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CELLULAR BASES OF THE EFFECT OF HEAVY METALS ON THE BODY

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Resume: In the light of the above, it becomes necessary to study the mechanism of toxic action of a particular xenobiotic, as well as their combination, which provides for the study of their effects on the structural state of cells of various tissues and their membrane components.

As a result of the large-scale reforms implemented over the years of independence, our country has achieved some success in preventing the toxic effects of pesticides and heavy metal salts on the human body and animals.

Key words: organophosphorus and organochlorine pesticides, morphometric and ultrastructural parameters of the liver and hepatocytes, butylcaptax, droppa and lead salts.

Relevance

An ecotoxicant is a toxic and environmentally stable substance that can accumulate in organisms to dangerous levels of concentrations. Chemicals alien to organisms that are not part of the natural biotic cycle are called xenobiotics. Xenobiotics are compounds alien to organisms (industrial pollutants, pesticides, household chemicals, medicines, heavy metal salts, etc.). Xenobiotics, entering organisms in significant quantities, can affect the genetic apparatus and cause their death. [1, 3, 9].

As a result of human economic activity, a large number of different xenobiotics, alien to humans and animals, circulate in the biosphere, many of which have extremely high toxicity. "Priority" organic compounds have been identified from pollutants, that is, those that pose the greatest danger to humans now and in the future [2, 7, 8].

The active work of industrial enterprises leads to a large intake of heavy metals into the environment, which can then lead to the deposition of toxicants on the earth's surface, at a very close distance from the source of pollution. The concentration of metals in close areas adjacent to industrial enterprises significantly exceeds the maximum permissible concentration [4, 6].

Currently, more than 1,500 types of pesticides have been registered in the world, the use of which in agriculture led to the mass death of birds and animals [5, 12].

Ecotoxicants are absorbed by living organisms and moving through food chains, increasing their concentrations many times, have a harmful effect on natural ecosystems, living organisms and humans. In recent decades, it has been increasingly

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recognized that success in protecting and promoting public health largely depends on social and economic factors, as well as the conditions and environmental conditions in which the current and future generations of people live [4,6].

In agriculture, there is no factor more closely related to the problem of nature protection, especially human health protection, than the chemicalization of the industry. The issues of safe handling of pesticides, agrochemicals and chemotherapeutic agents are extremely important. Their ability to circulate in environmental objects (water, soil) and their presence in agricultural products causes the possibility of chronic adverse effects on a living organism [7, 11].

In addition, many active substances of pesticides and agrochemicals have the ability to material biological accumulation – accumulation in human biological environments.

As a result of the action of herbicides on intermediate metabolism, the processes of decomposition and formation of low molecular weight organic compounds necessary for a new synthesis are disrupted; the effect on secondary metabolism is expressed in a violation of the synthesis of various specific components of plant cells such as alkaloids, pectins, coumarins, anthocyanin, tannins, etc. It is important to note the possibility of direct and indirect contact of herbicides with endogenous growth regulators such as phytohormones (auxins, gibberelens, cytokinins, abscisins and ethylene) and non-hormonal physiologically active substances (vitamins, phenolic compounds)

The herbicidal action of compounds may be accompanied by a change in their molecular structure. Derivatives of aryloxyacetic acids (2,4-D, 2M-4X), benzoic acid (bifenox), aryloxyphenoxypropionic acids (benzoyl propethyl), galloidalkanic acids (bidisin), urea, etc. are transformed and move around the plant in the form of acids and compounds conjugated with sugars [231; - P.597.]. It was found that some herbicides amiprofosmethyl, orizalin, trifluralin, as well as fungicides kaptan and dichlofluanide realize their effects through Ca2+ cell homeostasis, inducing 2H+/Ca2+ exchange of Mx [Hertel C., 1981]. In this case, the redistribution of Ca2+ ions between the Mx and the cytoplasm of the cell is disrupted. These herbicides have been shown to induce 2H+/Ca2+ exchange of Mx.

The ability of the compound to penetrate the membrane of a large area depends on its lipophilicity. Moreover, in some cases, there is a direct correlation between the activity of the pesticide and its lipophilicity. The penetration of pesticides through the membrane and their incorporation into the membrane leads to changes in the structure of the function and membranes.

The morphological and cytological effects of a number of herbicides on the processes of cell morphogenesis are carried out through interaction with the microtubule system. Obviously, inhibited assembly/disassembly of microtubules is the

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result of changes in the level of Ca2+ in the cytoplasm through interaction with the Ca2+ pump system of mitochondrial membranes, since Ca2+ ions play a leading role in regulating polymerization/dipolymerization of microtubules. Basically, the effect is realized through weakened absorption of Ca2+. Thus, ioxynyl can affect the absorption of Ca2+ indirectly, since it suppresses the energy generation system, on the other hand, which effectively induces 2H+/Ca2+ exchange of Mx without disconnecting OF.

To develop a toxic effect, the insecticide must penetrate into an animal or plant organism. In many ways, the realization of the effect is due to the physico-chemical characteristics of the compound. So, even highly active substances, but ionized ones are practically nontoxic in relation to the vast majority of arthropods.

One of the factors that ensure the penetration and specific distribution of the pesticide of the cell is its interaction with membrane lipids. The more lipotropic the substance, the easier it penetrates through cellular and intracellular membranes, affecting the functional state of subcellular structures. Another important factor is which membrane lipoids the insecticide predominantly binds to.

It has been shown that pesticides of different chemical nature are found in maximum amounts in the composition of various lipid fractions. In particular, DDT is a highly hydrophobic compound, found in the largest amounts in the fraction of cholesterol esters, g – HCG in triglycerides, and Sevin is less hydrophobic, the maximum amounts of it are found in phospholipids.

The neurotoxicity of chlorophos and other pesticides is based on changes in such important components of neuronal membranes as gangliosides, cerebrosido and cholesterol. The interaction of the pesticide with the lipid is obviously based on the formation of adsorption bonds.

The study of the interaction of DDT with the nerve membranes of squid showed that the drug accumulates in the plasma membrane of nerve fibers. At the same time, it inhibits potassium permeability and delays the opening of sodium channels in squid axons.

It was found that chlorophenviomphos and its analogues inhibit oxygen consumption in the V3 state in the rat brain Mx, however, at a concentration of 25-75 microns, these compounds do not affect the respiration rate in the V4 state when succinate is used as an oxidation substrate. In addition, the activity of succinate dehydrogenase and cytochrome c oxidase does not change.

When studying the effect of parathion, malothion and dimethoate on the respiration of rat liver Mx, it was shown that these drugs at concentrations above 26 micrograms /ml significantly inhibit the respiration rate of Mx activated in the presence of 2,4 – DNF, however, a similar depressing effect is found even without the addition of a disconnector.

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One of the manifestations of the activity of pesticides is their effect on the enzyme systems of biomembranes. DDT at a concentration of 53 microns suppresses invitroMg2+ - and Na+, K+ - ATPase of the liver, intestinal mucosa, cloacal bladder and kidneys of turtles. As a result of direct exposure to tokution and its metabolites, the activity of microsomal enzymes in rats changes. A number of organochlorine insecticides and carbamants reduce the activity of enzymes of the pentose phosphate cycle.

It should be noted that the effect of insecticides on most enzymes is non-specific. However, inhibited cholinesterases are characteristic of insecticides, especially organophosphate and carbonate compounds.

At the same time, an important role in the mechanism of action of a number of xenobiotics, along with the direct action of the drug, belongs to an indirect effect on metabolic processes through changes in the level of hormones, metabolites and other biologically active substances. Thus, insects poisoned with malothione have a significantly increased content. Since cGMP plays an important role in the mechanism of action of hormones, the author attaches pathogenetic importance to the fact established by him in the process of intoxication of insects with organophosphorus compounds.

In the mammalian body, individual groups of insecticides exhibit a directed effect due to different selective localization. Thus, methylnitrophos causes a sharp decrease in ATP and glycogen levels in the pectoral muscles and liver of chickens. Toxic effects on reproductive functions have been found for synthetic pyrethroid ambush, lindane and other pesticides.

Thus, from the above literature data, a multifaceted manifestation of the toxic effects of compounds with an insecticidal orientation on both the insect body and mammals and plant cells is visible. It is still difficult to more or less unambiguously determine the sequence of processes leading to the realization of the toxic effect. It seems that a more detailed study of the mechanism of action of compounds at the cellular and subcellular levels can solve this problem.

The effect of defoliants on the plant body also affects the metabolism of carbohydrates in it. A violation of carbohydrate metabolism may be associated with a change in the energy efficiency of respiration and photosynthesis, expressed in a decrease in ATP levels, a deficiency of which prevents both the movement and conversion of sugars.Despite the high defoliating activity of butyphosum, and its use in cotton growing in the Republic of Uzbekistan has now been discontinued due to its high toxicity to warm-blooded animals. These aspects of the effect of butyphos on the physiological and biochemical processes occurring in humans and animals will be analyzed in a number of subsequent sections. Here we will consider the properties of

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some other defoliants that are promising for use in cotton production due to their lower toxicity.

The membrane-damaging and cytotoxic effects of many xenobiotics are associated with GENDER. As an illustration of this position, data can be given: defoliants dropp and butylcaptax disrupt the ultrastructure of hepatocytes, induce NADP.N- and ascorbate-dependent SEX. The relationship of xenobiotic induction of SEX processes with modification of functional parameters of membranes is discussed in the monograph by A.K.Mirakhmedov et al. Defoliants butifos, butylcaptax, magnesium chlorate, dropp, ethylene-producing compounds significantly modify the course of the most important physiological and biochemical processes in the plant organism.

Thus, the literature data presented in this section indicate the versatile effect of pesticides on the structural and functional state of tissues and cells, both plant and animal organisms. Obviously, elucidating the mechanism of biological and toxic effects of compounds of various orientations will contribute to the creation of drugs with minimal negative effects on the human body and animals.

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