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XENOBIOTIC RESEARCH IN THE HISTORY OF THE DEVELOPMENT OF THE ENVIRONMENTAL DIRECTION OF TOXICOLOGY IN UKRAINE (SECOND HALF OF THE 20TH – BEGINNING OF THE 2I CENTURY)

The article continues the author's previous research on the evolution of scientific views on identifying the xenobiotic properties of synthetic substances used by humans in various sectors of the economy, with the development of modern ecology. In the second half of the XX century, when the idea (modern paradigm) of "the connection of everything with everything" became dominant in Environmental Research, the modern stage (1970 – present) of its development was formed in the history of the formation of ecology as a science. It was realized, albeit belatedly, the need for simultaneous and accurate consideration of all changes in the natural environment due to the development of the Earth's spheres and the impact of human activity on it. The problem of averting the global environmental crisis has raised the issue of combining all scientific knowledge and branches of practical activity on a single scientific basis and defined a single task for all: to investigate the nature and extent of environmental pollution associated with human activity, the degree of their danger and the possibility of neutralization, ways of ecologization of production, saving and reproduction of natural resources. There was a need for scientific knowledge on which to base regulations and safety assessment of synthetic chemicals and drugs, which became an important motivation for the study of xenobiotics. It is established that at this time the International Society for the Study of Xenobiotics (ISSX) was established, which became the main scientific organization for researchers interested in the metabolism and effects of foreign substances on living organisms. Since the 60s and 70s, the boundaries of toxicology have expanded significantly and it has developed into the science of the pathology of xenobiotics on living organisms, that is, ecological toxicology or environmental toxicology has emerged. In the late XX and early XXI centuries, much attention in Ukraine began to be paid to the issue of predicting *harm and risk assessment, including the «risk-benefit» criterion for toxic substances. Industrial and agricultural ecotoxicology is actively developing. Lev Ivanovich Medved (1905-1982) made a significant contribution to the development of agricultural labor and pesticide toxicology. His organizational activity as the director of the Kyiv Research Institute of Occupational Hygiene and Occupational Diseases from 1952 to 1964, and then from 1964 to 1982 as the director of the All-Union Research Institute of Hygiene and Toxicology of Pesticides, Polymers and Plastics contributed to the creation of creative scientific teams that occupy leading positions in the field of agricultural labor both in Ukraine and abroad. In modern scientific research, Ukrainian scientists have studied the dynamics of accumulation of residual amounts of pesticides produced in the late XX – early XXI centuries and continue to study the xenobiotic properties of pesticides used to protect crops. To this day, the Institute of Plant Protection of the National Academy of Agrarian Sciences of Ukraine remains the main institution of the Scientific and Methodological Center in our country for the implementation of the scientific research program «Plant Protection». The studies indicate the need to accelerate the study of the toxic properties of xenobiotics used in various spheres of life and their impact on the environment.*

Keywords: *ecology, evolution of scientific views, xenobiotics, xenobiotic research, ecotoxicology, pesticides.*

КСЕНОБІОТИЧНІ ДОСЛІДЖЕННЯ В ІСТОРІЇ РОЗВИТКУ ЕКОЛОГІЧНОГО НАПРЯМКУ ТОКСИКОЛОГІЇ В УКРАЇНІ (ДРУГА ПОЛОВИНА XX – ПОЧАТОК XXI ст.)

У статті продовжено попередні дослідження автора про еволюцію наукових поглядів на виявлення ксенобіотичних властивостей синтетичних речовин, які застосовує людина в різних галузях господарства з розвитком сучасної екології. У другій половині XX ст., коли домінуючим в екологічних дослідженнях стало уявлення (сучасна парадигма) про «пов'язаність усього з усім», в історії становлення екології як науки формується сучасний етап (1970 р. – дотепер) її розвитку. Було, хоч і з запізненням, усвідомлено необхідність одночасного і якнайточнішого врахування усіх змін природного середовища внаслідок розвитку сфер Землі та впливу на нього людської діяльності. Проблема відвернення глобальної екологічної кризи поставила питання об'єднання всіх наукових знань і галузей практичної діяльності на єдиній науковій основі та визначила для всіх єдине завдання: дослідити характер і обсяги забруднень довкілля, пов'язаних з діяльністю людини, ступінь їхньої небезпечності та можливості нейтралізації, шляхи екологізації виробництва, економії та відтворення природних ресурсів. Виникла потреба в наукових знаннях, на яких базуватимуться правила й оцінка безпеки синтетичних хімічних речовин і ліків, що стало важливою мотивацією для вивчення ксенобіотиків. Встановлено, що в цей час було створено Міжнародне товариство з вивчення ксенобіотиків (ISSX), що стало головною науковою організацією для дослідників, які цікавляться метаболізмом і розподілом чужорідних для живого речовин. Починаючи з 1960-1970-х рр. межі *токсикології значно розширилися і вона переросла в науку про патологію впливу ксенобіотиків на живі організми, тобто виникла екологічна токсикологія або токсикологія навколишнього середовища. В кінці XX – на початку XXI ст. велику увагу в Україні почали надавати питанням прогнозування шкідливості й оцінці ризику, включаючи критерій «ризик-користь» до токсичних речовин. Активно розвивається промислова та сільськогосподарська екотоксикологія. Значний внесок у розвиток сільськогосподарської праці та токсикології пестицидів вніс Лев Іванович Медведь (1905-1982). Його організаторська діяльність на посаді директора Київського НДІ гігієни праці та профзахворювань з 1952 по 1964 рр., а потім з 1964 по 1982 рр. директора Всесоюзного НДІ гігієни та токсикології пестицидів, полімерів та пластичних мас сприяла створенню творчих наукових колективів, які займають провідні позиції в галузі сільськогосподарської праці як в Україні, так і за її межами. В сучасних наукових дослідженнях українських учених досить добре вивчено динаміку накопичення залишкових кількостей пестицидів виробництва кінця XX – початку XXI ст. і продовжується дослідження ксенобіотичних властивостей пестицидів, які застосовують для захисту сільськогосподарських культур. Донині Інститут захисту рослин Національної академії аграрних наук України залишається головною установою Науково-методичного центру в нашій країні з виконання програми наукових досліджень «Захист рослин». Проведені дослідження вказують на необхідність форсування вивчення токсичних властивостей ксенобіотиків, які використовуються у різних сферах життя населення та їхнього впливу на навколишнє середовище.*

Ключові слова: *екологія, еволюція наукових поглядів, ксенобіотики, ксенобіотичні дослідження, екотоксикологія, пестициди.*

Statement of the problem. As it was noted earlier [19, p. 227], in the history of the formation of ecology as a science, the modern stage (1970 – till now) began when the dominant idea (modern paradigm) of the "connection of everything with everything" became dominant. It was realized, albeit belatedly, the need for simultaneous and accurate consideration of both the interaction between each other and with the material environment of all species and variants of the living environment, and changes in the natural environment due to the development of the Earth's spheres and the impact of human activity on it.

Interacting with nature, man has always sought to improve his well-being, make life more comfortable and financially secure. This led to an increase in the production of the necessary industrial and agricultural products, which, as is known, was associated with the generation of waste that got into the environment and polluted it. The process of irreversible transformation of parts of the biosphere into man-made objects and territories by humans is called technogenesis, and the part of the biosphere artificially transformed as a result of human activity and filled with its products is called technosphere (technogenically modified shell of the biosphere). The development of industrial production based on the use of resource and technological potential inevitably generates disharmony in the system "nature – society". Evidence of this is the man-made degradation of natural resources, landscapes, etc. For example, in Ukraine, relatively clean territories in the middle of the XX century do not exceed 7% of the total area, and 68% of the ecological situation is unfavorable for human health. In many countries, the area of environmental disasters reaches 1% of their total area. The grandiose scientific and technological achievements of recent decades are accompanied by the emergence of no less significant global environmental problems: the disappearance of hundreds of species, excessive pollution of natural waters, deforestation, degradation of arable land, the emergence of ozone "holes" and, ultimately, the deepening of the socio-economic crisis, which leads to hunger for hundreds of millions of people [18, pp. 211-212].

XX century is the century of chemistry. The chemical pollution of the biosphere has spread – an increase in the number of chemical components of a certain environment, as well as: penetration (introduction) of chemical substances that are not inherent to it or in concentrations that exceed the norm. The most dangerous for natural ecosystems and humans is chemical pollution, which poisons the environment with various toxicants (aerosols, chemicals, heavy metals, pesticides, plastics, detergents, etc.). According to experts, at the end of the XX century, the natural environment contained 7.0 - 8.6 million chemicals, and their number is annually replenished by another 250 thousand new compounds. Many chemicals have carcinogenic and mutagenic properties, among which 200 are particularly dangerous (the list is compiled by UNESCO experts): benzene, asbestos, benzopyrene, pesticides, heavy metals (especially mercury, lead, cadmium), food additives and various dyes. Particularly polluting the environment are enterprises that produce antibiotics, enzymes, vaccines, serums, feed protein, bioconcentrates, etc., i.e. enterprises of industrial biosynthesis, in the emissions of which there are living cells of microorganisms [18, p. 213].

By the end of the twentieth century, the chemical industry has created a huge number of new, mainly organic substances, but all these substances could already get the "right to life" only after passing the toxicological expertise [4]. The need for knowledge about the toxic effects of chemicals, measures to prevent their negative impact on the human body has become an everyday need both in everyday life and at production.

In previous studies [20, pp. 119-129], we found that at the end of the twentieth century, at the third stage of interaction between society and nature, when a functionally closed global socio-ecosystem had already been formed, there was a need for scientific knowledge on which to base the rules and safety assessment of synthetic chemicals and drugs, which became an important motivation for the study of xenobiotics, substances synthesized by humans and which remain unchanged in the natural environment for a long time. Applied branches of modern ecology began to actively develop, investigating the xenobiotic properties of synthetic substances and their impact on the environment. At this time, the International Society for the Study of Xenobiotics (ISSX) was established [1], which became the main scientific organization for researchers interested in the metabolism and distribution of substances foreign to living organisms.

This article continues the research aimed at studying the evolution of scientific views on the identification of xenobiotic properties of synthetic substances used by humans in various sectors of the economy, with the development of modern ecology. Very little space in modern literature is given to the study of the proposed research, which is their novelty.

Results of the research. Environmental degradation, the possibility of environmental disasters stimulated the development of not only ecology as a science, but also the ecologization of other sciences. First of all, it concerned those sciences that were related to chemical pollutants of the environment.

If toxicology at the beginning of the 20th century was mainly concerned only with the study of the toxic properties of chemical substances, then since the 60s and 70s its boundaries have expanded significantly and toxicology has evolved into the science of the pathology of the influence of toxic substances on living organisms, that is, environmental toxicology has emerged (Grygor'eva L. I., Tomilin Yu. A., 2015) or environmental toxicology. Much attention began to be paid to the issue of predicting harmfulness and risk assessment, including the "risk-benefit" criterion for toxic substances [9].

Toxicology and environmental toxicology share common methodologies and techniques, terminology and concepts. At the same time, environmental toxicology can be considered as a separate direction of applied ecology, with which it also has some methodological approaches, methods, terminology and concepts.

O. I. Tsyganenko, I. T. Matasar and, V. F. Torbin (1998) defined environmental toxicology as a science with an interdisciplinary nature that studies the laws of interaction of the organism (including at the population level) of humans, animals and plants with xenobiotics that enter the environment, their impact on living organisms, population-species, biocenosis and biosphere levels.

At this time, the science of toxicology is divided into separate areas: industrial, agricultural, forensic, food, and others. At the same time, it should be noted that there is no sharp enough limit in the implementation of preventive measures in case of negative effects of toxicants on the human body in one or another field. Thus, the impact of pesticides, heavy metals, and other toxic substances on the human body is studied by both agricultural and industrial, food, and municipal toxicology. It was on the basis of preventive ecology, which focused on the protection of all living things, that the development of environmental toxicology began.

Industrial ecotoxicology. A significant contribution to the development of industrial toxicology was made by the Soviet toxicologist Mykola Vasyliovych Lazarev (1895-1974). The scientist began a systematic study of the connection between the chemical structure of a substance and its biological effect, that is, the effect on the metabolism of a living organism and on the ecological system as a whole. These studies received further development and began to be applied by scientists from other areas of toxicology. It was this theory that was used for various methods of determining the maximum permissible concentration of a toxic substance that could be safe for human health (MPC).

In 1957, M. V. Lazarev initiates the idea of creating a new branch of hygiene - geohygiene. It should be noted that this idea of M. V. Lazarev was based on the theory of the Ukrainian scientist V. I. Vernadskyi about the biosphere – the area of active life on earth, which covers the lower part of the atmosphere (air environment), the hydrosphere (water environment), the upper part of the lithosphere (soil environment). The joint activity of living organisms, including humans, manifests itself as a geological factor of planetary scale and importance.

M. V. Lazarev raised the issue that the active transformative activity of man, associated with the spontaneous development of civilization, often has a detrimental effect on nature, causing negative changes in the environment.

Thus, in the fall of 1988, in the city of Chernivtsi (Ukraine), an outbreak of a disease unknown to doctors in children was registered, which later received the name "Chernivtsi chemical disease" [3, p. 7]. In his monograph, Ukrainian toxicologists V. I. Bilous and Bilous V. V. (2002) identified this disease as talotoxicosis. Thallium and other heavy metals enter the atmosphere of the city due to the imperfection of technological processes and violations of sanitary and technical rules and hygiene standards at enterprises. Toxic trace elements, a significant part of which are thallium, cadmium, lead, mercury, in the form of dust, smoke and soot pollute the environment, accumulating according to the laws of concentration of substances in trophic chains, in soil, water of open reservoirs, in plants, including berries, vegetables, fruits, in the bodies of birds, animals, and people.

In the form of fine aerosol, toxic thallium and other poisonous substances are constantly present in the surface dusty and smoky air layers. The contamination, which is considered insignificant when assessing the amount of toxic pollutants in the environment, becomes catastrophically dangerous due to the increase in concentration in trophic chains. This is dangerous, first of all, for people who are at the top of all trophic chains [10, pp. 99-100]. Thus, a zone of technogenic trace element pollution has gradually formed in the city and its surroundings.

However, the Chernivtsi tragedy is not the first thallium intoxication of man-made origin. Mass talotoxicosis of residents of one of the settlements was highlighted in his publication by A. Brockhaus et al. (1980), who with his co-authors was involved in the examination of the victims.

An important role in the emergence of a critical ecologically toxic situation in Chernivtsi was played by a number of factors that WHO recommended must be taken into account during the epidemiological study of diseases of unknown etiology, namely: 1) factors related to the physical environment; 2) anthropogenic environmental factors; 3) factors related to the injured individual [17].

Agricultural ecotoxicology. The middle of the last century was marked by the discovery of pesticidal properties of products of organic synthesis. The post-World War II period saw the rapid development of chemical plant protection agents and pesticides used to destroy organisms that harmed crops, domestic animals, and humans. Among the first pesticides to be widely used were a group of chlorinated hydrocarbons, including DDT (dichlorodiphenyltrichloroethane), dieldrin, and aldrin. Thus, in Ukraine, in 1948, the "Order of the RM of the Ukrainian SSR on the use of the drug DDT in measures to combat pests in agriculture" [2] was issued, according to which a commission was created to prepare the issue of the use of the drug DDT in the fight against blood-sucking insects of agricultural animals in collective farms and State farms of the Ukrainian SSR.

However, it soon became clear that DDT and other organochlorine drugs have high toxicity, are able to overcome long trophic networks and are resistant to the influence of both abiotic (temperature, humidity, acidity, etc.) and biotic factors of the environment. Therefore, these substances can be stored in natural objects for many years, and according to the law of concentration, when moving from one trophic level to another, their concentration increases tenfold.

So, according to N. Green and others (USA, 1990), in just four links of the trophic chain of the aquatic ecosystem, the concentration of DDT increased 1,875 times [10, p. 99]. This was the reason for a sharp reduction in the use of organochlorine compounds around the world.

In our country, in 1970, a decision was made to remove highly toxic insecticides from the range of pesticides used on fodder and food crops, but they continued to be actively used in agriculture until 1975 and later to combat infectious disease vectors.

The use of organochlorine pesticides was replaced by the active use of organophosphorus preparations (thiophos, etc.). Then fungicides (dithiocarbamates, phthalimides, thiuram) and herbicides (DNOK, triazines) were synthesized.

In the 1970s and 1980s, pyrethroid insecticides became widely used. By the beginning of the 1980s, the global production of pesticides reached 2.3-2.5 million tons of active substance. The wide range and growing scale of pesticide use, the increase in the frequency of treatments in conditions of crop rotation forces plant protection specialists to objectively and comprehensively take into account the possibility of their negative aftereffects [5, pp. 9-10].

The potential danger of using pesticides is due to their toxicity for humans and fauna, and in some places for plants, in addition, the ability to cause side effects and remote consequences. Thus, a correlation of 14 forms of pathologies out of 37 with the total load of pesticides was established. Among them are lesions of the upper respiratory tract, bronchial asthma, diseases of the liver and kidneys, effects on the endocrine system, disorders of the functions of the nervous system, an increase in the number of developmental anomalies (Moldova, Chuvashia), as well as a high level of general morbidity in newborns [6; 7; 11].

Much later, in 1998, at the proposal of the UN, as part of the environmental protection program, the Convention was adopted, which limited the trade in dangerous substances and pesticides such as DDT, organophosphates and mercury compounds. Numerous studies have shown that stable organochlorine compounds are found in almost all organisms living in water and on land. 95 countries took part in the new International Treaty. At the same time, DDT and hexachlorocyclohexane (HCCH) were included in the list of pesticides required for control.

A significant contribution to the development of agricultural work and toxicology of pesticides was made by the Ukrainian ecotoxicologist Lev Ivanovich Medved (1905-1982). His organizational activities as the director of the Kyiv Research Institute of Labor Hygiene and Occupational Diseases from 1952 to 1964, and then from 1964 to 1982 as the director of the All-Union Research Institute of Hygiene and Toxicology of Pesticides, Polymers and Plastic Masses contributed to the creation of creative scientific teams that occupy leading positions in the field agricultural labor both in our country and abroad. Monographs, a handbook on occupational hygiene and a handbook on pesticides, published under the editorship of L. I. Medvedya, and under his direct authorship, played an important role in preserving the health of the rural population, first of all.

In 1956, the Institute of Entomology and Phytopathology, the task of which was to improve plant protection methods and develop protective measures against the most dangerous pests and diseases of agricultural crops, was reorganized into the Ukrainian Research Institute of Plant Protection, subordinated first to the Ukrainian Academy of Agricultural Sciences, and later to the Ministry of Agriculture of the Ukrainian SSR, which acquired the status of the Republican Scientific and Methodological Center for Plant Protection. Since January 1971, the Institute became a component of the Southern Branch of the All-Union Academy of Agricultural Sciences (VASGNIL), and since 1992 – of the Ukrainian Academy of Agricultural Sciences, which in 2010 acquired the status of National. To this day, the Plant Protection Institute of the National Academy of Agrarian Sciences of Ukraine remains the main institution of the Scientific and Methodological Center in our country for the implementation of the scientific research program "Plant Protection" [4, p. 142].

Scientists of the Plant Protection Institute of the National Academy of Sciences of Ukraine and other institutions of the Scientific and Methodological Center have already improved chemical protection of plants over the years of the 21st century. Many innovations have been created in this direction. Thus, technological regulations for the use of pesticides of a modern range for the protection of the main agricultural crops have been developed. Great importance is attached to the rationalization and greening of the chemical method of protection, in particular measures to prevent resistance in pests and to reduce the danger of beneficial insects. A significant part of scientific developments is related to the use of effective methods of controlling the content of pesticide residues in plants, soil, water, plant products, as well as the quality of the process of treating seed material. Models of pesticide detoxification in agrocenoses and ecotoxicological indicators of this process have been developed. Scientific schools of *ecologists* (O. I. Borzykh) and *ecotoxicologists* (L. I. Bublyk) were formed at various stages of research to solve the most important issues regarding chemical protection of plants [4, p. 149].

In modern scientific researches of Ukrainian scientists, as evidenced by literary sources [5-8, 11-15, etc.], the dynamics of the accumulation of residual amounts of pesticides produced at the end of the 20th – beginning of the 21st centuries have been studied quite well, and the xenobiotic properties of drugs of different toxicity have been identified. used in intensive plant protection technologies. Organochlorine drugs (DDT, gamma-HCCG, PCP) and drugs of the sim-triazine group (atrazine and simazine) were noted for their high stability in environmental objects, the residual amounts of which can be stored in the soil from 1.5 to 20 years.

Organochlorine pesticides mainly show a general toxic effect and they have two features that make them extremely dangerous for the environment. First, they are extremely resistant to environmental factors, and for most of them, the metabolic period exceeds 10-20 years or even longer. For example, metabolites of DDT, which has been banned for use since the beginning of the 80s of the XX century, can still be detected in the soil of agricultural lands today. Secondly, organochlorine pesticides, due to their low solubility in water, have a low ability to migrate in the environment, but due to their high solubility in fats, they have the ability to bioaccumulate.

Organophosphorus pesticides have high biological activity, contact and systemic action. Therefore, most organophosphate preparations are highly toxic substances. A wide range of drugs are esters of phosphate or thiophosphate acids, and their feature is that pesticides retain their activity for a short period of time (2-6 weeks), after which they undergo metabolism with the formation of harmless components. Therefore, organophosphate pesticides practically do not accumulate in environmental objects. At the same time, most drugs of this group have high toxicity for warm-blooded animals, including humans. Pesticides of this class include metaphos, thiophos, chlorophos, phthalophos, phazolon, etc.

Synthetic pyrethroids or symtriazines are a large class of new-generation pesticides that are highly effective and relatively low-toxic to warm-blooded organisms. All drugs of this group are derivatives of heterocyclic organic compounds, but they have moderate resistance to environmental factors. As a rule, due to the peculiarities of the chemical nature of these compounds, they have high biological activity, but they are not characterized by bioaccumulation. It should be noted that sim-triazines and synthetic pyrethroids, which are often combined into one group of pesticides, are chemically related to different classes of organic compounds. Among sim-triazines, such drugs as simazine, promethrin, atrazine, propazine, etc. have become widespread. Decis, ambush, ripcord, karate, etc. have become widespread among synthetic pyrethroids.

Derivatives of carbamic and thiocarbamic acids mainly have fungicidal and insecticidal effects, the peculiarity of these compounds is their low toxicity for warm-blooded organisms, as well as their low ability to bioaccumulate. These drugs mainly have a contact effect, and also act as intestinal poisons.

Studies of recent decades show that the intensification of agriculture largely causes an increase in the pesticide load on agrocenoses, leads to a disturbance in their balance and to a possible increase in the resistance of harmful organisms.

Contamination of raw materials and food products can occur in two ways, direct and indirect. Direct pollution is the ingress of chemicals during direct processing of products. Indirect – pollution through air, soil, water, feed, through the migration of pesticides. The residual amount of pesticides depends on many factors, including the properties of the pesticides themselves (stability, solubility, physical state), the properties of raw materials and products (shape, density, surface condition), the rate of consumption and frequency of processing, the method of processing, and various environmental conditions.

Among the main negative environmental consequences of the use of pesticides, the following should be highlighted: their ability to accumulate in the soil and be transported along the trophic chain; decrease in biological productivity and normal functioning of soil biota; decrease in the intensity of soil self-cleaning processes; inhibition of biochemical processes and prevention of fertility recovery.

Important characteristics of pesticides that must be taken into account when using them: activity in relation to organisms, selective activity, safety for people and the environment.

The activity of pesticides depends on the methods of penetration into the body, migration and suppression of vital processes. These factors depend on the amount of pesticides and the time of action.

The selectivity of pesticides (the ability to destroy one type of organism without affecting others) depends on differences in biochemical processes, enzymes and substrates in organisms of different species, as well as on the doses used.

Environmental safety of pesticides is related to their selectivity, as well as their ability to persist for a certain period of time in the environment without losing their biological activity. The persistence of the same pesticide can differ significantly in different environmental objects and various conditions.

It should be noted that in recent decades, pesticides still remain an important link in the production of agricultural products. Modern agricultural production in developed countries is moving to integrated crop protection technologies and the use of pesticides of new generations, which are safer for people, animals and ecosystems in general. However, the use of pesticides in violation of recommended norms and regulations has negative environmental consequences, and there are still many problems with the use of plant protection products.

It follows from the resolution of the UN World Conference on Ecology in Rio de Janeiro (1992) that humanity lives in an unknown toxicological environment. Even medicines, it turns out, have been studied for only 40% of their nomenclature.

As for other xenobiotics, the share of their study is reduced to 1 in 10.

Conclusions. In the second half of the 20th century, when the idea (modern paradigm) of "the connection of everything with everything" became dominant, in the history of the formation of ecology as a science, the modern stage (1970 – until now) of its development was formed. There was a need for scientific knowledge on which to base the rules and safety assessment of synthetic chemicals and drugs, which became an important motivation for the study of xenobiotics.

It has been established that the International Society for the Study of Xenobiotics (ISSX) was founded at this time and became the main scientific organization for researchers interested in the metabolism and distribution of foreign substances. Starting from the 1960s and 1970s, the boundaries of toxicology expanded significantly and it grew into the science of the pathology of the influence of xenobiotics on living organisms, i.e. environmental toxicology or environmental toxicology arose. At the end of the 20th and the beginning of the 21st centuries, great attention was paid in Ukraine to the issue of hazard prediction and risk assessment, including the "risk-benefit" criterion for toxic substances. Industrial and agricultural ecotoxicology is actively developing. The conducted studies show that only a small part of man-made chemical compounds has a fairly complete toxicological and hygienic characteristic. This suggests the need to accelerate the study of the toxic properties of xenobiotics used in various spheres of life of the population and their impact on the environment.

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