

MORPHOLOGY, PHYSIOLOGY AND PATHOPHYSIOLOGY

STUDIES OF THE EFFECT OF INDOLE AND ITS DERIVATIVE 1-BENZYLINDOLE ON THE FUNCTIONAL STATE OF THE HEART AND BLOOD VALUES OF LABORATORY RATS

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ABSTRACT

Background. Indole and its derivatives are widely used in all areas of pharmaceutical production. The toxicometry of indole compounds has been sufficiently studied. At the same time, there is still no information on the toxic effect on individual organs and systems during long-term intake of most compounds.

The aim. To carry out an experimental study of the toxic effect of indole and its derivative 1-benzylindole on the functional state of the heart and blood values.

Material and methods. The work was carried out on 46 white rats, divided into groups: control group (n = 22); animals receiving indole once a day for 1 month (n = 12); animals receiving 1-benzylindole once a day for 1 month (n = 12). The substances were administered intragastrically 5 days a week. The condition of the animals was assessed by integral parameters, peripheral blood parameters and biochemical serum tests, and morphological data.

Results. Administration of indole and 1-benzylindole caused an increase in the electrical activity of the atria, a decrease in the duration of the QRS complex, and a statistically significant decrease in blood pressure and body temperature compared to the control group. The intake of indole and 1-benzylindole decreased the number of red blood cells and hemoglobin, increased the activity of aspartate aminotransferase and alanine aminotransferase, and increased the concentrations of urea, total cholesterol and triglycerides in the blood. Against the background of long-term exposure to indole and 1-benzylindole, dystrophic disorders, hypertrophic and atrophic changes in individual fibers with a pronounced congestion of the microcirculatory vessels were revealed in the heart of rats.

Conclusion. Indole and 1-benzylindole in case of long-term intake lead to functional disorders of the cardiovascular system, which cause the development of arterial hypertension, coronary heart disease, and atherosclerotic vascular lesions. Preventive measures in industries with possible contact with indole and its derivatives should include regular medical examinations of workers with mandatory monitoring of electrocardiography and advanced indicators of general and biochemical blood tests.

Key words: indole, 1-benzylindole, experimental rats, functional state of the heart, blood biochemistry, heart morphology

Received: 14.06.2022
Accepted: 10.11.2023
Published: 26.03.2024

For citation: Gorokhova L.G., Mikhailova N.N., Zhukova A.G., Kazitskaya A.S. Studies of the effect of indole and its derivative 1-benzylindole on the functional state of the heart and blood values of laboratory rats. *Acta biomedica scientifica*. 2024; 9(1): 64-72. doi: 10.29413/ABS.2024-9.1.7

ИССЛЕДОВАНИЯ ВОЗДЕЙСТВИЯ ИНДОЛА И ЕГО ПРОИЗВОДНОГО 1-БЕНЗИЛИНДОЛА НА ФУНКЦИОНАЛЬНОЕ СОСТОЯНИЕ СЕРДЦА И ПОКАЗАТЕЛИ КРОВИ ЛАБОРАТОРНЫХ КРЫС

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РЕЗЮМЕ

Обоснование. Индол и его производные широко используются во всех сферах фармацевтического производства. Токсикометрия индольных соединений достаточно изучена. Вместе с тем сведения о токсическом влиянии на отдельные органы и системы при длительном поступлении в организм большинства соединений до сих пор отсутствуют.

Цель исследования. Экспериментальное изучение токсического влияния индола и его производного 1-бензилиндола на функциональное состояние сердца и показатели крови.

Материал и методы. Работа проведена на 46 белых крысах, разделённых на группы: контрольная (n = 22); животные, получавшие индол 1 раз в день в течение 1 месяца (n = 12); животные, получавшие 1-бензилиндол 1 раз в день в течение 1 месяца (n = 12). Вещества вводили внутривенно 5 дней в неделю. Состояние животных оценивали по интегральным параметрам, показателям периферической крови и биохимическим анализам сыворотки, морфологическим данным.

Результаты. Введение индола и 1-бензилиндола приводило к увеличению электрической активности предсердий, уменьшению продолжительности комплекса QRS и статистически значимо снижало артериальное давление и температуру тела по сравнению с контролем. Поступление индола и 1-бензилиндола снижало количество эритроцитов и гемоглобина, повышало активность аспартатаминотрансферазы и аланинаминотрансферазы, увеличивало концентрации мочевины, общего холестерина и триглицеридов в крови. На фоне длительного воздействия индола и 1-бензилиндола в сердце крыс выявлены нарушения дистрофического характера, гипертрофические и атрофические изменения отдельных волокон с резко выраженным полнокровием сосудов микроциркуляторного русла.

Заключение. Индол и 1-бензилиндол в условиях длительного поступления в организм приводят к функциональным нарушениям сердечно-сосудистой системы, которые являются причиной развития артериальной гипертензии, ишемической болезни сердца, атеросклеротических поражений сосудов. Профилактические мероприятия на производствах, где возможен контакт с индолом и его производными, должны включать регулярные профосмотры работников с обязательным контролем электрокардиографии и расширенными показателями общего и биохимического анализов крови.

Ключевые слова: индол, 1-бензилиндол, экспериментальные крысы, функциональное состояние сердца, биохимия крови, морфология сердца

Статья поступила: 14.06.2022
Статья принята: 10.11.2023
Статья опубликована: 26.03.2024

Для цитирования: Горохова Л.Г., Михайлова Н.Н., Жукова А.Г., Казицкая А.С. Исследования воздействия индола и его производного 1-бензилиндола на функциональное состояние сердца и показатели крови лабораторных крыс. *Acta biomedica scientifica*. 2024; 9(1): 64-72. doi: 10.29413/ABS.2024-9.1.7

INTRODUCTION

The modern pharmaceutical industrial complex is characterised by the introduction of new compounds into production, often having a complex nature of action over the body. This process largely determines the change in the clinical and pathogenetic specificity of modern varieties of occupational intoxications and the emergence of new nonspecific reactions that may dominate the clinical picture of diseases. It has been revealed that the cardiovascular complex is highly sensitive to the toxic effect of chemical substances, which manifests itself in the form of dystrophic changes in the myocardium and autonomic-vascular dystonia [1, 2]. The identification of mechanisms of disorders, their nosological differentiation and diagnostics, however, is considerably complicated by the fact that lesions of the cardiovascular system with chemical etiology develop under the combined effect of a whole complex of technological factors affecting the organism. For this reason, conducting extended experimental studies makes it possible to isolate the factor of chemical exposure from the general complex of unfavourable factors and to rank its importance in the development of various pathologies of the cardiovascular system.

Indole (2,3-benzpyrrole) is an organic compound of a series of nitrogen-containing heterocycles, an ancestor of an extensive group of synthetic and naturally occurring compounds. Its content is quite high in coal tar, in some plant essential oils (e.g., in plants of the olive family, citrus). Indole and its numerous derivatives are widely used in chemical production, especially in the pharmaceutical industry. Among them, compounds with a high degree of biological activity and a wide range of pharmacological effects on the human body have been revealed [3]. Specifically, the indole derivative, 1-benzylindole, has been

revealed to have cardiotropic, antiarrhythmic, anti-inflammatory and local anaesthetic activity [4].

The extensive use of indole and its compounds has been reflected in detailed studies of the toxicometric parameters of the substances [5, 6]. However, there is still no information related to the toxic effect of indole and 1-benzylindole on the cardiovascular complex at their prolonged intake into the body. Accordingly, the aim of the study was to experimentally examine the toxic effect of indole and its derivative 1-benzylindole both on the functional state of the heart and blood parameters.

MATERIAL AND METHODS

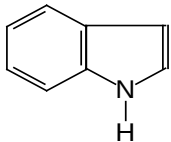
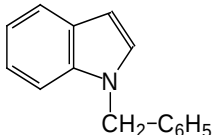
Design and proper testing environment. The physicochemical and toxicometric properties of indole and its derivative 1-benzylindole are summarized in Table 1.

The studies were performed on 46 white male sexually mature laboratory rats. Animals were kept and excluded from the experiment in accordance with the requirements of the guidelines of the Ministry of Health and Social Development of Russia "About the approval of the rules of laboratory practice" (No. 708-н dated August 23, 2010) and international rules «Guide for the Care and Use of Laboratory Animals» (Strasbourg, 1986).

Ethical review. A positive decision of the Biomedical Ethics Committee of the Research Institute of Complex Problems of Hygiene and Occupational Diseases (Minutes No. 3, § 1 dated May 12, 2022) was obtained for the experimental study. All animals underwent the necessary quarantine and were kept under standard housing conditions with natural light regime and free access to water. The rats were fed according to the standards established by the order of the Ministry of Health of the USSR № 1179 dated

TABLE 1

PHYSICOCHEMICAL AND TOXICOMETRIC PROPERTIES OF THE SUBSTANCES UNDER STUDY

Substance	Structural formula	Gross formula	Molecular weight	Aggregate state	DL ₅₀ (oral)	Substance hazard category
Indole (2,3-benzpyrrole) CAS Registry 120-72-9		C ₈ H ₇ N	117.15	Pale yellow crystalline powder with a pungent characteristic indole odour	Rats – 1200 mg/kg [7, 8]	III (moderately hazardous)
1-benzylindole CAS Registry 3377-71-7		C ₁₅ H ₁₃ N	207.262	Amorphous powder of pinkish-cream color with specific indole unpleasant odor	Rats – 5800 mg/kg	IV (low-hazardous)

October 10, 1983 "About the approval of the feed cost standards for laboratory animals in health care institutions".

Study duration, description, and methods of enrollment. Two series of experiments were conducted simultaneously. In the first, the rats were divided into a control group ($n = 11$) and a group of animals receiving indole ($n = 12$). In the second series, the rats were divided into a control group ($n = 11$) and a group of animals receiving 1-benzylindole ($n = 12$). The duration of substance administration was 1 month with weekend breaks. The study substances were administered intragastrically with a metal probe at a dose of 0.1 DL_{50} as a 20 % suspension on a starch gel 5 days a week, once a day. Control animals received starch gel intragastrically at appropriate doses. External examination of each animal was performed within the first hour after drug administration and every 10 days. Animals were weighed weekly and variations in feed and water intake in individual cages each day were visually observed.

Conclusions about the degree of the substances effect over the general condition of the animals were made considering the dynamics of body weight and rectal temperature measurement using TPEM-1 electrothermometer; motor activity and the value of the sum-threshold index (STI) were evaluated. Blood pressure readings were taken in animals by a noninvasive method using a LE 5001 tonometer (PANLAB, S.L. Energia, 112 08940 Cornell, Spain).

In the course of the experiment, on the 10th and 20th days, the rats had electrocardiogram (ECG) readings recorded in the second standard lead according to the method of L.V. Lierman (1962).

Blood sampling was performed in rats from the tail vein. The studies were performed according to a number of common clinical studies of peripheral blood: the number of erythrocytes, hemoglobin, leukocytes, analysis of leukocyte formula. The standard cyanmethemoglobin photometric method was used to determine hemoglobin content [9]. The number of erythrocytes and leukocytes was counted using the test tube method in a Goryaev chamber. Erythrocyte and leucocyte number were calculated according to standard formulae.

The following serum biochemical parameters were measured by standard methods using Vector-Best diagnostic kits (Russia): activity of serum aspartate amino transferase (AspAT), alanine aminotransferase (ALAT), glucose, urea, total cholesterol and triglycerides.

Histomorphologic examination of heart, liver, and kidney tissue was performed. A 12 % formalin solution was used as a fixative. After histological processing using the AGP-1 apparatus (Russia), the samples were embedded in paraffin. Sections 5–7 μm thick were prepared on a rotary microtome MZP-01 (Russia). The deparaffinised sections were stained with haematoxylin and eosin and Van Gieson picrofuchsin in order to reveal elastic and collagen fibres. Histological preparations were examined by light microscopy method using Nikon Eclipse E 200 (Nikon, Japan) with digital image transmission to the monitor and processing in BioVision 4.0 software.

Statistical analysis. Statistical processing was performed using Statistica software for Windows v. 10 (StatSoft Inc., USA) by methods of variation statistics with calculation of the following parameters: mean value, standard error of the mean, statistical significance of differences between comparison groups using the parametric Student's t -test (t) if normally distributed.

RESULTS

The conducted studies revealed significant disturbances in the organism of experimental animals exposed to indole and 1-benzylindole. Electrocardiographic examination of the experimental group of indole-injected animals revealed a statistically significant increase in heart rate (HR) and a 10 % increase in the duration of the P wave, which is an identifier of an increase in the electrical activity of the atria (Table 2) [10]. In addition, ECG of rats that had received both indole and 1-benzylindole revealed a decrease in the duration of the QRS complex.

A statistically significant increase in the elevation of the R wave during ECG acquisition from rats that survived 1-benzylindole poisoning is also an indicator of the presence of functional cardiac abnormalities.

The indices of electrical activity of the heart muscle during indole intake correlate with a decrease in the level of general excitability of experimental animals, which was manifested in STI and motor activity changes (Table 3). The negative effect of indole and 1-benzylindole administration over physiological and behavioural reactions was expressed as an increase in the ability of the nervous system to sum up subthreshold impulses by 12 % and a decrease in the motor activity of animals in the maze: total horizontal activity by 30 %; directed horizontal and vertical activity by 40 %, integral index by 20 %. During the subacute administration a statistically significant decrease in body temperature by 0.4–0.6 °C was observed. In animals that survived indole poisoning, a statistically significant pronounced decrease in blood pressure was revealed.

Analysis of the peripheral blood components composition revealed that administration of the studied toxicants to animals resulted in relative erythropenia and decreased haemoglobin concentration (Table 4). In the quantitative characteristic of white blood, relative leucopenia was observed, developing as a result of a 21–23 % decrease in the number of paleonuclear and segmented neutrophils. The decrease in leucocyte number resulted in a relative lymphocytosis. A statistically insignificantly expressed tendency to increase by 12–15 % the number of eosinophils in the blood of indole-poisoned animals was observed.

Glycemic level is a significant diagnostic marker showing the severity of biochemical disorders in intoxication. In rats poisoned with indole, an increase in serum glucose levels was observed by 24 %, with 1-benzylindole – by 14 % (Table 4). There was a 20 % increase in blood urea concentration.

TABLE 2

ELECTROCARDIOGRAM PARAMETERS OF RATS DURING SUBACUTE INTRAGASTRIC ADMINISTRATION OF SUBSTANCES (M ± M)

Indices	Animal groups (number)	Indole	1-benzylindole
HR, min	Experience (n = 12)	524.0 ± 7.50*	540.0 ± 9.54
	Control (n = 11)	496.9 ± 7.74	528.0 ± 11.53
Duration of the P wave, ms	Experience (n = 12)	21.2 ± 0.73*	19.9 ± 0.21
	Control (n = 11)	19.2 ± 0.34	19.7 ± 0.22
P wave height, mV	Experience (n = 12)	0.12 ± 0.02	0.13 ± 0.02
	Control (n = 11)	0.15 ± 0.019	0.16 ± 0.01
P-Q interval duration, ms	Experience (n = 12)	44.5 ± 1.25	43.4 ± 0.73
	Control (n = 11)	44.1 ± 1.16	43.1 ± 1.19
QRS complex duration, ms	Experience (n = 12)	19.5 ± 0.25*	19.4 ± 0.21**
	Control (n = 11)	20.6 ± 0.46	20.3 ± 0.21
R wave height, mV	Experience (n = 12)	0.62 ± 0.07	0.77 ± 0.07*
	Control (n = 11)	0.65 ± 0.07	0.95 ± 0.05

Note. Differences with the control group of animals are statistically significant: * – at $p < 0,05$; ** – at $p < 0,01$.

TABLE 3

INTEGRAL INDICES OF RAT CONDITION DURING SUBACUTE INTRAGASTRIC ADMINISTRATION OF SUBSTANCES (M ± M)

Indices		Animal groups (number)	Indole	1-benzylindole
Cumulative-threshold indicator, B		Experience (<i>n</i> = 12)	4.9 ± 0.19*	4.8 ± 0.10
		Control (<i>n</i> = 11)	4.4 ± 0.15	4.6 ± 0.10
Body temperature, °C		Experience (<i>n</i> = 12)	37.7 ± 0.12**	37.5 ± 0.14***
		Control (<i>n</i> = 11)	38.1 ± 0.08	38.1 ± 0.06
Blood pressure, mmHg	systolic	Experience (<i>n</i> = 12)	132.2 ± 5.81	–
		Control (<i>n</i> = 11)	136.3 ± 3.72	–
	diastolic	Experience (<i>n</i> = 12)	81.5 ± 4.01*	–
		Control (<i>n</i> = 11)	93.5 ± 3.65	–
	mean	Experience (<i>n</i> = 12)	98.2 ± 3.18*	–
		Control (<i>n</i> = 11)	108.5 ± 3.61	–
	horizontal total	Experience (<i>n</i> = 12)	21.8 ± 2.78*	24.0 ± 3.91
		Control (<i>n</i> = 11)	28.9 ± 1.76	27.8 ± 2.68
Motor activity	horizontal directional	Experience (<i>n</i> = 12)	5.7 ± 1.03	5.3 ± 1.03
		Control (<i>n</i> = 11)	8.2 ± 1.04	7.2 ± 1.03
	vertical	Experience (<i>n</i> = 12)	6.3 ± 1.12	5.3 ± 1.03*
		Control (<i>n</i> = 11)	9.2 ± 0.77	8.3 ± 1.04
	integral activity indicator	Experience (<i>n</i> = 12)	11.8 ± 1.05*	13.0 ± 1.04
		Control (<i>n</i> = 11)	14.8 ± 0.32	13.8 ± 0.41

Note. Differences with the control group of animals are statistically significant: * – at $p < 0,05$; ** – at $p < 0,01$.

When both indole and 1-benzylindole were administered, statistically significantly increased 1.2-1.3-fold AspAT and ALAT activities were revealed in serum. The study of lipid metabolism revealed an increase in serum total cholesterol concentration by 25 % with indole

administration and by 40 % with 1-benzylindole administration, and triglycerides by 45 and 50 %, respectively.

The changes revealed at the functional and biochemical levels are confirmed by the data of morphological studies of heart, liver and kidney tissue. For instance,

TABLE 4

HAEMATOLOGICAL AND BIOCHEMICAL PARAMETERS OF BLOOD SERUM OF RATS DURING SUBACUTE INTRAGASTRIC ADMINISTRATION OF SUBSTANCES (M ± M)

Indices	Animal groups (number)	Indole	1-benzylindole
Peripheral blood values			
HGB, g/L	Experience (n = 12)	156.2 ± 3.87	148.5 ± 4.48*
	Control (n = 11)	161.6 ± 3.26	161.0 ± 3.36
RBC, 10 ¹² /L	Experience (n = 12)	7.10 ± 0.12	6.65 ± 0.12*
	Control (n = 11)	7.30 ± 0.11	7.0 ± 0.11
WBC, 10 ⁹ /L	Experience (n = 12)	12.0 ± 1.22	12.5 ± 1.08
	Control (n = 11)	13.6 ± 1.47	15.2 ± 1.34
Banded neutrophils, %	Experience (n = 12)	1.0 ± 0.01	0.9 ± 0.12
	Control (n = 11)	1.3 ± 0.12	1.0 ± 0.24
Segmented neutrophils, %	Experience (n = 12)	14.9 ± 1.12	20.1 ± 1.83
	Control (n = 11)	21.7 ± 1.84	24.1 ± 2.82
Eosinophils, %	Experience (n = 12)	2.8 ± 0.62	2.8 ± 0.62
	Control (n = 11)	2.2 ± 0.87	2.2 ± 0.37
Monocytes, %	Experience (n = 12)	6.1 ± 0.50	6.6 ± 0.37
	Control (n = 11)	7.1 ± 0.74	6.8 ± 0.74
Lymphocytes, %	Experience (n = 12)	76.6 ± 1.12	67.8 ± 1.85
	Control (n = 11)	67.6 ± 3.36	63.0 ± 3.48
Serum biochemical indicators			
AspAT activity, mmol/(h · l)	Experience (n = 12)	1.99 ± 0.074***	1.73 ± 0.040***
	Control (n = 11)	1.49 ± 0.075	1.47 ± 0.047
ALAT activity, mmol/(h · l)	Experience (n = 12)	1.27 ± 0.115***	0.77 ± 0.073
	Control (n = 11)	0.62 ± 0.050	0.67 ± 0.044
Cholesterol, mmol/L	Experience (n = 12)	2.0 ± 0.097**	2.0 ± 0.125***
	Control (n = 11)	1.6 ± 0.086	1.4 ± 0.051
Triglycerides, mmol/l	Experience (n = 12)	0.67 ± 0.054**	0.65 ± 0.042*
	Control (n = 11)	0.45 ± 0.054	0.43 ± 0.078
Urea, mmol/L	Experience (n = 12)	5.9 ± 0.164	6.7 ± 0.470**
	Control (n = 11)	4.9 ± 0.122	5.2 ± 0.156
Glucose, mmol/L	Experience (n = 12)	7.7 ± 0.222***	8.0 ± 0.347
	Control (n = 11)	6.2 ± 0.261	7.0 ± 0.295

Note. Differences with the control group of animals are statistically significant: * – at $p < 0.05$; ** – at $p < 0.01$.

the following changes were revealed in myocardium: cardiomyocytes were thinned, with the presence of underlined striation; microcirculatory vessels were markedly full blooded; intermuscular spaces were dilated; residual traces of round cell infiltration were observed in some areas of myocardium. Due to some «homogenisation» of the middle layer of the vascular wall, thickening of vessels is observed; slight infiltration with elements of lymphoid series is revealed in them. In the vascular lumen – stasis phenomena with aggregation of aggregated erythrocytes.

The liver revealed moderately pronounced fatty dystrophy accompanied by a significant decrease in the glycogen content in the cytoplasm of hepatocytes compared to the control.

The ingestion of toxicants caused a compensatory-adaptive response of the organism, which manifested itself in diffuse proliferation of kupffer cells. Renal lesions are expressed in the form of enlarged tubules; as a result of swelling of capillary endothelium, the lumen of the Shumlansky – Bowman capsule is narrowed, the epithelium of renal tubules is swollen, loose protein masses are found in the lumen of tubules.

DISCUSSION

Data about the toxic effect of indole and 1-benzylindole on the cardiovascular system in Russian and foreign open sources are insignificant, while indole and its derivatives are valuable industrial raw materials for the chemical and pharmaceutical industries. The conducted studies have revealed the studied xenobiotics as moderately and low hazardous at acute intragastric intake into the organism, but it does not exclude possible toxic effect, especially to heart and blood system, at subacute and chronic exposure.

The results of the conducted experiment revealed functional abnormalities in the heart. ECG monitoring of the group of animals receiving indole revealed signs of increased atrial electrical activity. The shortening of the QRS complex duration revealed on the ECG of rats poisoned by both substances compared to the control may indicate an acceleration of the depolarisation process and serve as a sign of myocardial electrical instability [11].

Lesions of the cardiovascular tract are not isolated, but develop in combination with other general and specific manifestations of the damaging effect of a chemical agent to the organism. Administration of both indole and 1-benzylindole statistically significantly decreased blood pressure and body temperature, caused changes in the indices of motor activity and STI, which demonstrates a decrease in the general excitability of the animals' organism.

Being universal, the body's defense system elicits a range of monotypic hematologic responses. The ingestion of substances in the body causes systemic damage to the processes of haemopoiesis, which manifests itself as a decrease in the number of erythrocytes and haemoglobin concentration [12, 13]. A change in the percentage of white blood elements can be considered the most typical

defence reaction of the organism to toxins. In the study of white blood composition, relative leucopenia was observed due to a decrease in the number of rod-shaped and segmented neutrophils, which may be of diagnostic value. The decrease in leucocyte number resulted in a relative lymphocytosis. The number of eosinophils in the blood of animals exposed to indole poisoning is increased.

The increased level of enzyme activity in biomedical studies serves as a marker of a diseased organ, reflecting the level of its morphological destructive changes and physiological intensity of metabolism. Glycemic levels reflect the magnitude of severity of biochemical disorders in intoxication. In rats poisoned with indole and 1-benzylindole, an increase in serum glucose levels was observed, which may indicate impaired oxidation of the main energy substrates in the organs as a result of their toxic damage.

In standard clinical studies, the determination of changes in aminotransferase activity is considered one of the most highly sensitive marker assays for studying the functional status of the cardiovascular system. These enzymes are indicators of the state of organ membranes, which are characterised by their highest activity. For AspAT, the myocardium is primarily such an organ [14, 15]. Consequently, the increased AsAT activity in the serum of animals that had received indole and 1-benzylindole reflects probable membrane abnormalities accompanied by release of the enzyme into the blood. In this case, the increase in ALAT activity may signal not only hepatocyte damage, but also anabolic processes dominating in the organism of experimental animals [16].

The study of lipid metabolism revealed an increase in the concentration of total cholesterol and triglycerides in the blood serum of experimental groups of animals. The proatherogenic effect of toxicants may be one of the premorbid factors causing the development of arterial hypertension in chronic poisoning. The hypercholesterolaemia that develops under conditions of intoxication may be associated with both the ability of xenobiotics to activate a number of enzymes involved in cholesterol biosynthesis and the parallel inhibition of enzymes involved in its breakdown [17].

The 20 % increase in serum urea concentration revealed in the experiment may signal the initial stages of portal circulation disorder with the accession of renal failure.

Morphohistological studies confirmed the toxic effect towards the heart of animals poisoned with indole and 1-benzylindole. In the structure of the rat heart poisoned by these compounds, changes of dystrophic character, hypertrophic and atrophic changes of separate fibres were observed, in the microcirculatory vascular bed the walls were thickened at the expense of hypertrophy of cells of the muscular layer, full blood vessels were sharply pronounced.

Study limitations. The study is limited by examining the toxicological characteristics of indole and 1-benzylindole. In vivo experiments undertaken in accordance with guidelines for the protection of experimental animals limit their number as a result of animal hazards and public ethical views towards in vivo experiments.

CONCLUSION

The results of experimental studies have revealed that indole and 1-benzylindole under conditions of long-term intake into the organism lead to heart disorders, clinical manifestations of which can be such diseases as arterial hypertension, cardiosclerosis, angina pectoris, cardiac arrhythmias, atherosclerotic lesions of blood vessels. For the purpose of prophylaxis at the production facilities where contact of employees with indole and its derivatives is possible, in addition to constant monitoring of workplaces and mandatory use of personal protective equipment, regular occupational examinations of employees with extended indices of general and biochemical blood tests and mandatory control of ECG are necessary.

Conflict of interest

The authors declare no apparent and potential conflicts of interest in connection with the publication of this article.

Funding

The study had no financial support.

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