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MATHEMATICAL MODEL OF FUNCTIONAL RESPIRATORY SYSTEM FOR THE INVESTIGATION OF HARMFUL ORGANIC COMPOUNDS INFLUENCES IN INDUSTRIAL REGIONS

Introduction. *The areas around industrial objects, and now in regions of military actions are characterized by a high content of pollutants. Qualitative spectrum of these pollutants is extremely broad and contains both inorganic and organic elements and compounds. In particular, environmental pollution is caused by hydrocarbons with wide range of chemical structures, the study of which is very important due to their harmful and toxic influences on living organisms. The methods, currently used in medicine, give only a "thin slice" of current pathological state of organism, but they cannot predict the long-term consequences of such lesions. That is why it seems appropriate to use mathematical models that simulate the*

movement of organic compounds in the respiratory and circulatory systems and thus to predict possible pathologies in organs and tissues caused by hypoxic states that occur when these organs and tissues are affected.

***Purpose of the paper is** to create a mathematical model of functional respiratory system, which simulates the influence of external environment on the parameters of self-organization of human respiratory system in the dynamics of respiratory cycle; and thus to predict hypoxic conditions during tissue damage by hydrocarbons.*

***Results.** The mathematical model for respiratory gases transport and mass transfer in human organism is represented as a system of differential equations, which is a controlled dynamic system, and the states of which are determined by oxygen and carbon dioxide stresses in each structural link of the respiratory system (alveoli, blood, and tissues) at each moment of time. The model is supplemented by the equations of transport of the substances in each structural link as well as by the mathematical model of organism oxygen regimes regulation. The model includes seven groups of tissues - brain, heart, liver and gastrointestinal tissues, kidneys, muscle tissue etc. The algorithm of the work and iterative procedure of research with application of suggested complex are given.*

***Conclusion.** The proposed mathematical model for studying of the transport of organic substances in human organism which consists of differential equations of respiratory gases transport and mass transfer in it, and for the transport of organic compounds is theoretical only for today. However, in the presence of appropriate array of experimental data, it will be able to monitor the state of functional respiratory system after the pathogenic organic compounds inquiry, which may be useful in choosing of strategies and tactics for the treatment of particular lesion.*

***Keywords:** functional respiratory system, regulation of organism oxygen regimes, harmful organic substances, hypoxic state, mathematical model of respiratory system, transport of gases by blood, self-regulation of respiratory system.*

INTRODUCTION

In contemporary reality the great attention is attracted to problems of environmental pollution, and numerus researchers, environmentalists study effects of toxic and harmful environmental substances influence on living organisms. Industrial polluted territories are characterized by high content of contaminating substances, the qualitative spectrum of which is extremely wide, containing both inorganic and organic elements and compounds. Among such environmental chemical pollutants there are hydrocarbons (with linear and/or cyclic structures) for example, the derivatives of phenols with polyamine radicals of different lengths and branches. Such substances were registered among a wide range of environmentally harmful pollutants appeared as a result of industrial objects functioning, as well as damages of chemical plants, contamination of accident sites by fuels and lubricants, consequences of air crashes, fires at objects of oil and gas industries etc. Numerous works are devoted to study of these problems [1, 2], but many questions still are unanswered [2].

Numerical facts of environment industrial pollution with hydrocarbons of wide range of chemical structures were described [1, 2, 3], as well as the facts of their harmful and toxic effects on living organisms. However, the studies of mechanisms of such compounds influences on organisms, details of their physiological effects, results of monitoring of their pressure on organisms over long time periods are absolutely insufficient because of number of reasons. Such reasons are: the great diversity of such compounds in pollutant emissions, their insufficient chemical identification, variability of chemical structures of such compounds over time as a result of their continued chemical transformation in

the environment, other. The grounding of such substances computer identification with further studying was already done [4].

The practice of contemporary science demonstrates that usage of mathematical methods, including the methods of mathematic modeling permits to overcome such difficulties. Such methods have to be used in cases when direct experimental study is or impossible, or rather expensive [5]. The methods existing in medicine for such substances influences studying give only imagination about current pathological state of organism, which, of course, is very important for the treatment of specific lesions, but cannot predict the long-term consequences of such lesions for organism. Therefore, it is advisable to use mathematical models that allow ones to simulate the processes, pathways of organic compounds transportation by respiratory and/or blood circulation systems; and thereby to predict possible pathologies in organs and tissues. In this research we use mathematical model of functional respiratory system [6–8], which is supplemented by the equations of substances transportation in organism [9, 10].

The purpose of the paper is to develop mathematical models to study the influences of organic pollutants (derivatives of aromatic hydrocarbons) on the state of functional systems of living organisms.

Problem of environment pollution by harmful and toxic organic substances in industrial regions. Hydrocarbons are the major component of liquid and gaseous fuels that cause toxic effects on living organisms. Different types of fuels (gasoline, kerosene etc.) differ in their content of paraffin, petroleum and aromatic hydrocarbons [1, 2, 3]. The wastewater of production areas of airports, other aviation industry objects contains benzene, petroleum products that occur damaging effect on organisms of these enterprises service personnel and surrounding population. For example, an increased risk for the health of population was registered within the 10 km wide band surrounding the aviation objects [2]. Hydrocarbons are sources of environmental pollution by carcinogens, the most powerful of which are polycyclic hydrocarbons, as well as aromatic amines, which are products of functioning and emissions of aviation industry, chemical and petrochemical industries [3]. Hydrocarbons are also the components of transport fuels, their quantity is growing in metropolitan areas and, consequently, the risk of related diseases of population is increased in Ukrainian cities [3].

Oil pollution of sewages is especially noticeable in industrial regions, however, the molecular mechanisms of action of these hydrocarbons have not been studied yet [3]. At the same time, it is known that oil and petroleum products are too harmful for water reservoirs in nature (sea, lakes etc.), their physiological toxic effects on living organisms are widely known [1, 2, 3]. The authors tried to investigate effects of such hydrocarbons derivatives, which are parts of the abovementioned pollutants. Namely, the effects of aromatic hydrocarbons influence on organism (phenol derivatives with hydrocarbon radicals of different length and structure) were investigated. In previous works by Klyuchko O.M. was demonstrated that investigated molecular mechanisms of such substances action are common to a broad class of such compounds. In addition, the differences in properties of the action of toxic substances depending on the length of the polyamine radical were demonstrated [4, 5].

It should be noted that the most common of coal products are indene-coumar resins containing chemical compounds with similar structure of molecules. Inden-coumar resins are products of polymerization of non-organic compounds of xylene fraction ($T_{кип} = 160^0 – 180^0$ C): coumarone, indene, styrene and their homologues. These resins are used to increase the stickiness of the rubber mixtures. There are no fundamental differences between such compounds - low molecular weight and high molecular weight polymers [11]. The results obtained by some authors [1–3, 11] can be used to improve the safety of personnel working in coal mining or processing enterprises, chemical plants, places of industrial accidents etc.

Mathematical model of respiratory system. Using a systematic approach to describe the process of mass transfer of respiratory gases in organism, lets imagine the respiratory system in the form of controlled system in which the mass transfer of oxygen, carbon dioxide and nitrogen is going, and the controlling system, which produces certain effects that ensure the normal course of the process of mass transfer of gases. The mathematical model of controlled part of respiratory system is represented by a system of ordinary differential equations that describe the dynamics of oxygen tensions at all stages of its ways in organism.

We represent the mathematical model of the functional respiratory system in following form.

The block diagram of the model is shown in Fig. 1.

Let's denote as pO_2, pCO_2, and pN_2 partial pressures of oxygen, carbon and nitrogen respectively in breathing mixture, taking into account that

$$B = pO_2 + pCO_2 + pN_2, \tag{1}$$

where B is a value of atmospheric pressure.

Lets suppose that $p_{j_{RW}}$, $j = \overline{1,3}$ are the partial pressures of oxygen, carbon dioxide and nitrogen in the respiratory tract, and p_{j_A}, $j = \overline{1,3}$ — in the alveolar space.

Then the equation describing the dynamics of respiratory gases in the respiratory tract can be represented as:

$$\frac{dp_{j_{RW}}}{d\tau} = \frac{\dot{V}}{V_{RW}}(\vec{p}_{j_{RW}} - \overline{p}_{j_A}), \tag{2}$$

where the gas number corresponds to the index j — oxygen, carbon dioxide, nitrogen, V_{RW} — airway volume, $\dot{V}$ — lung ventilation.

$$\dot{V} = \begin{cases} \dfrac{RV \cdot \tau}{T_a} \sin \dfrac{\tau - \tau 0}{T_a} n_i, \textit{during a breathing act (inhalation and expiration)} \\ 0, \textit{during a breathing pause} \end{cases} \tag{3}$$

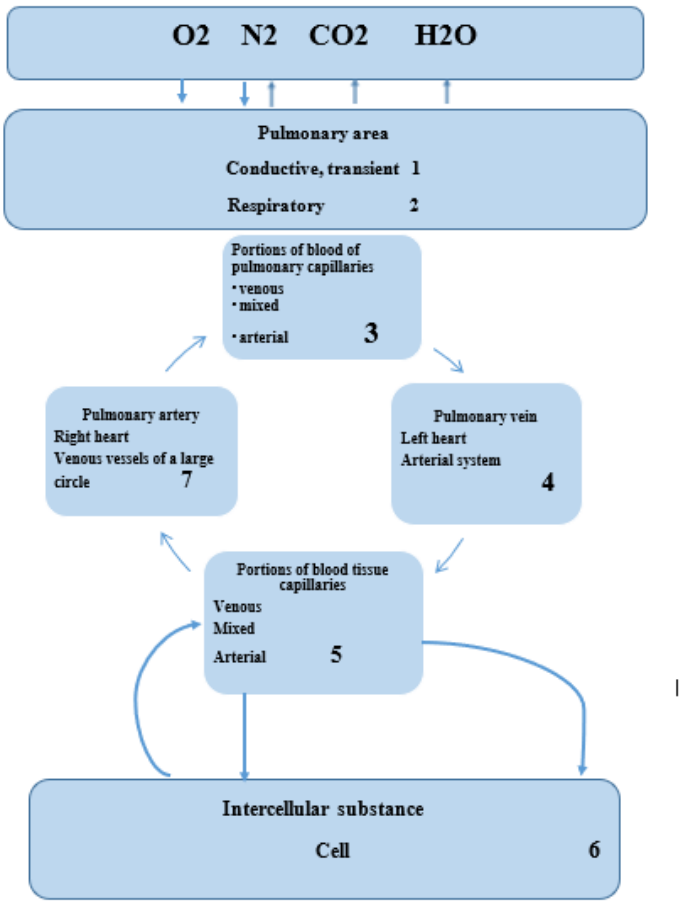

Fig. 1. Block diagram of the model

$$\text{and} \quad p_{jRW} = \begin{cases} p_j, at\, \dot{V} > 0 \\ p_{jRW}, at\, \dot{V} \le 0 \end{cases} \tag{4}$$

$$p_{j_A} = \begin{cases} p_{j_{RW}}, at\, \dot{V} > 0 \\ p_{j_A}, at\, \dot{V} \le 0 \end{cases}, \tag{5}$$

where T_α is the duration of the respiratory act, τ_0 — the time of its onset, RV — the respiratory volume. Using the same principles of material balance and flow continuity, we can write the equation for the dynamics of respiratory gases in the alveolar space:

$$\frac{dp_{j_A}}{d\tau} = \frac{1}{n_j(V_L - V_{RW})}[n_j \cdot p_{j_A} \cdot \widetilde{V} - G_{j_A} - n_j p_{j_A} \frac{dV_L}{d\tau}], \tag{6}$$

where G_{jA} is the flow of gas through the alveolar-capillary membrane, V_L is the lungs' volume, n_j — transfer coefficients. The algebraic analogue of Fick's law is used for G_{jA}:

$$G_{j_A} = k_j \cdot n_j \cdot S \cdot (p_{j_A} - p_{j_{Lc}}), \tag{7}$$

where *k, n* are coefficients of gases permeability through the membrane, *S* — is the surface area of mass transfer.

The peculiarities of mass transfer of gases convectively should be taken into account during obtaining of equations for the transport of respiratory gases by the blood. Oxygen is transported being dissolved in blood plasma as well as being chemically coupled to hemoglobin (*Hb)*; carbon dioxide — being dissolved as well as chemically coupled to hemoglobin and blood buffer bases *(BH);* nitrogen — being only dissolved in blood plasma.

Let suppose that p_aO_2, p_aCO_2, p_aN_2 — are the tensions of respiratory gases in the arterial blood; $p_{\bar{v}}O_2$, $p_{\bar{v}}CO_2$, $p_{\bar{v}}N_2$ — in mixed venous blood, ($p_{Lc}O_2$, $p_{Lc}CO_2$, $p_{Lc}N_2$) — in pulmonary capillary blood; ($p_{ct_i}O_2$, $p_{ct_i}CO_2$, $p_{ct_i}N_2$) — in tissue capillary blood; and ($p_{t_i}O_2$, $p_{t_i}CO_2$, $p_{t_i}N_2$)— in tissue fluid, respectively.

Applying the principles of material balance and continuity of flows, we can obtain the equation for changes of gases tensions in the blood of pulmonary capillaries as follows:

$$\frac{dp_{Lc}O_2}{d\tau} = \frac{1}{V_{Lc}(\alpha_1 + \gamma \cdot Hb \frac{\partial \eta_{Lc}}{\partial p_{Lc}O_2})}[\alpha_1(Q - Q_{sh})(p_a - p_{Lc}O_2) - \tag{8}$$

$$-\gamma \cdot Hb \cdot (Q - Q_{sh})(\eta_{\bar{v}} - \eta_{Lc}) + G_AO_2]$$

$$\frac{dp_{Дc}CO_2}{d\tau} = \frac{1}{V_c(\alpha_2 + \gamma_{BH} \cdot BH \frac{\partial z_{Lc}}{\partial p_{Lc}CO_2} + \gamma \cdot Hb(1 - \eta_{Lc}) \frac{\partial z_{Lc}}{\partial p_{Lc}CO_2})} \cdot \tag{9}$$

$$\cdot[\alpha_2(Q - Q_{sh})(p_{\bar{v}}CO_2 - p_{Lc}CO_2) + G_ACO_2 + (Q - Q_{sh}) \cdot \gamma_{BH} \cdot BH \cdot Q_{t_i} \cdot (z_{\bar{v}} - z_{Lc}) +$$

$$+ (1 - \eta_{Lc}) \cdot \gamma_{BH} \cdot BH \cdot (Q - Q_{sh}) \cdot z_{\bar{v}} - z_{Lc}] + \tag{10}$$

$$\frac{dp_{Lc}N_2}{d\tau} = \frac{1}{V_{Lc}\alpha_3}(\alpha_3(Q - Q_{sh})(p_{\bar{v}}N_2 - p_{Lc}N_2) + G_AN_2),$$

where Q, Q_{sh} — are volumetric rates of systemic circulation and circulation in conditions of the lungs bypass; α_1 α_2 α_3 — are coefficients of gases solubility in the blood plasma; *Hb*, *BH* — hemoglobin and buffer concentrations in the blood; γ, γ_{BH} — are Güfner constants, and the degree of oxygen saturation is determined by the ratios (20)–(23) relatively to the blood of pulmonary capillaries.

The equations of tensions change for gases and studied chemical compounds in the blood of arterial vessels were obtained in the same way. It is necessary to note only that the levels of gases tensions are formed as a result of quick mixing of their flows, coming from the blood of pulmonary capillaries and mixed venous blood with the gases in arterial vessels. That is why

$$\frac{dp_aO_2}{d\tau}=\frac{1}{V_a(\alpha_1+\gamma\cdot Hb\dfrac{\partial\eta_a}{\partial p_aO_2})}[\alpha_1(Q-Q_{sh})p_{Lc}O_2+\gamma\cdot Hb\cdot(Q-Q_{sh})(\eta_{Lc}-\eta_a)+$$
$$+\alpha_1Q_{sh}p_{\bar{v}}O_2]+\frac{1}{V_a(\alpha_1+\gamma\cdot Hb\dfrac{\partial\eta_a}{\partial p_aO_2})}+[\gamma\cdot BH\cdot Q_{sh}\eta_{\bar{v}}-\alpha_1Qp_aO_2-\gamma\cdot BH\cdot q\,\eta_a] \quad (11)$$

$$\frac{dp_aCO_2}{d\tau}=\frac{1}{V_c(\alpha_2+\gamma_{BH}\cdot BH\dfrac{\partial z_a}{\partial p_aCO_2}+\gamma\cdot Hb(1-\eta_a)\dfrac{\partial z_a}{\partial p_aCO_2})}\cdot$$
$$[\alpha_2(Q-Q_{sh}p_{Lc}CO_2)+\alpha_2Q_{sh}p_{\bar{v}}+(Q-Q_{sh})\cdot\gamma_{BH}\cdot BH\cdot Q_{t_i}\cdot(z_{Lc_i}-z_a)+(1-\eta_{Lc})\cdot\gamma_{BH}\cdot \quad (12)$$
$$\frac{(1-\eta_c)\cdot\gamma\cdot Hb\cdot(Q-Q_{sh})\cdot z_{Lc}+(1-\eta_{\bar{v}})\cdot\gamma\cdot Hb\cdot Q_{sh}\cdot\cdot z_{\bar{v}}-(1-\eta_c\cdot\gamma\cdot Hb\cdot Q\cdot z_a}{V_c(\alpha_2+\gamma_{BH}\cdot BH\dfrac{\partial z_a}{\partial p_aCO_2}+\gamma\cdot Hb(1-\eta_a)\dfrac{\partial z_a}{\partial p_aCO_2})}.$$

$$\frac{dp_aN_2}{d\tau}=\frac{1}{V_a\alpha_3}(\alpha_3(Q-Q_{sh})p_{Lc}N_2-\alpha_3\cdot Q_{sh}\cdot p_{\bar{v}}N_2\cdot Q_{t_i}-\alpha_3\cdot Q\cdot p_aN_2) \quad (13)$$

Here is an equation that characterizes the changes in the tensions of respiratory gases in the blood of tissue capillaries and tissue fluid of the organ:

$$\frac{dp_{ct_i}O_2}{d\tau}=\frac{1}{V_{ct_i}(\alpha_1+\gamma\cdot Hb\dfrac{\partial\eta_{ct_i}}{\partial p_{ct_i}O_2})}(\alpha_1Q_{t_i}(p_aO_2-p_{ct_i}O_2)+\gamma\cdot Hb\cdot Q_{t_i}(\eta_a-\eta_{ct_i})-G_{t_i}O_2), \quad (14)$$

$$\frac{dp_{ct_i}CO_2}{d\tau}=\frac{1}{V_{ct_i}(\alpha_{21}+\gamma_{BH}\cdot BH\dfrac{\partial z_{ct_i}}{\partial p_{ct_i}CO_2})}(\alpha_2Q_{t_i}(p_aCO_2-p_{ct_i}CO_2)+ \quad (15)$$
$$+\gamma_{BH}\cdot BH\cdot Q_{t_i}\cdot Hb\cdot Q_tz_a-G_{t_i}CO_2)-(\alpha_2Q_{t_i}-(1-\eta_{ct})\cdot\gamma_{Hb}\cdot Hb\cdot V_{ct\,i}\frac{\partial\eta_{ct\,i}}{\partial\tau})$$

$$\frac{dp_{ct_i}N_2}{d\tau}=\frac{1}{V_{ct_i}\alpha_3}(\alpha_3 Q_{t_i}p_aN_2-\alpha_3 p_{ct_i}N_2\cdot Q_{t_i}-G_{t_i}N_2), \tag{16}$$

$$\frac{dp_{t_i}O_2}{d\tau}=\frac{1}{V_{t_i}(\alpha_1+\gamma_{Mb}\cdot Mb\dfrac{\partial\eta_{t_i}}{\partial p_{t_i}O_2})}(G_{t_i}O_2-q_{t_i}O_2) \tag{17}$$

$$\frac{dp_{t_i}CO_2}{d\tau}=\frac{1}{V_{t_i}\alpha_2}(G_{t_i}CO_2+q_{t_i}CO_2) \tag{18}$$

$$\frac{dp_{t_i}N_2}{d\tau}=\frac{G_{t_i}N_2}{V_{t_i}\alpha_3}, \tag{19}$$

where

$$\eta_{ct_i}=1-1{,}75\exp(-0{,}052m_{ct_i}p_{ct_i}O_2)+0{,}75\exp(-0{,}12m_{ct_i}p_{ct_i}O_2) \tag{20}$$

$$m_{ct_i}=0{,}25(pH_{ct_i}-7{,}4)+1 \tag{21}$$

$$pH_{ct_i}=6{,}1+\lg\frac{BH}{\alpha_2 p_{ct_i}CO_2}, \tag{22}$$

$$z_{ct_i}=\frac{p_{ct_i}CO_2}{p_{ct_i}CO_2+35} \tag{23}$$

α_1, α_2, α_3, α_{1t_i}, α_{2t_i}, α_{3t_i} are solubility coefficients of respiratory gases in blood and tissue fluid; Q_{t_i} — volume circulation velocity in the capillary channel of the tissue reservoir; t_i, V_{ct_i}, V_{t_i} — volume of blood and tissue fluid, respectively.

Tissue blood which partially gave off oxygen and saturated with carbon dioxide, returns to the lungs through circulation. There tissue blood is enriched with oxygen, but left the carbon dioxide during each respiratory cycle. Respiratory gas tension equations for mixed venous blood can be written as:

$$\frac{dp_{\bar{v}}O_2}{d\tau}=\frac{1}{V_{\bar{v}}(\alpha_1+\gamma\cdot Hb\dfrac{\partial\eta_{\bar{v}}}{\partial p_{\bar{v}}O_2})}[\alpha_1(\sum_{ti}Q_{ti}\cdot p_{ct}O_2-Q\cdot p_{\bar{v}}O_2)-\gamma\cdot Hb\cdot Q\cdot\eta_{\bar{v}}], \tag{24}$$

$$\frac{dp_{\bar{v}}CO_2}{d\tau} = \frac{1}{V_{\bar{v}}(\alpha_2 + \gamma_{BH} \cdot BH \frac{\partial z_{\bar{v}}}{\partial p_{\bar{v}}CO_2})}[\alpha_2(\sum_{t_i} Q_{t_i} - Qp_{\bar{v}}CO_2) + (\sum_{t_i} \gamma_{BH} \cdot BH \cdot Q_{t_i} \cdot z_{2ct_i} -$$

$$\gamma_{BH} \cdot BH \cdot Q \cdot z_{2\bar{v}}) + (\sum_{t_i} (1 - \eta_{ct_i}) \cdot \gamma_{Hb} \cdot Hb \cdot Q \cdot z_{\bar{v}} - (1 - \eta_{\bar{v}}) \cdot \gamma_{Hb} \cdot Hb \cdot Q \cdot z_{\bar{v}}) + \quad (25)$$

$$+ \sum_{t_i} \gamma_{Hb} \cdot Hb \cdot V_{ct_i} \frac{\partial \eta_{ct_i}}{\partial \tau}$$

$$\frac{dp_{\bar{v}}N_2}{d\tau} = \frac{1}{V_{\bar{v}}\alpha_3}(\sum_{t_i} \alpha_3 \cdot Q_{t_i} \cdot p_{ct_i}N_2 - \alpha_3 \cdot p_{\bar{v}}N_2 \cdot Q_{t_i}). \quad (26)$$

System (1)–(26) for given $\dot{V}$, Q, Q_t, describes changes in the partial pressures and tensions of respiratory gases in the blood and tissue fluids of organism regions and organs during the respiratory cycle; η is the degree of hemoglobin saturation with oxygen; Q — is volumetric rate of systemic and Q_t — of local blood flows; $q_{t_i}O_2$ — is velocity of oxygen consumption by *i*-th tissue reservoir; $q_{t_i}CO_2$ — is velocity of carbon dioxide emission in *i*-th tissue reservoir. Velocities $G_{t_i}O_2$ of oxygen flow from the blood into the tissue and $G_{t_i}CO_2$ — of the carbon dioxide from the tissue to the blood are determined by the ratio

$$G_{t_i} = D_{t_i}S_{t_i}(p_{ct_i} - p_{t_i}), \quad (27)$$

where D_{t_i} — coefficients of gas permeability through the aerohematic barrier, S_{t_i} is area of the surface of gas exchange.

The task of optimal control. The purpose of control [12] is to output the perturbed system to a steady state mode, where following relations are true:

$$|G_{t_i}O_2 - q_{t_i}O_2| \le \varepsilon_1, \quad |G_{t_i}CO_2 + q_{t_i}CO_2| \le \varepsilon_2, \quad (28)$$

where, ε_1 and ε_2 are sufficiently small positive numbers that were stated in advance. In this case, the control parameters are in limits:

$$0 \le \dot{V} \le \dot{V}_{\max}, \; 0 \le Q \le Q_{\max}, \; 0 \le Q_{t_i} \le Q, \; \sum_{i=1}^{m} Q_{t_i} = Q, \quad (29)$$

where m — is the number of tissue reservoirs in organism.

In addition, to resolve the conflict situation between the executive organs of regulation (respiratory muscles, cardiac muscles and smooth muscles of vessels), being at that time consumers of oxygen, and other tissues and organs, following relations were suggested

$$q_{resp.m}O_2 = f(V)\ q_{card.m}O_2 = \varphi(Q)\ q_{smooth.m}O_2 = \psi(Q)\,. \tag{30}$$

We consider following functional as a criterion for regulation

$$I = \min_{\substack{0\le \dot V \le \dot V_{\max} \\ 0\le Q_{t_i} \le Q_{\max}}} \int_{\tau_0}^{T} [\rho_1 \sum_{t_i} \lambda_{t_i} (G_{t_i}O_2 - q_{t_i}O_2)^2 + \rho_2 \sum_{t_i} \lambda_{t_i} (G_{t_i}CO_2 + q_{t_i}CO_2)^2]d\tau\,, \tag{31}$$

where τ_0 is moment of the start of perturbated influence on the system, T is the duration of this effect, ρ_1 and ρ_2 — the coefficients characterizing the sensitivity of individual organism to hypoxia and hypercapnia, λ_{t_i} are coefficients reflecting the morphological features of the individual tissue reservoir i, $i = \overline{1,m}$.

Such control minimizes the total oxygen consumption in organism and in each tissue region, as well as accumulation of carbon dioxide.

Mathematical model of studied substances transport in organism. Let's denote $c_{f_{rw}}$ as concentration of organic substance in respiratory tract (in moles), and as d_f — its dose, then the equation of the dynamics of respiratory gases in the respiratory tract (1)–(31) should be supplemented by the equations of studied organic compound concentration [8–10]:

$$\frac{dc_{f_{RW}}}{d\tau} = \frac{\dot V}{V}(\tilde c_{f_{RW}} - \tilde c_{f_A}) \tag{32}$$

$$\tilde c_{f_{RW}} = \begin{cases} \xi d_f, \xi = 1, with\ inhalation of\ the\ drug (\dot V > 0) \\ \xi = 0, in\ the absence of\ inhalation during\ a\ respiratory\ break\ (\dot V > 0) \\ \tilde c f_{RW}, at\ \dot V \le 0 \end{cases} \tag{33}$$

$$\tilde c f_A = \begin{cases} c f_{RW}\ npu\ \dot V > 0 \\ c f_A\ npu\ \dot V \le 0 \end{cases}. \tag{34}$$

The level p_AO_2, p_ACO_2, p_AN_2 as well as c_{f_A} in alveolar space is formed due to the mixing of the gases and dispersion of studied organic compounds coming from the airways into the alveoli with those ones that are present in the alveolar space, and taking into account the flows of gases and chemical substances through the alveolar-capillary membrane. Then the equation of the dynamics of respiratory gases in the alveolar space (6) should be supplemented by the equations

$$\frac{dc_{f_A}}{d\tau} = \frac{1}{V_L}(\tilde{c}_{f_A}(\tau)\dot{V} - G_{f_A} - c_{f_A}\frac{dV_L}{d\tau}) \tag{35}$$

$$G_{j_A} = D_j S(p_{f_A} - p_{j_{lc}}) \tag{36}$$

$$G_{f_A} = D_f S(c_{f_A} - c_{j_{lc}}), \tag{37}$$

where D_j, are coefficients of permeability of gases and studied organic compound through the alveolar-capillary membrane with the surface area S

It should be noted that respiratory gases are transported by the blood in different ways: being dissolved in blood plasma and chemically bound to hemoglobin (*Hb*) carbon dioxide in dissolved plasma and chemically bound to bicarbonate compounds (*BH*); nitrogen is transported in dissolved form only. We assume that studied organic compound is transported in the blood too.

Using the principles of material balance and continuity of flow it is possible to obtain the equations of changes in gases tensions and concentrations of studied organic molecules in the blood of pulmonary capillaries, supplementing equations (8)–(10) by the equation

$$\frac{dc_{f_{lc}}}{d\tau} = \frac{1}{V_{lc}}((Q - Q_{sh})(c_{f_{\bar{v}}} - c_{f_{lc}}) - G_{f_A}. \tag{38}$$

The equations of tensions changes of respiratory gases and studied organic compound in the blood of arterial vessels can be written in the same way. Only it should be taken into account that the levels of gases tensions and concentrations of studied organic compounds can be formed as a result of instantaneous mixing of streams coming from the blood of pulmonary capillaries and mixed venous blood with gases and substance in arterial vessel. Then equations (11)–(13) for portions of arterial blood have to be supplemented by the equation.

$$\frac{dc_{f_a}}{d\tau} = \frac{1}{V_a}((Q - Q_{sh})c_{f_{lc}} + Q_{sh}c_{f_{\bar{v}}} - Qc_{f_a}. \tag{39}$$

The arterial blood flow branches to the microcirculatory networks of organs and tissues. The classical mathematical model of mass transfer and mass exchange of respiratory gases describes the dynamics of tensions of respiratory gases in ***m*** tissue reservoirs among which, as a rule, there are tissues of the brain, kidneys, liver, gastrointestinal tract, cardiac and skeletal muscles, bone and fat tissues. The structure of tissue reservoir is described usually as “Krog cylinder” whose axis is a generalized capillary. Equations (14)–(16) describing changes in tensions of respiratory gases in the blood washing the tissue, and in the tissue fluid of the reservoir can be supplemented by following equations of studied substances’ concentrations for the blood of tissue capillaries:

$$\frac{dc_{f_{ct_i}}}{d\tau} = \frac{1}{V_{ct_i}}(Q_{t_i}(c_{f_a} - c_{f_{ct_i}}) - G_{f_{t_i}}) \tag{40}$$

and for tissue fluid we supplement equations (16)–(18) with the expression

$$\frac{dc_{f_{t_i}}}{d\tau} = \frac{G_{f_{t_i}}}{V_{t_i}}, \tag{41}$$

where

$$G_{f_{t_i}} = D_{f_{t_i}} S_{t_i}(c_{f_{ct_i}} - c_{f_{t_i}}). \tag{42}$$

During the development of mathematical model for the transport and mass exchange of respiratory gases and aromatic derivatives, it was assumed that this substance does not participate directly in the metabolic processes.

In the venous vessels, the blood from organs and tissues is mixed and transported to the lungs for oxygen enrichment. Therefore, the equations for respiratory gases transport in mixed venous blood (24)–(26) are supplemented by the equation of concentration of the substance

$$\frac{dc_{f_v}}{d\tau} = \frac{1}{V_{\bar{v}}}(\sum_{t_i} Q_{t_i} c_{f_{t_i}} + c_{f_a} Q_{f_{t_i}} - Q c_{f_v}). \tag{43}$$

It is assumed that the excretion of organic compounds f from organism is carried out through the kidneys. The changes in concentrations of this compound f in the renal tissue are determined by the equation

$$\alpha_{f_i} V_{t_i} \frac{dc_{f_{t_i}}}{d\tau} = G_{f_{i_i}} - \alpha_{t_i} Q_f c_{t_i}, \tag{44}$$

where Q_f is velocity of the liquid filtration. It was assumed that the value of volumetric filtration rate was 0, 035 mg / s.

Then the iterative procedure for studying the effect of organic matter on the human respiratory system can be represented as follows (Fig. 2).

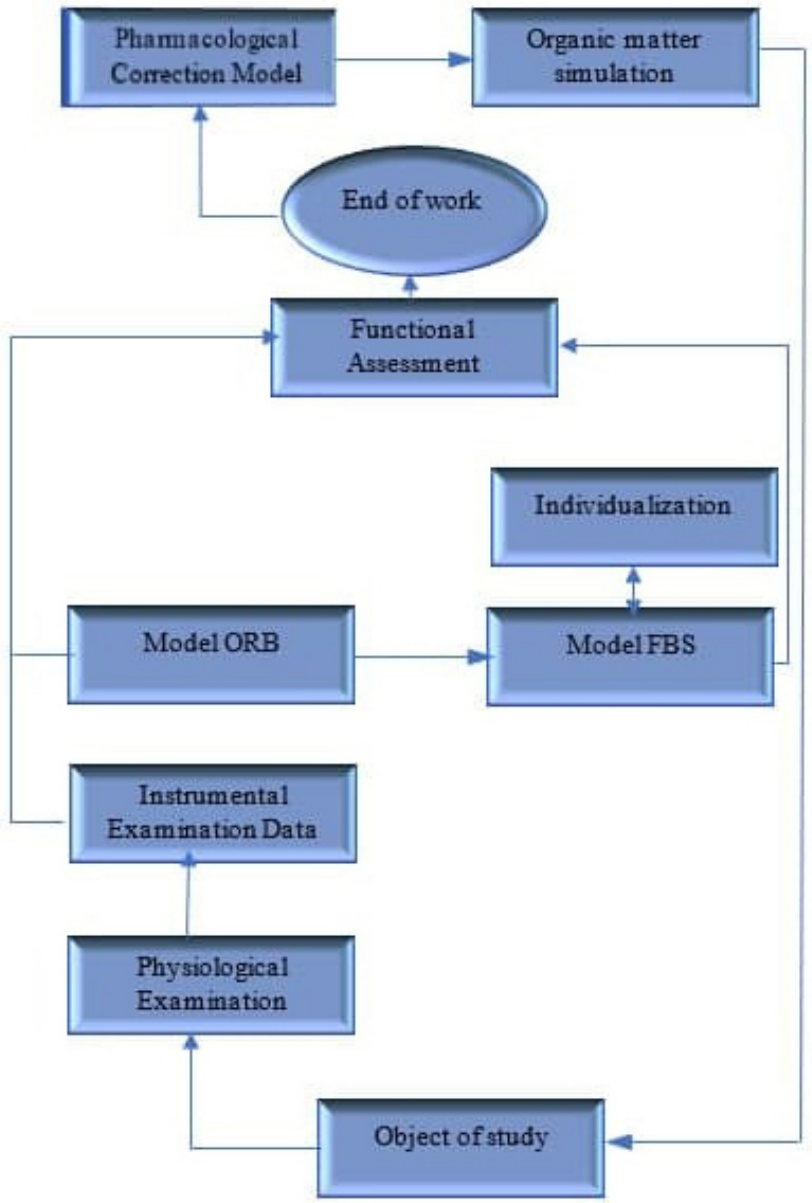

Fig. 2. Iterative procedure for studying the effect of organic matter on the human respiratory system

The iterative procedure for applying the proposed software package in this case will be:

1. An instrumental examination of the patient is carried out. We get data on lung ventilation, composition of the alveolar and exhaled air, respiratory rate, blood pressure, heart rate, hemoglobin, blood acidity etc., which are the source for the model of oxygen regimes of the body (ORB)[8, 13–15].

2. Based on the data of instrumental examination, we calculate indicators such as minute volume of respiration, minute volume of blood, rate of oxygen

consumption by the body, profitability, intensity and effectiveness of oxygen modes of the body, data characterizing the hypoxic state.

3. The data of instrumental examination and part of the data obtained in the calculation of the oxygen regimes of the body are used as the source for the model of respiratory gas transport. Thus, individualization of the model is carried out.

4. We simulate the introduction of organic matter into the body of a particular person on an individualized model [8, 16]. We obtain the values of the stresses of oxygen and carbon dioxide in the tissues of individual organs, which allow us to judge the degree of tissue hypoxia and get information about the state of seven groups of tissues represented in the mathematical model.

CONCLUSIONS

Proposed mathematical model for studying of organic compounds transport in human organism, consisting from the equations of mass transfer and mass exchange of respiratory gases, mathematical model of self-organization of respiration functional system and equations of substances transport in the systems of respiration and circulation have only theoretical value for today. However, in case of obtaining of experimental data array, these models will allow to monitor the state of respiratory system and blood circulation when harmful organic compounds enter the human organism. Presented models will allow the physicians to optimize the strategy and tactics of medical treatment.

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МАТЕМАТИЧНА МОДЕЛЬ ФУНКЦІОНАЛЬНОЇ СИСТЕМИ ДИХАННЯ ДЛЯ ДОСЛІДЖЕННЯ ВПЛИВУ ШКІДЛИВИХ ОРГАНІЧНИХ СПОЛУК У ПРОМИСЛОВИХ РЕГІОНАХ

Вступ. Території навколо промислових об’єктів, а натепер і в місцях проведення бойових дій характеризуються підвищеним вмістом сполук-забруднювачів, якісний спектр яких є надзвичайно широким та містить як неорганічні, так і органічні елементи та сполуки. Зокрема, відбувається забруднення атмосфери вуглеводнями широкого спектру хімічної будови, дослідження яких є дуже важливим внаслідок їхньої токсичної дії на живі організми. Методики, які наразі застосовують в медицині, дають лише деякий зріз поточного патологічного стану організму, проте не можуть прогнозувати довготермінові наслідки такого ураження. Саме тому видається доцільним застосувати математичні моделі, які дають змогу імітувати процес пересування органічної сполуки системою дихання та кровообігу і тим самим прогнозувати можливі патології в органах та тканинах, спричинені гіпоксичним станом, який виникає внаслідок ураження цих органів та тканин.

Мета. Побудувати математичну модель функціональної системи дихання, яка імітує вплив зовнішнього середовища на параметри самоорганізації системи дихання людини в динаміці дихального циклу і таким чином дає змогу прогнозувати гіпоксичні стани внаслідок ураження тканини вуглеводнями.

Результати. Надано математичну модель транспорту та масообміну респіраторних газів в організмі людини як систему диференційних рівнянь, яка є керованою динамічною системою, стани якої визначаються у кожен момент часу рівнями напруження кисню та вуглекислого газу в кожній структурній ланці системи дихання (альвеолах, крові, тканинах). Модель доповнено рівняннями транспорту речовини у кожній структурній ланці і математичною моделлю регулювання кисневих режимів організму.

У моделі передбачено сім груп тканин — тканини мозку, серця, печінки та ШКТ, нирок, м'язові тканини тощо. Наведено алгоритм роботи та ітераційну процедуру дослідження із застосуванням запропонованого комплексу.

Висновки. Запропонована математична модель для вивчення транспорту органічних речовин в організмі людини, яка складається з диференційних рівнянь транспорту та масообміну респіраторних газів в організмі людини і транспорту органічної сполуки, наразі має лише теоретичний характер. Проте за наявності відповідного масиву експериментальних даних вона надасть можливість відстежити стан функціональної системи дихання у разі потрапляння патогенних органічних сполук, що може виявитися корисним для вибору стратегії та тактики лікування конкретного ураження організму.

Ключові слова: *функціональна система дихання, регулювання кисневих режимів організму, шкідливі органічні речовини, гіпоксичний стан, математична модель системи дихання, транспорт газів кров'ю, саморегуляція системи дихання.*