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APPLICATION OF GAS CHROMATOGRAPHY METHODS FOR ANALYSIS OF EXHALED AIR BY PATIENTS WITH RESPIRATORY DISEASES

А.С. Зайцев, Н.А. Мацегора, С.В. Зайцев, С.О. Камінська, В.М. Тіхенко. **Застосування методів газової хроматографії для аналізу повітря, що видихають пацієнти із захворюваннями органів дихання.** Удосконалення методів газової хроматографії для аналізу видихуваного повітря пацієнтів при діагностуванні наявності та розвитку патологій їх органів дихання є актуальним завданням. Метою роботи є аналіз апробованих та перспективних методів контролю вмісту пароподібних та (або) газоподібних біологічних маркерів у видихуваному повітрі пацієнтів, а також вибір оптимальних методик вимірювань методами газової хроматографії. Виконано: аналіз наукових досліджень та публікацій у галузі сучасних методів контролю вмісту пароподібних та(або) газоподібних біологічних маркерів у видихуваному повітрі пацієнтів; визначення технічних вимог та удосконалено структурну схему багатоканального газового хроматографа для вимірювання вмісту пароподібних та(або) газоподібних біологічних маркерів у повітрі, що видихається пацієнтами; визначення основних метрологічних характеристик результатів вимірювань концентрацій пароподібних та/або газоподібних біологічних маркерів у повітрі з використанням методів газової хроматографії. Визначено, що межі сумарної відносної похибки результатів вимірювань при довірчій ймовірності $P = 0{,}95$ залежать від діапазонів концентрацій біологічних маркерів у повітрі, що видихається пацієнтами. Отримані результати дозволяють спростити процедури визначення вмісту біологічних маркерів методами газової хроматографії в повітрі, що видихається, а також неінвазивно діагностувати наявність і розвиток патологій органів дихання пацієнтів.Удосконалено структурну схему багатоканального газового хроматографа для вимірювання вмісту пароподібних та (або) газоподібних біологічних маркерів у повітрі, що видихається.
Ключові слова: органи дихання, видихуване повітря, біологічні маркери, хроматографія

A. Zaitsev, N. Matsegora, S. Zaitsev, S. Kaminska, V. Tikhenko. **Application of gas chromatography methods for analysis of exhaled air by patients with respiratory diseases.** Improvement of gas chromatography methods for analyzing the exhaled air of patients when diagnosing the presence and development of pathologies of their respiratory organs is an urgent task. The aim of this work is to analyze proven and promising methods for monitoring the content of vaporous and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies, as well as the choice of optimal measurement techniques using gas chromatography methods. The analysis of scientific researches and publications in the field of modern methods of control of the content of vapor and (or) gaseous biological markers in the exhaled air of patients is made. The technical requirements are determined and the structural scheme of the multichannel gas chromatograph for measuring the content of vapor and (or) gaseous biological markers in the air exhaled by patients is improved. The main metrological characteristics of the results of measurements of concentrations of vapor and / or gaseous biological markers in air using gas chromatography methods are determined. The main technical requirements for a multichannel gas chromatograph for determining the content of vaporous and (or) gaseous biological markers in exhaled air have been determined. It has been determined that the boundaries of the total relative error of the measurement results at a confidence level of $P = 0.95$ depend on the ranges of the concentrations of biological markers in the exhaled air of patients. The obtained results make it possible to simplify the procedures for determining the content of biological markers by gas chromatography in the exhaled air, as well as non-invasively to diagnose the presence and development of pathologies of the patients' respiratory organs.
Keywords: respiratory organs, exhaled air, biological markers, chromatography

Introduction

The introduction of invasive diagnostic methods in clinical settings complemented by scientific searches for more accessible and informative non-invasive approaches, for example, methods for assessing the air exhaled by patients, thanks to the creation of standardized equipment for its analysis. Currently, for analyzing the air exhaled by patients, they use gas chromatography (GC) with mass spectrometry [1, 2], proton mass spectrometry (PTR-MS), proton mass spectrometry with a transit-time analyzer (PTR-TOF- MS), separated ion flux mass spectrometry (SIFT-MS) [3], ion mobility

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spectrometry [1], diode laser absorption spectroscopy [1]. The air exhaled by patients is a complex gas mixture containing, in addition to atmospheric gases, basic metabolic products (CO_2, H_2O), also gaseous molecules, some of which can be used as biological markers, such as: CO, NO, NO_2, N_2O, NH_3, H_2O_2, C_2H_4, C_2H_6, CH_2O, CH_4, CH_3OH, C_2H_5OH, CS_2, H_2S, C_5H_{12}, CH_2OHS. When studying the composition of the air exhaled by patients, the development and application of multichannel analytical measuring systems is relevant. Simultaneous analysis of the content of several gaseous or vaporous biological markers allows one to observe correlations in their release with exhaled air and to investigate the relationship between various physiological and biochemical processes in the patient's body. Diagnostics based on multicomponent gas analysis can have a high probability, versatility, and will make it possible to carry out comprehensive studies of the patient's body and expand the range of solutions to biomedical problems [1]. Thus, there is a need for continuous improvement and development of new methods for analyzing gaseous or vaporous biological markers in the air exhaled by patients, taking into account the continuous development of measuring equipment [4].

Analysis of recent research and publications

In work [2] it is noted that: bronchopulmonary diseases make the main contribution to mortality from cancer. Non-invasive diagnostics of bronchopulmonary diseases based on the analysis of the component composition of air samples exhaled by patients is promising. In comparison with the air exhaled by healthy people, in lung cancer, there is an increased content of biological markers, such as hexane, methylpentane, sterol, acetone, methyl ketones and n-propanol, derivatives of benzene, heptane, decane, cyclopentane, octane, butadiene-cyclohexane, heptanal, nonane. It is noted that these results were obtained by GC-MS. In works [5, 6] it is shown that the quantitative and qualitative composition of the air exhaled by patients includes at least 600 volatile and non-volatile compounds. They contain information about the functional state of the human body. In work [7] it is noted that at present, studies are underway to diagnose lung cancer by the air exhaled by patients using mass spectrometry using metabolites such as: isoprene; acetone; acetonitrile; 1.3-cyclohexane; 2-butanone; 2, – butadiene. Among the promising specific significant compounds for the diagnosis of asthma: NO, pentane, acetone, isoprene, benzene. In [8], a method was developed for measuring the concentrations of acetone, butanol-1, butanone-2, hexanal, pentanal, isoprene, butyric, propionic, and acetic acids in the exhaled air of a patient by the method of gas chromatography-mass spectrometry with thermal desorption (GC TD-TS) . In works [9 – 7] it is indicated that the analysis of the qualitative and quantitative composition of the air exhaled by patients by various physicochemical methods makes it possible to detect many diseases at the early stages of their development. In work [18] it is noted that lipid peroxidation (LPO) is one of the most important oxidative processes in the human body. The main initiators of free radical oxidation are reactive oxygen species (ROS), which can increase under the influence of unfavorable factors and cause oxidative stress.

As a result of oxidative stress in the body, there is an accumulation of toxic products of LPO, which cause metabolic disorders in the body, disruption of the functional state of various systems and changes in the immune status. It was shown that the scientific literature reflects data on the involvement of ROS in the pathogenesis of such pathological processes as inflammatory, hepatotoxic, postischemic and reperfusion disorders. The results of these processes affect the quantitative and qualitative composition of the exhaled air by patients. In [19] it is noted that the study of the gas composition of exhaled air was carried out using an array of metal oxide resistive semiconductor gas sensors. The sensors differed from each other in the composition of the sensitive layer and were selected so as to have preferential selectivity to certain groups of substances, namely: sensor 1 – alkanes; sensor 2 – oxidizing agents, short-chain carboxylic acids; sensor 3 – alcohols, oxidants; sensor 4 – ammonia, alcohols; sensor 5 – acetone and ketone bodies, ammonia. In work [20] the characteristics of a new class of signaling molecules – gas transmitters are given: NO, H_2S, CO.

The mechanisms of formation of these molecules, their functions in the body, molecular mechanisms of signal transmission with the participation of gases are briefly described. The data obtained in this work can be used in the development of new pathogenetically substantiated approaches to the therapy of malignant neoplasms. At the same time, the work does not indicate methods for determining the content of gases NO, H_2S, CO in the objects under study. In [21], it was noted that NO in the respiratory tract is produced by nitrooxide synthases (NOS) of epithelial cells, endothelial cells, proinflammatory cells of the immune system (macrophages, neutrophils, mast cells, T-lymphocytes), and

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neurons. Of the many processes in the body that regulated by NO, its pro-inflammatory effect is of particular importance in the pathology of the respiratory system. The spectrum of the biological action of NO depends on the level of its concentration. At low levels of concentration, NO has a cytoprotective effect. Under conditions of high concentration, NO has a cytotoxic effect. A high concentration of NO also has an antibacterial, antiviral, antifungal effect, promotes the development of an inflammatory process, causes DNA damage, inhibits tissue respiration, enhances cell apoptosis, and modulates the functional activity of various immunocytes. At the same time, the work does not indicate methods for determining the content of NO gas in the objects under study. The works [22, 23] provide information on diseases and the corresponding biological markers in the exhaled air of patients with respiratory pathologies. This information are presented in Table 1.

Table 1

Biological markers and typical patient diseases with pathologies of the respiratory system

Biological markers and typical patient diseases
CO: oxidative stress; hemoglobinuria, upper respiratory tract infection; asthma
NO: chronic obstructive pulmonary disease; asthma, bronchiectasis; rhinitis; upper respiratory tract infection; severe sepsis
NH_3: metabolism of monoamines in the lungs; lungs' cancer; liver pathology with COVID-19 disease
$H_2O_{2(vapor)}$: weakened respiratory function of the lungs; asthma
Alkanes (C_nH_{2n+2}: CH_4, C_2H_6, C_3H_8, C_4H_{10}, C_5H_{12}, C_6H_{14}, C_7H_{16}, C_8H_{18}, C_9H_{20}, $C_{10}H_{22}$ with $n=1...10$); short chain carboxylic acids ($C_nH_{2n+1}COOH$: CH_2O_2, $C_2H_4O_2$, $C_3H_6O_2$, $C_4H_8O_2$, $C_5H_{10}O_2$, $C_6H_{12}O_2$ with $n=0…6$); monohydric alcohols ($C_nH_{2n+1}OH$: CH_3OH, C_2H_5OH, C_3H_7OH, C_4H_9OH, $C_5H_{11}OH$, $C_6H_{13}OH$, $C_7H_{15}OH$, $C_8H_{17}OH$, $C_9H_{19}OH$, $C_{10}H_{21}OH$ with $n=1...10$); monohydric alcohols $+NH_3$; $NH_3+C_3H_6O$ (acetone): chronic tonsillitis (compensated and decompensated forms)
C_2H_4: oxidative stress, lipid peroxidation; chronic asthma
C_2H_6: E-ubiquinol status in lipid peroxidation
C_2H_6 and pentanes (n–C_5H_{12}; iso–C_5H_{12}; neo–C_5H_{12}): lipid peroxidation
O_2: oxygenation index in acute respiratory failure, including infectious disease COVID-19
Bhutans (n–C_4H_{10}; iso–C_4H_{10}) and pentanes (n–C_5H_{12}; iso–C_5H_{12}; neo–C_5H_{12}): lipid peroxidation
H_2: digestive or gastrointestinal tract disorders; lactose deficiency in the treatment of medicines for pathologies of the respiratory system
C_3H_6O (acetone): lung cancer
C_5H_{12} and its derivatives: exacerbation of bronchial asthma
$H_2O_{(vapor)}$: deficiency in the formation of condensate from the exhaled air with pathologies of the respiratory system

A wide range of analyzed components (biological markers) in the exhaled air of patients with respiratory pathologies, and the ranges of measured values of the concentrations of these components, require the use of several gas chromatographs and measurement techniques with the necessary indicators of the accuracy of the measurement results. This complicates the measurement procedures, requires special training of personnel and increases the cost of the measurement results. Thus, it is necessary to perform a set of studies to simplify the procedures for determining the content of biological markers by gas chromatography (GCh) methods in the exhaled air of patients with respiratory pathologies [4].

The aim of this work is to analyze the proven and promising methods of gas chromatographic control of the content of vaporous and gaseous biological markers in the exhaled air of patients with respiratory pathologies, as well as to select the optimal measurement techniques using gas chromatography methods.

This goal was achieved by solving the following tasks:

– analysis of scientific research and publications in the field of modern methods for monitoring the content of vaporous and (or) gaseous biological markers in the exhaled air for diagnosing respiratory pathologies of patients;

– determination of technical requirements for a multichannel gas chromatograph for measuring the content of vaporous and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies;

– improvement of the structural diagram of a multichannel gas chromatograph for determining the content of vaporous and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies;

– determination of the main metrological characteristics of the results of measurements of the concentrations of vaporous and (or) gaseous biological markers in the air using gas chromatography methods.

Presentation of the main material

The analysis of well-known proven methods for monitoring the content of gaseous and (or) vaporous biological markers in the exhaled air of patients with diseases of internal organs, including pathologies of the respiratory system, was used. To calculate the thresholds for C_{no} determination of the concentrations of biological markers H_2, CH_4, C_2H_6, C_2H_4, C_2H_2, CO, CO_2, O_2, N_2, C_3H_6, C_3H_8, butane, pentane, hexane, heptane, octane isomers in air, as well as for gas chromatograph calibration, used gas mixtures of these substances with a concentration of each substance from 0.05 to 0.5% by volume (% vol.) in argon or nitrogen. To calculate the thresholds for determining the concentrations of H_2O and H_2O_2 vapors and calibrate the gas chromatograph, mixtures of vapors of these substances were used at their concentrations from 0.17 g/m^3 to 17 g/m^3 in argon (Ar) or nitrogen (N_2).

To calculate the thresholds for determining the concentration of vapors of biological markers of ethanol, acetaldehyde, ethyl acetate, methyl acetate, methanol, 2-propanol, 1-propanol, 2-methyl-1-propanol, 1-butanol, 3-methyl-1-butanol, acetone, benzene, toluene, chlorobenzene, ethylbenzene, styrene, aniline, nitrobenzene, phenol, xylene isomers, as well as for the calibration of the gas chromatograph, vapor-gas mixtures of these biological markers were used, obtained by bubbling. Ar or N_2 gas flows through liquid biological markers at temperatures from 20 to 30 °C with dilution of streams of gas mixtures with pure gases Ar or N_2.

The vapor concentrations of these biological markers in gas flows were 0.01 mg/m^3 and higher. The measurements were performed using gas chromatographs with thermal conductivity detector (TCD) and flame ionization detectors (FID). When determining the content of H_2O_2 vapors in air, the well-known chemical reaction of catalytic thermal decomposition of H_2O_2 at temperatures t = 300-350 °C in an inert gas flow was used:

$$2H_2O_{2(vapor)} = 2H_2O_{(vapor)} + O_2. \qquad (1)$$

The concentration of H_2O_2 vapor in the air sample is calculated from the concentration of the O_2 formed as a result of chemical reaction (1) using the gas chromatography method and the TCD detector in the gas chromatograph. The structural diagrams of multichannel gas chromatographs presented in [24, 25] were subject to improvement. Ar, N_2, helium (He) were used as carrier gases of the gas chromatograph.

Results

Figure 1 shows an improved structural diagram of a 7-channel gas chromatograph for determining the content of vapor and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies.

Table 2 shows the main technical requirements for a multichannel gas chromatograph for determining the content of vapor and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies.

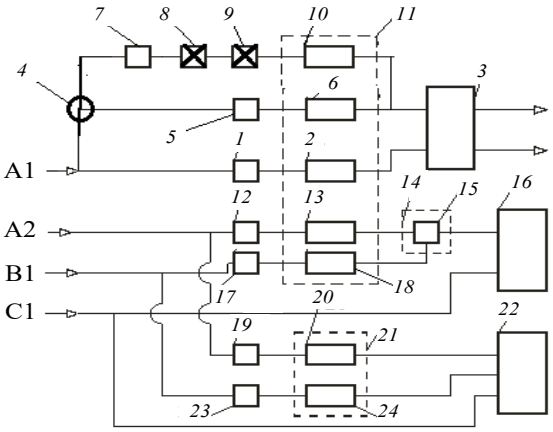

Fig. 1. Improved structural diagram of a 7-channel gas chromatograph for determining the content of vapor and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies: *1* – heated gas metering valve; *2*, *6*, *10*, *13*, *18*, *20*, *24* – chromatographic columns; *3* – TCD; *4* – gas valve-switch; *5*, *7*, *12*, *17* – gas metering valves; *8* – thermal desorber; *9* – catalytic reactor; *11*, *14*, *21* – thermostats; *15* – methanator; *16*, *22* – FID; *19*, *23* – evaporators; A1 – carrier gas No. 1; A2 – carrier gas No. 2; B1 – hydrogen; C1 – air

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Table 2

Basic technical requirements for a gas chromatograph*

Characteristics
1. Measuring channel № 1 to determine the contents H_2, O_2, N_2. Elements: gas valve switch position 4, t_s = 20...30 °C; gas metering valve position 5, t_d = 20...30 °C; GCh column position 6 – sorbent in GCh column "CaA", t_{ci} = 40 °C; TCD detector (working chamber) position 3, carrier gas line A1, t_{TCD} = 200 °C
2. Measuring channel № 2 for vapor content determination H_2O_2. Elements: gas switch valve position 4, t_s = 20...30 °C; gas metering valve position 7, t_d = 50 °C; thermodesorber position 8, adsorbent-absorber in a thermal desorber "Al_2O_3", t_{ci} =40 °C, υ_t=15 °C/c from t_{ci} to t_{cf} = 350 °C; catalytic reactor position 9, catalyst "powder Cu", t_{kr} = 350 °C; GCh column position 10 – sorbent in GCh column "CaA", t_{ci} = 60 °C; TCD detector (working chamber) position 3, carrier gas line A1, t_{TCD} = 200 °C
3. Measuring channel № 3 for vapor content determination H_2O. Elements: gas metering valve position 1, t_d = 120 °C; GCh column position 2 – sorbent in GCh column "Polysorb-1", t_{ci} = 120 °C; TCD detector (comparison camera) position 3, carrier gas line A1, t_{TCD}=150 °C
4. Measuring channel № 4 to determine the contents CO, CH_4, CO_2, C_2H_4, C_2H_6, C_2H_2. Elements: gas metering valve position 12, t_d = 20...30 °C; GCh column position 13 – sorbent in GCh column «Porapak N 80/100», t_{ci} = 40 °C, υ_k = 12 °C/min from t_{ci} = 40 °C to t_{cf} = 180 °C; methanator position 15, t_m = 325 °C; FID detector position 16, carrier gas line A2, t_{FID} = 200 °C
5. Measuring channel № 5 to determine the contents CH_4, C_2H_6, C_3H_8, isomers of butane, pentane, hexane, heptane, octane. Elements: gas metering valve position 17, t_d = 20...30 °C; GCh column position 18 – sorbent in GCh column "Porapak R", t_{ci} = 40 °C, υ_k = 15 °C/min from t_{ci} = 40 °C to t_{cf} = 200 °C; FID detector position 16, hydrogen line B1, t_{FID} = 300 °C
6. Measuring channel No. 6 for determining the content of vapors of ethanol, acetaldehyde, ethyl acetate, methyl acetate, methanol, 2-propanol, 1-propanol, 2-methyl-1-propanol, 1-butanol, 3-methyl-1-butanol. Elements: gas metering valve position 19, t_d = 40...50 °C; GCh column position 20 – length 50 m, inner diameter 0.32 mm, thickness of the sorbent layer 0.52 μm, sorbent in GCh column "HP-FFAP", t_{ci} = 75 °C, υ_k =15°C/min from t_{ci} = 75 °C to t_{cf} = 180 °C; FID detector position 22, carrier gas line A2, t_{FID} = 250 °C
7. Measuring channel No. 7 for determining the content of vapors of methanol, acetone, benzene, toluene, chlorobenzene, ethylbenzene, xylenes, styrene, aniline, nitrobenzene, phenol. Elements: gas metering valve position 23, t_d = 40...50 °C; GCh column position 24 – quartz glass, length 25 m, inner diameter 0.3 mm, sorbent layer thickness 5 μm sorbent in GCh column "SE-54"; t_{ci} = 50 °C, υ_k = 10 °C/min from t_{ci} = 50 °C to t_{cf} = 250 °C, FID detector position 22, hydrogen line B1, t_{FID} = 250 °C

Table 3 shows the experimentally obtained values of the thresholds for determining the concentrations C_{tc} of biological markers in air samples when performing measurements by gas chromatography methods. Each value of the concentration of a biological marker was obtained as result of five (n = 5) parallel measurements with a confidence level of P = 0.95 with a coefficient of normalized deviations t = 2.78 depending on the number of degrees of freedom $f = n-1$ at n = 5.

* Notes: 1. tci – the initial temperature of the GCh column; tTCD is the TCD temperature; tFID – FID temperature; tm is the temperature of the methanator; td is the temperature of the gas metering valve with calibrated metering loops; tcf is the final temperature of the GCh column; ts is the temperature of the gas switch valve; tt is the temperature of the thermal desorber; tkr is the temperature of the catalytic reactor; υk is the speed of programming the temperature GCh of the column; υt is the speed of programming the temperature of the thermal desorber 2. In measuring channels No. 5, No. 6 and No. 7, other GCh columns can be installed to determine the corresponding biological markers in the air.

Table 3

Thresholds for the determination of biological markers in the air

№	Component	C_{tc}	№	Component	C_{tc}
1	H_2	$2\cdot10^{-4}$ % vol.	8	Ethanol, acetaldehyde, ethyl acetate, methyl acetate, methanol, 2-propanol, 1-propanol, 2-methy l-1-propanol, 1-butanol, 3-methy l-1-butanol, acetone, benzene, toluene, chlorobenzene, styrene, ethylbenzene, aniline, phenol, nitrobenzene, xylene isomers	0.01 mg/m^3
2	CH_4, C_2H_6, C_2H_4, C_3H_8	$1\cdot10^{-4}$ % vol.			
3	C_2H_2	$5\cdot10^{-5}$ % vol.			
4	CO, CO_2	$5\cdot10^{-4}$ % vol.			
5	O_2, N_2	$7\cdot10^{-4}$ % vol.			
6	$H_2O_{(vapor)}$	0.2 g/m^3 ($2.5\cdot10^{-2}$ % vol.)			
7	$H_2O_{2(vapor)}$	10 mg/m^3 ($7\cdot10^{-4}$ % vol.)	9	Isomers of butane, pentane, hexane, heptane, octane	$5\cdot10^{-4}$ % vol.

Table 4 shows the values of the limits of the permissible relative error δ_i (% relative) for determining the concentrations of gaseous and (or) vaporous biological markers in the air, depending on the values of their concentrations C_i (% by volume).

Table 4

Values of the limits of the permissible relative error δ_i for determining the concentrations of gaseous and (or) vaporous biological markers in the air, depending on the values of their concentrations C_i

Concentration range of biological markers in air, C_i,% by volume				δ_i, %
H_2; O_2; N_2; $H_2O_{(vapor)}$; $H_2O_{2(vapor)}$ in the form of O_2	CH; C_2H_4; C_2H_6; C_3H_6; C_3H_8; Isomers of butane, pentane, hexane, heptane, octane	C_2H_2	CO; CO_2	
$< 5\cdot10^{-3}$	$< 10^{-3}$	$< 5\cdot10^{-4}$	$< 5\cdot10^{-3}$	≥ 50
$(5...25)\cdot10^{-3}$	$(1...3)\cdot10^{-3}$	$(5...15)\cdot10^{-4}$	$(5...25)\cdot10^{-3}$	< 50
$(25...50)\cdot10^{-3}$	$(3...50)\cdot10^{-3}$	$(1.5...25)\cdot10^{-3}$	$(25...100)\cdot10^{-3}$	≤ 20
$> 5\cdot10^{-2}$	$> 5\cdot10^{-2}$	$> 5\cdot10^{-2}$	> 0.1	≤ 10

Table 5 shows the values of the standard deviation (RSD, % relative) of the output signal for the TCD and FID of a gas chromatograph (height, area, retention time of the gas chromatographic peak of the corresponding biological marker) depending on the concentration range of C_i, vol %, in air.

Table 5

Gas Chromatograph TCD and FID Output RMS Values

C_i, % volumetric	< 0.002	0.002...0.01	0.01...0.1	0.1...1	1...10
RSD, % relative	> 10	10	2	2	1

The limits of the total relative error of the measurement results of the concentrations of vaporous biological markers in the exhaled air do not exceed 25 % relative at a confidence level of $P = 0.95$. The limits of the total relative error of the results of measuring the concentrations of gaseous biological markers in the exhaled air does not exceed 50% relative at a confidence level of $P = 0.95$.

The boundaries of the total relative error of the results of measuring the concentrations of gaseous and (or) vaporous biological markers in the exhaled air depend on the ranges of concentrations of these biological markers.

The basic principles of operation of the improved gas chromatograph are similar to those given in [24, 25].

Conclusions

To achieve this goal, the following tasks were solved in the work:

1. The analysis of scientific research and publications in the field of modern methods for monitoring the content of vaporous and (or) gaseous biological markers in the exhaled air for diagnosing

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respiratory pathologies in patients has been carried out. It has been established that a wide range of analyzed biological markers in the exhaled air of patients with respiratory pathologies, and ranges of measured values, require the use of several gas chromatographs and measurement techniques with the required accuracy of measurement results. This complicates the measurement procedures, requires special training of personnel and increases the cost of the results.

2. The technical requirements for a 7-channel gas chromatograph for measuring the content of vaporous and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies have been determined. In this case, measurements are allowed to be performed both in isothermal modes of using chromatographic columns, and in modes of their temperature programming.

3. The structural diagram of a 7-channel gas chromatograph has been improved for determining the content of vaporous and (or) gaseous biological markers in the exhaled air of patients with respiratory pathologies. Measurements can be performed using one TCD gas chromatography detector and two FID gas chromatography detectors.

4. he main metrological characteristics of the results of measuring the concentrations of vaporous and (or) gaseous biological markers in air using gas chromatography methods have been determined. It was determined that the boundaries of the total relative error of the results of measuring the concentrations of biological markers in the exhaled air: do not exceed 25 % relative at a confidence level of $P = 0.95$ when determining vaporous biological markers; do not exceed 50 % relative at a confidence level of $P = 0.95$ when determining gaseous biological markers; depend on the concentration ranges of biological markers in the exhaled air.

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