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**Application of the method of absorption diode laser spectroscopy for measuring the content of  $^{13}\text{C}$  and  $^{12}\text{C}$  in exhaled air**

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The paper reports on experimental studies of the absorption of  $^{13}\text{C}^{16}\text{O}_2$  in a mixture with  $^{12}\text{C}^{16}\text{O}_2$  in exhaled air by laser absorption spectroscopy using a diode laser tunable in the frequency range 4860–4880  $\text{cm}^{-1}$ . The results of the studies showed that the minimum detectable concentration of  $^{13}\text{C}^{16}\text{O}_2$  is at a level of less than 20 ppm, and this approach is promising for measuring the content of  $^{13}\text{C}^{16}\text{O}_2$  in exhaled air for non-invasive online diagnosis of oncological diseases of the gastrointestinal tract at early stages.

**Keywords:** diode laser spectroscopy, carbon dioxide, breath tests, oncological diseases of the gastrointestinal tract.

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## Introduction

As has been repeatedly noted earlier [1,2], the problem of early diagnosis of oncological diseases, particularly severe diseases of the gastro-intestinal tract (GIT), is highly relevant. According to the data from the International Agency on Research for Cancer, approximately 900 000 new cases of gastro-intestinal cancer occur in the world every year, and about 650 000 deaths caused by this disease are recorded. Gastro-intestinal oncological diseases are the most common form of malignant tumors in many countries of Asia, Eastern Europe, South America, the Russian Federation and the Baltic states [3].

It is known that the harbinger of the development of gastro-intestinal cancer is the appearance of the H. Pylori urease [4–6] infection in the human body, as a result of which the availability of methods for diagnosing this infection is important for detecting gastro-intestinal cancer in the early stages and preventing its further development in the body.

The main currently existing methods of diagnosing H. Pylori urease include such as morphological, bacteriological, histological and biochemical [7,8]. However, these methods require endoscopic examinations and biopsy samples, i.e. they are invasive and difficult to implement for frequent reuse. Moreover, these methods are characterized by frequent cases of false negative diagnoses due to the local limitations of the biopsy area. For the prevention and early detection of gastro-intestinal oncological diseases, simpler and more convenient non-invasive methods are needed that allow measurements to be carried out online and can be used repeatedly.

More recently, methods called breathing tests have been actively developing in the world. They are based on the measurement of the carbon-13 content in the exhaled air, which is formed in the form of a molecule  $^{13}\text{C}^{16}\text{O}_2$  as a result of cleavage of labeled urea in the stomach during its reactions with H. Pylori [9]. For the successful application of breath tests, it is necessary that they meet the following requirements: firstly, the measurement error  $^{13}\text{C}^{16}\text{O}_2$  mixed with  $^{12}\text{C}^{16}\text{O}_2$ , the content of which in the exhaled air can be more than 2 orders of magnitude compared to  $^{13}\text{C}^{16}\text{O}_2$ , should not exceed 1% [10], secondly (taking into account the fact that the total proportion of carbon dioxide in the exhaled air is approximately 2–4%), the value of the minimum detectable concentration  $^{13}\text{C}^{16}\text{O}_2$  (sensitivity) should be at the level of tens of ppm. In other words, it is necessary to measure concentrations  $^{13}\text{C}^{16}\text{O}_2$  at the level  $< 10^{15} \text{ cm}^{-3}$  with the error maximum 1%. Meeting these requirements allows you to minimize the number of false positive and false negative diagnostic results.

There are a large number of measurement methods  $^{13}\text{C}^{16}\text{O}_2$  in exhaled air [11]. Among them, one of the most promising, allowing to achieve high sensitivity and accuracy in real time, is a method based on the method of absorption laser spectroscopy, in which frequency tunable diode lasers [12–20] are used as sources, which emit in the near and middle infrared spectral ranges, where  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  there are intense absorption bands. This method has obtained the generally accepted name TDLAS (tunable diode laser spectroscopy).

The analysis of spectral ranges that we conducted earlier in [11] is the most preferred for detection  $^{13}\text{C}^{16}\text{O}_2$  in the exhaled air, showed that such there are ranges near the wavelengths 4.3, 2.0 and 1.6  $\mu\text{m}$ .

The absorption coefficients of CO<sub>2</sub> reach the highest values near the wavelength of 4.3 μm. Therefore, this region of the spectrum is the most promising for obtaining the best detection sensitivity <sup>13</sup>C<sup>16</sup>O<sub>2</sub> and the accuracy of measuring its concentration in a mixture with <sup>12</sup>C<sup>16</sup>O<sub>2</sub>. However, in this region of the spectrum, it is necessary to cool the photodetector detectors to cryogenic temperatures and, in more-over, to use rather expensive quantum cascade lasers [9,15].

Near the wavelength of 1.6 μm absorption <sup>12</sup>C<sup>16</sup>O<sub>2</sub> and <sup>13</sup>C<sup>16</sup>O<sub>2</sub> drops by about 5 orders of magnitude, and this inevitably leads to a significant decrease in sensitivity and detection accuracy <sup>13</sup>C<sup>16</sup>O<sub>2</sub>. However, the use of fiber optics is possible in this spectral region, which attracts the authors of a number of publications [18].

From our point of view, taking measurements near the wavelength of 2 μm is the most promising. This is due to the fact that the values of the absorption coefficients CO<sub>2</sub> in this region are about 3 orders of magnitude greater compared to the region near 1.6 μm, and, in addition, relatively inexpensive tunable diode lasers can be used in this spectral region, and also photodetectors operating at room temperature.

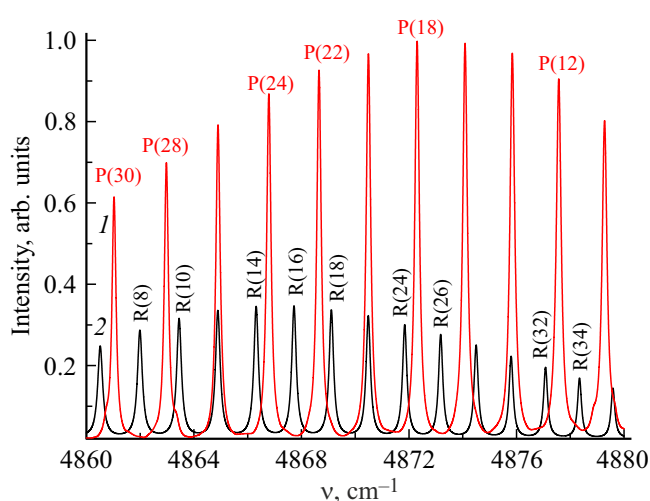
In this paper, experimental studies of absorption spectra are reported <sup>12</sup>C<sup>16</sup>O<sub>2</sub> and <sup>13</sup>C<sup>16</sup>O<sub>2</sub> near wavelength 2 μm. The obtained results allowed us to propose a method for detecting these molecules that are mixed with each other in exhaled air.

## Justification of the choice of the spectral range proposed for measurements

At the first stage, we selected the range of the spectrum that is optimal for measuring the content <sup>12</sup>C<sup>16</sup>O<sub>2</sub> and <sup>13</sup>C<sup>16</sup>O<sub>2</sub> in exhaled air. For this purpose, computational modeling of the absorption spectra of these molecules near the wavelength 2 μm (5000 cm<sup>-1</sup>) was carried out using the HITRAN [21] spectroscopic database.

Calculations have shown that such a range is the area 4860–4880 cm<sup>-1</sup>, in which there are a number of rotational absorption lines <sup>12</sup>C<sup>16</sup>O<sub>2</sub> (R-branch) and <sup>13</sup> *text*C<sup>16</sup>O<sub>2</sub> (P-branch) belonging to the vibrational bands 20013-00001 and 20012-00001 of these molecules, respectively (Fig. 1, where a value proportional to the coefficients of carbon dioxide absorption at atmospheric pressure is deposited along the vertical axis:  $k_{\text{abs}}(\nu) = \sigma(\nu)n$ , where  $\sigma(\nu)$  — the cross section of carbon dioxide absorption at the frequency  $\nu$ ,  $n$  — CO concentration).

It can be seen that for selective detection <sup>12</sup>C<sup>16</sup>O<sub>2</sub> and <sup>13</sup>C<sup>16</sup>O<sub>2</sub> a number of frequency combinations can be used to make measurements that coincide with the centers of the absorption lines of these molecules that overlap to the smallest extent. Such lines can be the lines P(12), P(18), P(22), P(24), P(28) and P(30) molecules <sup>13</sup>C<sup>16</sup>O<sub>2</sub> and adjacent pairs of lines of the molecule <sup>12</sup>C<sup>16</sup>O<sub>2</sub> (indicated in Fig. 1). We have selected absorption lines P(12) (frequency



**Figure 1.** Calculated absorption spectra <sup>13</sup>C<sup>16</sup>O<sub>2</sub> (red curve) and <sup>12</sup>C<sup>16</sup>O<sub>2</sub> (black curve) in the spectral range 4860–4880 cm<sup>-1</sup> at atmospheric pressure of each of the gases.

in the center of the line  $\nu_0 = 4877.5739$  cm<sup>-1</sup>) and P(18) ( $\nu_0 = 4872.3034$  cm<sup>-1</sup>) for the research) molecules <sup>13</sup>C<sup>16</sup>O<sub>2</sub> for the following reasons. Firstly, the values of the absorption coefficients in the frequency centers of these lines are close to the maximum in the range of 4860–4880 cm<sup>-1</sup>, and secondly, the ratio of the absorption coefficients in the frequency centers of the lines P(12) and P(18) to the values of the coefficients is also close to the maximum absorption in the frequency centers of adjacent pairs of absorption lines of the molecule <sup>12</sup>C<sup>16</sup>O<sub>2</sub> — R(32) ( $\nu_0 = 4877.0305$  cm<sup>-1</sup>), R(34) ( $\nu_0 = 4878.2931$  cm<sup>-1</sup>) and R(24) ( $\nu_0 = 4871.7917$  cm<sup>-1</sup>), R(26) ( $\nu_0 = 4873.1290$  cm<sup>-1</sup>) respectively.

## Experimental equipment

For experimental studies of absorption spectra <sup>12</sup>C<sup>16</sup>O<sub>2</sub> and <sup>13</sup>C<sup>16</sup>O<sub>2</sub> a tunable diode laser based on the InGaAlAs/InP compound was used. Laser generation was carried out in single-frequency mode — one longitudinal mode with a frequency of approximately 4876 cm<sup>-1</sup> at room temperature of the diode. The laser radiation frequency was adjusted by modulating the pump current in the range of approximately 3.5–9.7 mA at different temperatures of the laser diode in the range of 20–35°C, for which a special control unit was used. The temperature change of the diode occurred in manual mode, and amplitude scanning was used to modulate the pumping current using a built-in sawtooth pulse generator, the frequency of which was approximately 10 kHz. The laser generation power was approximately 1 mW.

To calibrate the frequency of laser radiation — to obtain its dependence on the pump current and temperature of the laser diode — it is necessary first to conduct experimental studies of absorption spectra <sup>12</sup>C<sup>16</sup>O<sub>2</sub> and <sup>13</sup>C<sup>16</sup>O<sub>2</sub>, and

then compare the results with the HITRAN data. During the experimental studies, the laser radiation was modulated by the generator of the control unit and passed through a multi-pass cell, the optical length of which was 4.8 m. A vacuum gauge was used to measure the pressure in the cell (which could vary in the range from 8 mbar to 1 atm using a pre-vacuum pump). The laser radiation passed through the cell was recorded by a photodetector (hereinafter — PD) based on the PbS compound. Fourier filtering of the registered signals was used to process the experimental results obtained. The cutoff frequency was  $5 \cdot 10^{-3}$  Hz, which significantly reduced the noise component. The signals from the PD were processed using an analog-to-digital converter (ADC) built into the computer.

## Experimental Studies

At the first stage of experimental studies, the cell was filled with a gas mixture containing molecules  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  at a temperature of 296 K in the concentration ratio  $[^{13}\text{C}^{16}\text{O}_2]/[^{12}\text{C}^{16}\text{O}_2] = 7 \cdot 10^{-3}$ . This ratio is chosen because it is characteristic of the exhalation of a healthy person.

Fig. 2 shows as an example the experimental dependences of the intensity of the laser radiation transmitted through the cell on the pump current in two spectral regions. The abscissa axis is the time sweep of the signal received by the ADC. The observed dips in the recorded signals occur when the laser frequency coincides with the absorption lines  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$ . Several absorption lines were recorded in each frequency tuning range of the laser (at different diode temperatures), while 24 rotational absorption lines of both molecules were recorded in the entire temperature range of the diode 20–35°C.

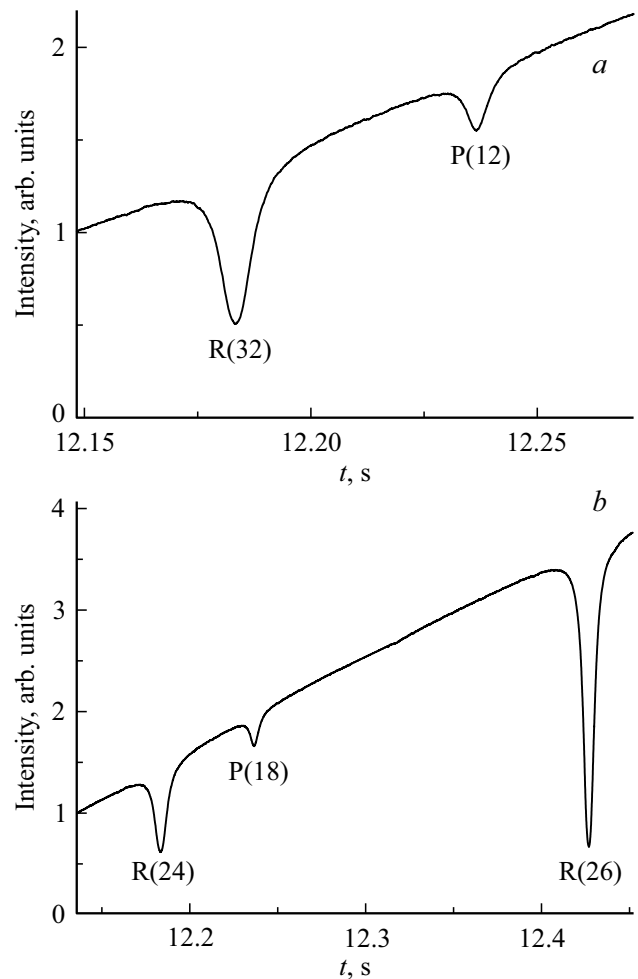
Next, the values of the absorption coefficients of  $k_{\text{abs}}$  molecules were calculated  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$ .

After passing through the cell filled with the analyzed gas mixture  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$ , the PD registers the intensity of  $I = I_0 T$ , where  $I_0$  — the registered PD intensity of the laser radiation passed through an empty cell of length  $L$ ,  $T = 1 - (I_0 - I)/I_0$  — transmission of the analyzed gas mixture. In accordance with the Booger-Lambert-Baer law

$$I_0 - I = I_0(1 - T) = I_0 \exp(-k_{\text{abs}}L),$$

$$k_{\text{abs}} = L^{-1} \ln(1 - T).$$

The values of the absorption coefficients obtained experimentally were compared with the corresponding values from the HITRAN database, which contains data on the frequencies of the centers of absorption lines  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  and the values of their absorption coefficients at different pressures. Fig. 3 shows the experimental dependences of the absorption coefficients  $^{13}\text{C}^{16}\text{O}_2$  and HITRAN data in the range 4870–4880  $\text{cm}^{-1}$ . The agreement of experimental results and calculated data is very good — for



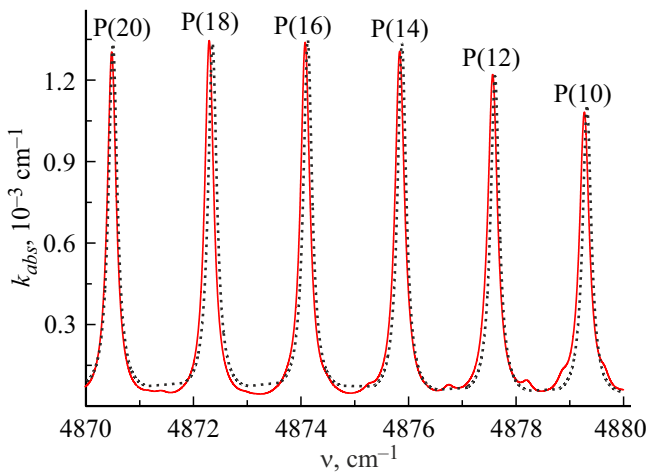
**Figure 2.** Experimental dependences of the intensity of laser radiation transmitted through a cell containing a mixture  $^{13}\text{C}^{16}\text{O}_2$  and  $^{12}\text{C}^{16}\text{O}_2$  at full pressure 210 mbar and at laser diode temperatures 20.2°C (a) and 25.8°C (b). Lines R refer to carbon-12, and lines P — to carbon-13.

all absorption lines  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  their difference did not exceed 8%.

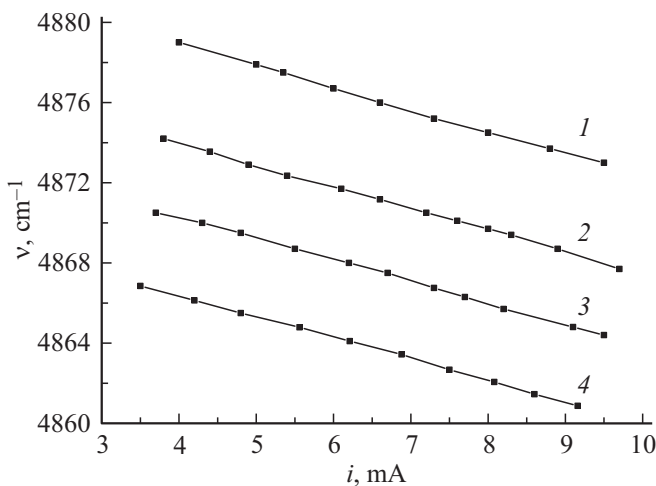
After that, the dependence of the laser radiation frequency on the pump current at different temperatures of the laser diode was graded. Fig. 4 shows several dependencies obtained as an example.

At the next stage of experimental studies, the cell was filled with exhaled air, in various samples of which the content of  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  fluctuated in the range of 1.5–3.5% with the ratio of the share  $^{12}\text{C}^{16}\text{O}_2$  to share  $^{13}\text{C}^{16}\text{O}_2$  from 70 to 140 at atmospheric pressure. The samples also contained a certain amount of water vapor, the concentration of which was still below the sensitivity threshold of the experimental scheme used and therefore did not affect the recorded signals.

Fig. 5 shows the dependences of the intensity of the laser radiation transmitted through the cell with the studied mixture for one of the exhaled air samples containing absorption



**Figure 3.** Experimental absorption spectrum  $^{13}\text{C}^{16}\text{O}_2$  (solid red curve) and HITRAN data (dots). Pressure  $^{13}\text{C}^{16}\text{O}_2$  — 0.57 mbar, total pressure in the cell 1 atm. For a better reading of the drawing, significantly more intense absorption lines  $^{12}\text{C}^{16}\text{O}_2$  on it have been removed.



**Figure 4.** Dependences of the laser generation frequency on the pump current at laser diode temperatures 20.2 (1), 25.8 (2), 29.5 (3) and 34.1°C (4).

lines P(12) and P(18) molecules  $^{13}\text{C}^{16}\text{O}_2$ . In this sample, the ratio of concentrations  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  was 135 with the total share  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  in it 2.8%. Compared with the line P(12) against the background of the absorption lines R(32) and R(34) closest to it, the line P(18) is less contrasting against the background of the absorption lines R(24) and R(26) closest to it. This is due to the fact that the values of the absorption coefficients of the lines P(12) and P(18) differ slightly (the difference between them is less than 10%), while the values of the coefficients of the lines R(24) and R(26) are noticeably greater compared to the values of the absorption coefficients of the lines R(32) and R(34).

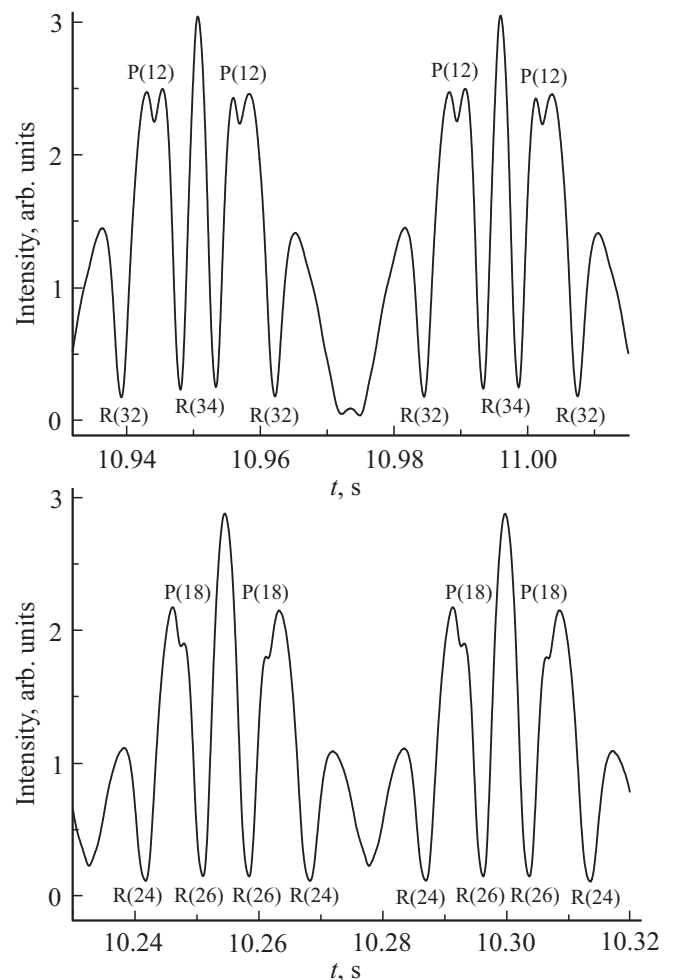
### Analysis of obtained results

The experimental results obtained made it possible to estimate the maximum detectable minimum concentration  $^{13}\text{C}^{16}\text{O}_2$  (sensitivity) and measurement accuracy mixed with  $^{12}\text{C}^{16}\text{O}_2$  in exhaled air. To do this, Alan's variation [22] was used, according to which the error  $\Delta_1$  of measuring the ratio of absorption coefficients was calculated  $^{13}\text{C}^{16}\text{O}_2$  and  $^{12}\text{C}^{16}\text{O}_2$  and the error  $\Delta_2$  of the absorption coefficient measurement  $^{13}\text{C}^{16}\text{O}_2$  in the analyzed mixture according to the formula

$$\Delta_I = \frac{1}{2(N-1)} \frac{\sqrt{\sum_{j=1}^N (x_{j+1} - x_j)^2}}{\bar{x}_N} \cdot 100,$$

where  $x_j$  — values of registered experimental signals processed using a Fourier filter,  $N$  — number of measurements,  $\bar{x}_N$  — mean value on the set  $x_j$  ( $j = 1 \dots N$ ).

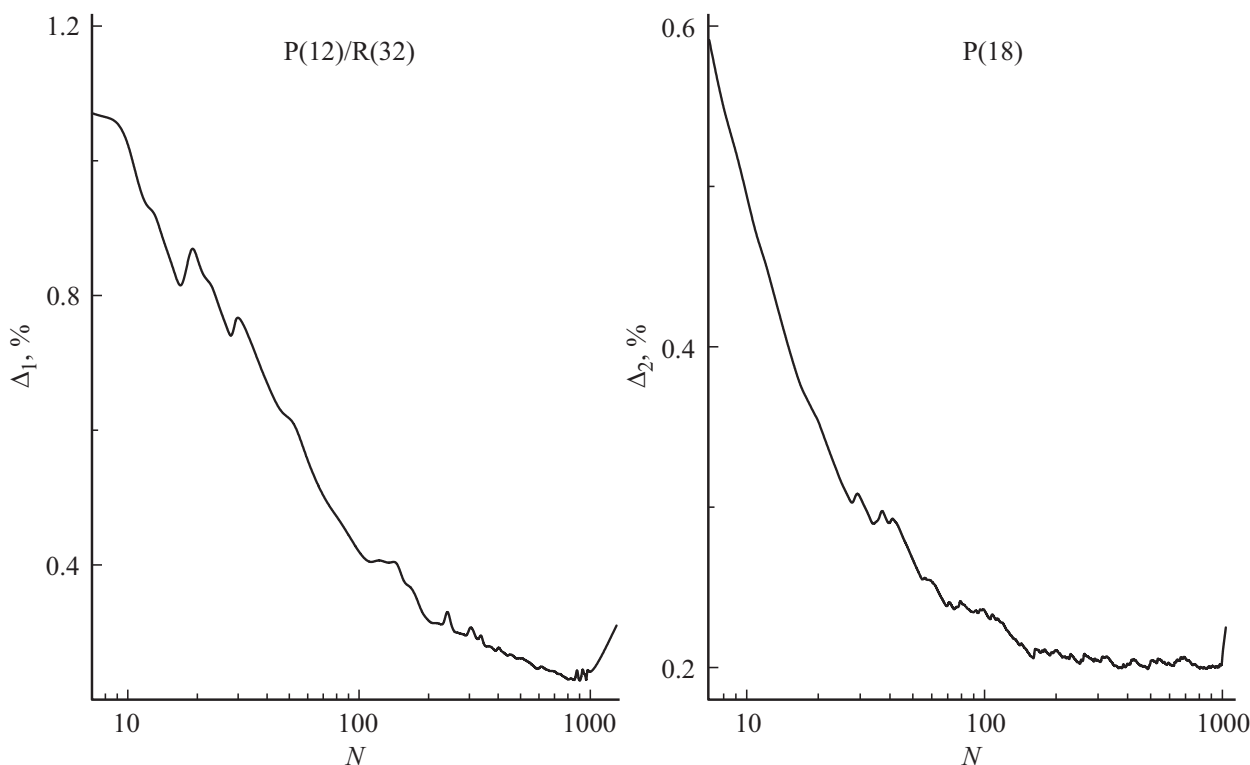
As  $x_j$ , when calculating the error of  $\Delta_1$ , the values of the ratios of the intensities recorded at frequencies correspond-



**Figure 5.** Experimental dependences of the intensity of the laser radiation transmitted through the cell with the studied mixture  $^{13}\text{C}^{16}\text{O}_2$  and  $^{12}\text{C}^{16}\text{O}_2$  containing absorption lines of P(12) and P(18) molecules  $^{13}\text{C}^{16}\text{O}_2$ .

Sensitivity and accuracy of content measurement  $^{13}\text{C}^{16}\text{O}_2$ 

Results	Pairs of lines $^{13}\text{C}^{16}\text{O}_2$ and $^{12}\text{C}^{16}\text{O}_2$ , for which are registered ratios of measured signals at their centers			
	P(12)/R(32)	P(12)/R(34)	P(18)/R(24)	P(18)/R(26)
$\Delta_1, \%$	0.17	0.2	0.22	0.2
$\Delta_2, \%$	0.23	0.23	0.3	0.27
$[\text{}^{13}\text{C}^{16}\text{O}_2]/[\text{}^{12}\text{C}^{16}\text{O}_2]_{\min}$	$1.7 \cdot 10^{-5}$	$1.7 \cdot 10^{-5}$	$2.1 \cdot 10^{-5}$	$2.0 \cdot 10^{-5}$
$[\text{}^{13}\text{C}^{16}\text{O}_2]_{\min}$	$4.6 \cdot 10^{14}$	$4.6 \cdot 10^{14}$	$5.6 \cdot 10^{14}$	$5.4 \cdot 10^{14}$



**Figure 6.** Dependences of errors  $\Delta_1$  for the ratio P(12)/R(32) and  $\Delta_2$  for the line P(18) on the number of measurements  $N$ .

ing to the centers of the absorption lines P(12) and P(18) to the intensities recorded at frequencies corresponding to the centers of the absorption lines R(32), R(34) and R(24), R(26) respectively — 4 the relations denoted further by P(12)/R(32), P(12)/R(34), P(18)/R(24), P(18)/R(26). When calculating the error  $\Delta_2$ , the values of the intensity recorded at the frequency corresponding to the center of the absorption line P(12) or P(18) were used as  $x_j$ .

The table shows the results obtained for a sample of exhaled air, the transmission spectrum of which is shown in Fig. 5. Fig. 6 shows as an example the dependencies of  $\Delta_1$  for the ratio P(12)/R(32) and  $\Delta_2$  for the line P(18) on the number of dimensions. In all cases, it turned out that the minimum error values of  $\Delta_1$  and  $\Delta_2$  are reached with the number of measurements noticeably exceeding 100 (most often closer to 1000). The results were similar for all exhaled air samples used.

Results obtained using absorption lines of the P(12) molecule  $^{13}\text{C}^{16}\text{O}_2$  and R(32), R(34) molecules  $^{12}\text{C}^{16}\text{O}_2$  for their detection turned out to be somewhat better compared to the results obtained using absorption lines of the P(18) molecule  $^{13}\text{C}^{16}\text{O}_2$  and R(24), R(26) molecules  $^{12}\text{C}^{16}\text{O}_2$ . This seems to be due to the fact that, as already noted, the line P(12) is more contrasting compared to the line P(18).

The obtained minimum error values are  $\Delta_1$  (0.17%) and  $\Delta_2$  (0.23%) for an air sample in which the fraction  $^{13}\text{C}^{16}\text{O}_2$  is 1/135 relative to the fraction  $^{12}\text{C}^{16}\text{O}_2$  at atmospheric pressure and total fraction  $^{12}\text{C}^{16}\text{O}_2$  and  $^{13}\text{C}^{16}\text{O}_2$  in the mix 2.8%, correspond to the minimum detectable concentration  $^{13}\text{C}^{16}\text{O}_2 \sim 4.6 \cdot 10^{14} \text{ cm}^{-3}$  (17 ppm) with a signal-to-noise ratio of  $= 1$  and when using a cell with an optical length of 4.8 m. Minimum detectable fraction  $^{13}\text{C}^{16}\text{O}_2$  mixed with  $^{12}\text{C}^{16}\text{O}_2$  was  $4.6 \cdot 10^{-5}$ .

## Conclusion

The results of the studies carried out in this paper indicate that the use of the method of diode laser absorption spectroscopy (TDLAS) with the use of diode lasers tunable near the wavelength of  $2\ \mu\text{m}$  is promising for measuring the content of  $^{13}\text{C}^{16}\text{O}_2$  mixed with  $^{12}\text{C}^{16}\text{O}_2$  in exhaled air for noninvasive online diagnostics of gastro-intestinal oncological diseases in the early stages. The received sensitivity and accuracy of detection  $^{13}\text{C}^{16}\text{O}_2$  meet the requirements for breath tests, the method itself seems quite simple and does not require expensive equipment, which is important for its practical application.

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## Conflict of interest

The authors declare that they have no conflict of interest.

## References

- [1] R.W. Hulst, B.W. Hoff, A. Ende, G.N.J. Tytgat. *Nederlands Tijdschrift Voor Geneeskunde*, **143** (8), 395 (1993).
- [2] V.T. Ivashkin. *Helicobacter pylori: Revolution in gastroenterology* (Triad-X, M., 1999), p. 255.
- [3] L.E. Wroblewski, R.M. Peek, K.T. Wilson. *Clin. Microbiol. Rev.*, **23**, 713 (2010). DOI: 10.1128/CMR.00011-10
- [4] A.I. Shmak, F.V. Yezikyan, M.Yu. Revtovich, E.P. Martynov, A.A. Kotov, A.V. Eroshenko. *Zdravookhranenie (Minsk)*, **6**, 36 (2018). (in Russian).
- [5] V.I. Chissoy, V.V. Starinsky, G.V. Petrova. *Malignant neoplasms in Russia in 2011 (Morbidity and mortality)* (FSBI „MNIOI named after P.A. Herzen“ Ministry of Health of Russia, Moscow, 2013), p. 28.
- [6] A.S. Loginov, Yu.V. Vasiliev, V.I. Kasyanenko, S.A. Zelenikin. *Russian Gastroenterological Journal*, **1**, 19 (1997).
- [7] T.A. Byrne, R.L. Persinger, L.S. Young. *Ann. Surg.*, **222**, 243 (1995). DOI: 10.1177/0148607196020005375
- [8] P. Greenberg, J. Koch, J. Cello. *Am. J. Gastroenterol.*, **91** (2), 228 (1996).
- [9] M. Kato, M. Saito, S. Fukuda. *J. Gastroenterol.*, **39**, 629 (2004). DOI: 10.1007/s00535-003-1357-7
- [10] E.V. Stepanov. *Trudy Instituta Obschey Fiziki RAN im. A.M. Prokhorov*, **61**, 253 (2005). (in Russian)
- [11] S.V. Kireev, A.A. Kondrashov, S.L. Shnyrev, I.G. Simanovsky. *Laser Phys.*, **27** (10), (2017). DOI: 10.1088/1555-6611/aa7549
- [12] E.S. Mironchuk, I.V. Nikolaev, V.N. Ochkin, S.S. Rodionova, M.V. Spiridonova, S.N. Tskhai. *Kvant. elektron.*, **39** (4), 388 (2009). (in Russian).
- [13] H. Shirin, G. Kenet, O. Shevah, J. Wardi, S. Birkenfeld, M. Shahmurov, R. Bruck, Y. Niv, S.F. Moss, Y. Anvi. *Aliment. Pharmacol. Ther.*, **15** (3), 389 (2001). DOI: 10.1046/j.1365-2036.2001.00926.x
- [14] R.G. Plavnik.  *$^{13}\text{C}$ -urease respiratory test for *Helicobacter Pylori* (clinical and organizational aspects)* (Medpraktika-M, M., 2017), p. 36.
- [15] M. Erdely, D. Richter, F.K. Tittel. *Appl. Phys. B*, **75**, 289 (2002). DOI: 10.1007/s00340-002-0960-2
- [16] E.I. Korotkova, T.M. Gindullina, N.M. Dubova, O.A. Voronova. *Physico-chemical methods of research and analysis* (Publishing House of Tomsk Polytechnic University, Tomsk, 2011), p. 177.
- [17] D.D. Nelson, J.B. McManus, S.C. Herndon, M.S. Zahniser, B. Tuzson, L. Emmenegger. *Appl. Phys. B*, **90**, 301 (2008). DOI: 10.1007/s00340-007-2894-1
- [18] D.E. Cooper, R.U. Martinelli, C.B. Carlisle, H. Riris, D.B. Bour, R.J. Menna. *Appl. Optics*, **32** (33), 6727 (1993). DOI: 10.1364/AO.32.006727
- [19] E.V. Stepanov. *Diode laser spectroscopy and analysis of biomarker molecules* (Fizmatlit, M., 2009), p. 291.
- [20] S.V. Kireev, A.A. Kondrashov, M.A. Rybakov, S.L. Shnyrev, A.I. Sultangulova. *Laser Phys. Lett.*, **19** (2), 025701 (2022). DOI: 10.1088/1612-202X/ac4590
- [21] L.S. Rothman, I.E. Gordon, Y. Babikov, A. Barbe, D. Chris-Benner, P.F. Bernath, M. Birk, L. Bizzocchi, V. Boudon, L.R. Brown, A. Campargue, K. Chance, E.A. Cohen, L.H. Coudert, V.M. Devi, B.J. Drouin, A. Fayt, J.-M. Flaud, R.R. Gamache, J.J. Harrison, J.-M. Hartmann, C. Hill, J.T. Hodges, D. Jacquemart, A. Jolly, J. Lamouroux, R.J. LeRoy, G. Li, D.A. Long, O.M. Lyulin, C.J. Mackie, S.T. Massie, S. Mikhailenko, H.S.P. Müller, O.V. Naumenko, A.V. Nikitin, J. Orphal, V. Perevalov, A. Perrin, E.R. Polovtseva, C. Richard, M.A.H. Smith, E. Starikova, K. Sung, S. Tashkun, J. Tennyson, G.C. Toon, V.I.G. Tyuterev, G. Wagner. *J. Quant. Spectrosc. Radiat. Transfer*, **130**, 4-50 (2013).
- [22] N.V. Smirnov, I.V. Dunin-Barkovsky. *Course of probability theory and Mathematical statistics for technical applications* (Nauka, M., 1969), p. 511.