Received: 6 April 2023 | Revised: 15 May 2023 | Accepted: 24 May 2023

DOI: 10.1002/jbio.202300120

RESEARCH ARTICLE

JOURNAL OF BIOPHOTONICS

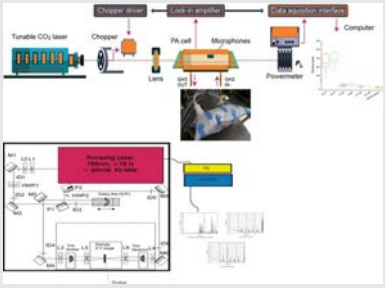
NIR and THz spectroscopy: An experimental investigation toward nicotine-related devices

Ana-Maria Bratu | **Mihaela Bojan** | **Stefan Banita** | **Mioara Petrus** | **Cristina Popa**

National Institute for Laser, Plasma and Radiation Physics, Bucharest, PO, Romania

Correspondence
Cristina Popa and Mioara Petrus, National Institute for Laser, Plasma and Radiation Physics, 409 Atomistilor St., PO Box MG-36, 077125 Bucharest, Romania.
Email: cristina.achim@inflpr.ro; mioara.petrus@inflpr.ro

Abstract



This study examined the content of nicotine-delivery products using terahertz time-domain spectroscopy (THz-TDS) and breath ethylene investigated with CO_2 laser photoacoustic spectroscopy (CO_2 LPAS) system as a biomarker of oxidative stress after smoking. The THz-TDS method provided valuable information on the transmission spectra of tobacco and nicotine in smoking products. From the CO_2 LPAS data it was observed that in cigarette (TC) smoking the mean breath ethylene was 687 parts per billion (ppb), while in electronic cigarettes and tobacco heating devices smoking the mean ethylene was 56 ppb and 48 ppb, respectively. The main finding was that TC showed higher transmission in the THz region producing a higher oxidative stress on the body.

KEYWORDS

ethylene, human health, laser photoacoustic spectroscopy, nicotine-related devices, THz spectroscopy

1 | INTRODUCTION

When you light a cigarette, the tobacco burns and creates smoke. There are approximately 600 ingredients in cigarettes (TCs), some of which are toxic substances present in the tobacco plant itself, and others are additives that enhance the effects of nicotine and make smoking more attractive to consumers [1]. The majority of smokers are addicted to nicotine, responsible for the harmful effects of using tobacco product known to cause physical and psychological addiction [2]. Burning process that releases the tobacco flavors and nicotine produces more than 8000 chemicals in cigarette smoke and about 100 substances are known to cause diseases such as lung cancer, cardiovascular disease, and emphysema [3, 4]. In an effort of quitting smoking cigarettes, electronic cigarette (ECs; vapes) tobacco heating device (THDs) are marketed as alternatives for smokers who do not want or cannot stop smoking.

An immediate reaction of the body after smoking is the increase of oxidative stress determined by the generation of reactive oxygen species. Membrane lipids are highly susceptible to free radical damage and is generated the process of lipid peroxidation [5]. Some of the end-products of lipid peroxidation like ethane, ethylene, and pentane can be used for estimation of cellular damage because after their formation in tissues these species are generated in the breath [6]. One of the first by-products of lipid peroxidation studied as a breath biomarker was ethylene. Studies on animals and humans demonstrated

the generation of ethylene as an end-product lipid peroxidation process induced by ultraviolet radiation, x rays or as a result of inflammatory diseases [7–11]. Ethylene was one of the first breath compounds studied, being reported to range between 3 and 100 parts per billion (ppb) [10, 12, 13]. Preliminary work showed that smoking cigarettes may induce ethylene formation in large quantities of hundreds of ppb in human body [14].

Therefore, the risk assessment strategy of smoking TCs, ECs, and THDs can be determined by evaluating the specific biomarker ethylene that gives us information on the absorption and cellular damage of toxic substances in smokers. Although there are many methods used for breath analysis, most of them do not have high sensitivity or are not considered practical due to the need for sample preparation and the use of a trained operator [15–18]. Laser photoacoustic spectroscopy (LPAS) method has been successfully applied to the detection of breath ethylene due to its advantages such as high sensitivity and selectivity, no need for sample preparation, operational simplicity, good time response, and large dynamic range to measure concentrations below the level of ppb [19, 20]. Because there is limited information available regarding the relationship between the effects of smoking on the body and the manufacturing ingredients, spectral data of smoking products content can be obtained using terahertz time-domain spectroscopy (THz-TDS). The THz spectral domain (0.1–10 THz) offers information about vibrational spectra of the molecules. Having the properties of seeing behind the dielectric substances but being nonionizing, the THz systems became a standard for detection of dangerous and hazardous substances [21, 22]. Considering these properties, THz-TDS method can give us valuable information about the transmission spectra of tobacco and nicotine from smoking products.

Therefore, we propose an approach in which the ingredients of smoking products are analyzed with the THz-TDS method and the results are related to the body's response to the consumption of these products by indicating the level of ethylene in the breath with the help of LPAS. Our study results in useful information that can help raise awareness of the constituents in smoking products and a better understanding of the potential health impact of smoking.

2 | MATERIALS AND METHODS

2.1 | THz-TDS materials and method

Three types of nicotine delivery devices were used in 4-min smoking sessions with 15 puffs from each device: tobacco from a traditional cigarette with the specification tar 10 mg, nicotine 0.8 mg, carbon monoxide 10 mg; e-liquid with specifications of 20 mg nicotine in 10 mL propylene glycol 50% and vegetable glycerine 50% providing 0.06 mg nicotine/puff (that means 0.9 mg in 15 puffs), and tobacco heating devices providing 0.5 mg nicotine.

These nicotine delivery devices were analyzed using this THz-TDS, to detect the signature of nicotine and tobacco. The samples were classic tobacco, without menthol, sticks of THD, and e-liquid. We have measured the transmission for each one, having as reference the holder (for the solid tobacco) and respectively the absorbent paper for the liquid substances (glycerin and nicotine have been measured in a liquid form). The transmission spectrum for each substance is obtained by diving the spectrum of the sample to the spectrum of the reference (Figure 1).

The experimental setup was built using a THz-TDS kit from Ekspla. The system uses a Toptica Photonics FFS Erbium-YAG laser in ultrashort pulses, emitting at 780 nm, with pulse duration <70 fs and power >60 mW, having a 30-mW input pulse on the 10 μW transmitting antenna [22]. The laser beam is split using a splitter cube and a P1 polarizer into two beams with adjustable powers of approximately 60/40%. The transmit beam is directed to the transmit antenna via an optical delay line. The second 40% beam is directed directly to the detector. The signal obtained on the detector is synchronized and detected by a lock-in amplifier. The THz spectroscopy set-up is software controlled under LabView™ in order to speed up and simplify data collection.

The measurement procedure for this system requires a preliminary measurement; first one of reference and then of the sample. The LabView program generates an image of this measurement, but at the same time it is possible to save an ASCII data set of the numerical results. In this set, we directly have transmission data correlated with frequency. The transmission data of the samples are obtained by dividing the measured spectra by the reference spectrum. To increase the efficiency, two Teflon lenses (L5 and L6) are fixed in front of the detector and the receiver. The role of the lenses is to focus the THz beam on the photoconductive antennas. The route that the laser beam takes to finally obtain electromagnetic radiation in the THz range is presented in Figure 2.

2.2 | CO_2 LPAS materials and method

The breath collection bags from QuinTron are used to collect up to approximately 0.75-L in a single alveolar breath sample from individuals. GaSampler Test Kits contain all the necessary components to easily collect breath samples: a disposable mouthpiece, a

FIGURE 1 Content of different nicotine delivery devices: (A) tobacco from traditional cigarette, (B) e-liquid containing nicotine, (C) tobacco from heating devices.

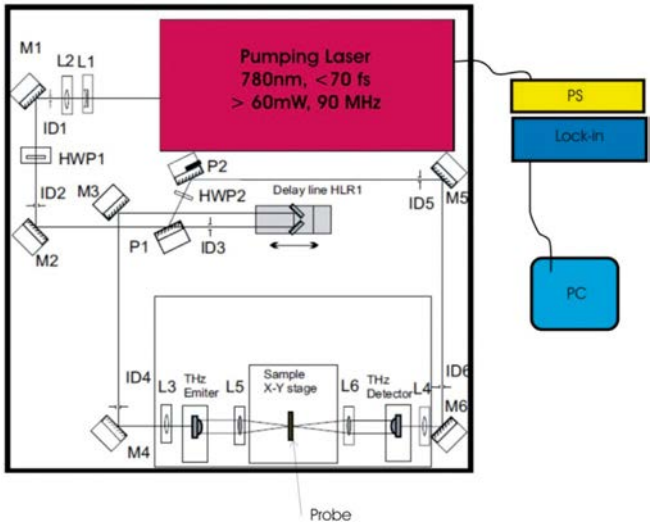


FIGURE 2 Scheme of the experimental terahertz time-domain spectroscopy (THz-TDS) system.

tee-mouthpiece assembly (it includes a plastic mouthpiece and a tee connector), and a discard bag designed to remove the first approximate 400 mL of air (named "dead space" air).

Breath of participants was analyzed before and after the use of nicotine-delivery devices by CO_2 LPAS. This method is well known in the field of trace gas detection. The LPAS system involves a line-tunable CO_2 laser, a resonant photoacoustic (PA) cell where the gas concentration is detected and analyzed and a gas flow-through system. Line-tunable CO_2 lasers provide required selectivity for analyzing multicomponent mixtures for molecules that own characteristic absorption pattern in the 9.2–10.8 μm region [19, 20]. The frequency stabilized CO_2 laser emits continuous-wave radiation on 54 different vibrational-rotational lines with power between 0.5 and 6.5 W determined by the selected line. The PA cell chosen for the measurements is a longitudinal H-type cell, designed for extracavity operation, which presents a stable operation at a relatively low frequency, with a low sensitivity to environmental changes, negligible noises and a sufficiently large PA amplitude. The CO_2 laser beam is intensity-modulated by a mechanical chopper functioning at the resonant frequency of the PA cell, then is focused by a ZnSe lens, and directed to the PA cell. The PA cell is dispensed with four miniature microphones having a sensitivity of 20 mV/Pa each that are used as sensors of the acoustic waves initiated by the heat deposition of the absorbing molecules. The electrical output from microphones is totalized and the signal is lead into a lock-in amplifier that displays the amplitude and the phase of the PA signal. The laser beam power is measured by a powermeter located after the PA cell, and its digital output together with the output from the lock-in amplifier are introduced in a data acquisition interface module. All experimental data are processed and stored by a computer (see Figure 3).

The calibration of the system was performed by filling the PA cell with 1ppmV ethylene in nitrogen at a total pressure of 1 atm, and tuning the CO_2 laser on 10P (14) line where ethylene exhibits the maximum coefficient absorption of 30.4 cm^{-1} atm^{-1}. For this PA cell the experimentally determined resonance frequency is 564 Hz yielding a quality factor of 16.1 and a cell constant of 5.41×10^3 Pa cm/W. The cell constant is multiplied by the responsivity of the microphone and another parameter, that characterize the PA cell, named responsivity can be measured $R = 433$ cmV/W at 1 atm. The PA signal in our instrument is linearly dependent on the absorption coefficient (α), cell

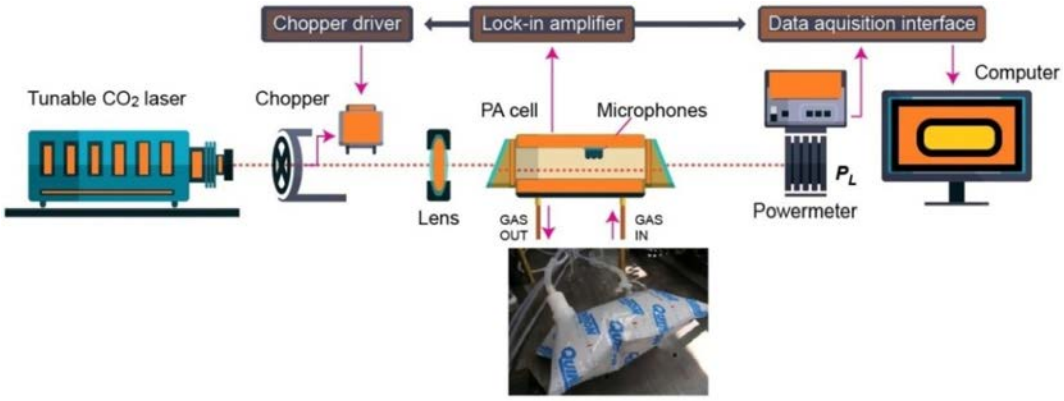


FIGURE 3 Scheme of the experimental laser photoacoustic spectroscopy (LPAS) system for breath ethylene detection.

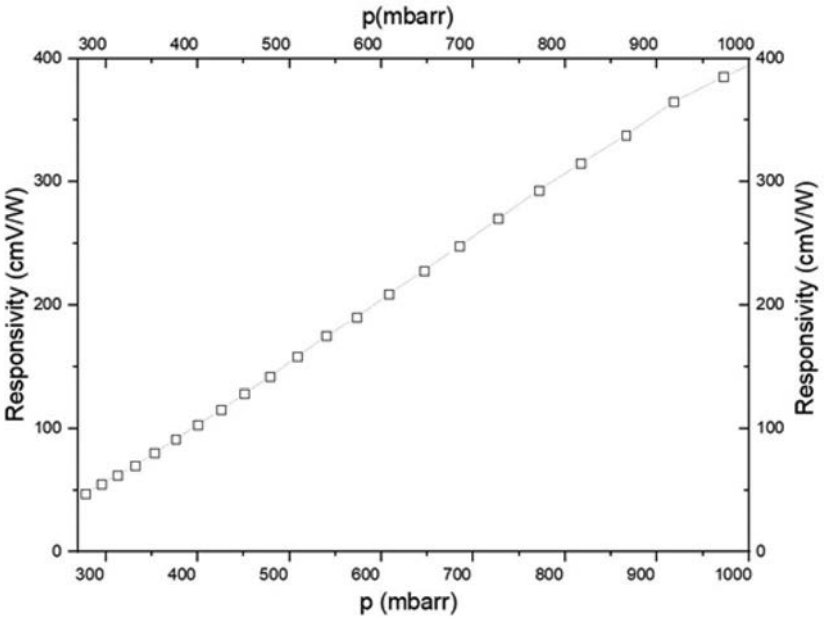


FIGURE 4 The responsivity of the photoacoustic (PA) cell against the pressure.

constant (C), microphone responsivity (S_M), incident laser power (P_L), and absorbent trace gas concentration (c). When cell constant is multiplied by the responsivity of the microphones PA signal is obtained after formula $V = \alpha RP_Lc$. From this formula the gas concentration can be deduced as $V/\alpha RP_L$ ratio. Responsivity R is influenced by the pressure of the gas inside the PA; therefore, it is important to establish the dependence of R on the gas pressure, presented in Figure 4.

Participants were asked to fill the special sample bags after smoking TC, EC, and THD. The breath sample were collected in the aluminum coated-bags and connected to the system. A preliminary cleaning of the system performed by alternating nitrogen flushing and vacuum procedures until the background signal in nitrogen is around 20 μV. The expired air is transferred at a controlled flow rate of 600 sccm (standard cubic centimeters per minute) and is passed through a potassium hydroxide scrubber to retain the interfering gases. Carbon dioxide and water vapor are gases found in large amounts in the breath, which absorb CO_2 laser radiation and can impede detection of ethylene in the ppbV range. By using the potassium hydroxide scrubber these interfering gases can be reduced in young, healthy, and nonsmoking person by a factor equal to 90, from 3.9% to 0.043% [23]. After passing through the potassium hydroxide scrubber the expired air is introduced in the PA cell where the ethylene molecules absorb the laser radiation and their concentration is determined in real time.

The pressure of the gas in the cell was measured, applying then the correction factor for the responsivity according to the calibration curve.

The detection limit is defined at signal-to-noise ratio of unity (SNR = 1) where the limiting sensitivity of the system is 2.5×10^{-9} cm^{-1} at 4 W laser power. With the minimum detectable absorptivity of 1.8×10^{-8} cm^{-1}, CO_2 LPAS system is design to provide interference-free

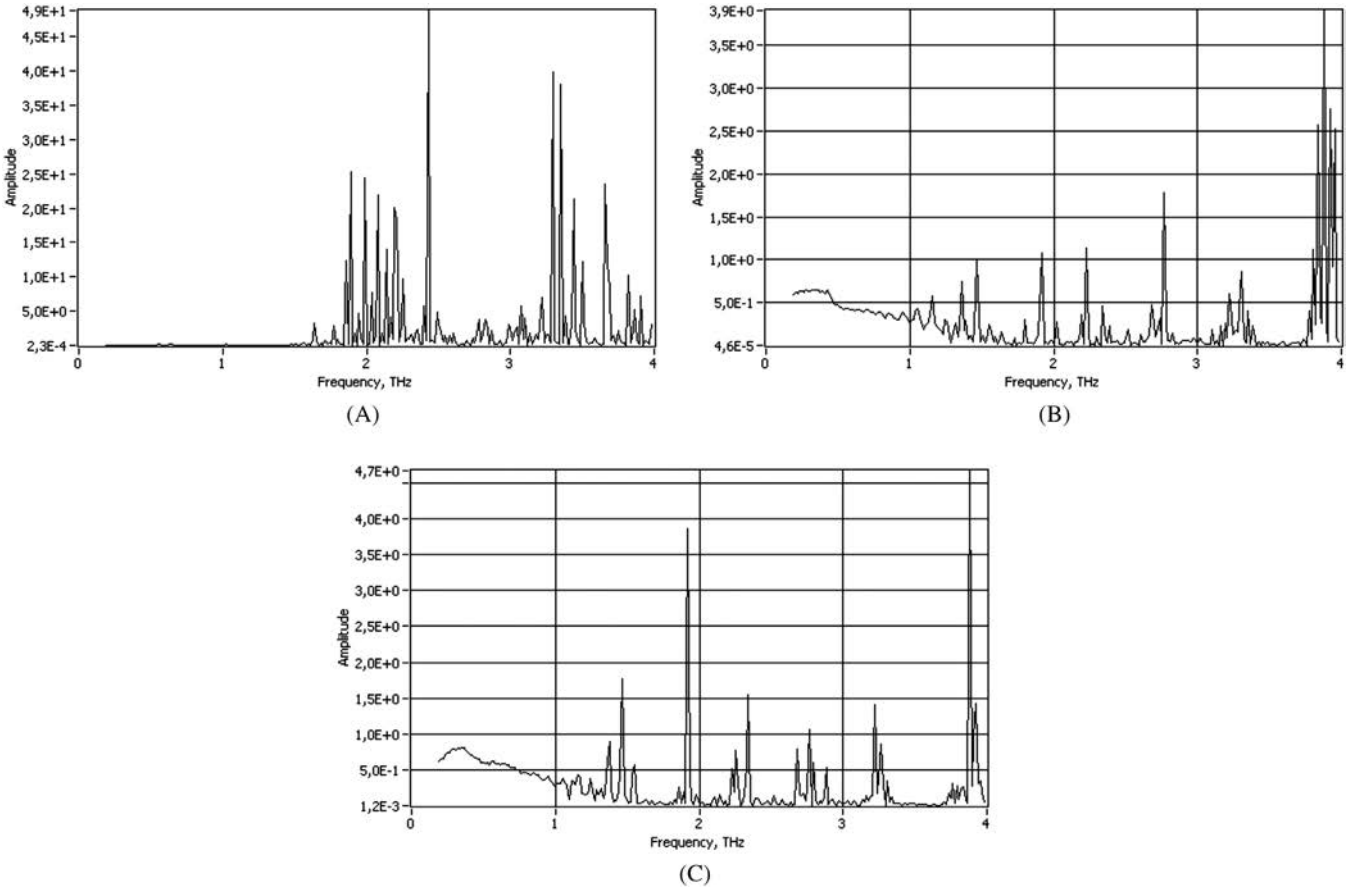


FIGURE 5 Transmission spectra for: (A) absorbant paper, (B) e-liquid base, and (C) nicotine shot in e-liquid base.

minimum detectable and minimum detectable concentration between 0.6 ppbV and 270 ppbV for gases with absorption coefficients of 30–0.1 cm^{-1} atm^{-1}.

3 | RESULTS

3.1 | Nondestructive detection of elements from different nicotine-delivery devices using THZ-TDS

THz-TDS spectroscopy uses short THz broadband pulses that are generated using a laser in ultra-short pulses. A single laser radiation pulse is required to illuminate the photoconductive surface of the emitting antenna so that it generates the entire spectrum of terahertz frequencies from 0.1 THz to 5 THz.

3.1.1 | Liquid substances (glycerin and nicotine)

Figure 5 shows the transmission spectra of absorbent paper, e-liquid base without nicotine and nicotine. E-liquid base without nicotine has a good transmission at 2.7 THz and at 3.9 THz from the range of 0.1 to 4 THz. The absorbent paper transmission spectra are shown in Figure 5(B) observing peaks at 2.5 and 3.5 THz. The transmission of nicotine has a maximum at 1.9 THz and in the same graph we can identify also one of the signatures of glycerin at 3.9 THz (Figure 5 (C)).

Using THz-TDS spectroscopy, we have found a good transmission for nicotine in a 1–3 THz regime, at 1.9 THz, terahertz technology being a promising application for the detection of elements from different nicotine-delivery devices.

3.1.2 | Solid substances (classical cigarettes and HEETS)

In Figure 6, we have the transmission data of the samples correlated with frequency and obtained by dividing the measured spectra by the reference spectrum. Practically, Figure 6 shows the transmission spectra of a holder that is used as reference for the solid samples–Figure 6(A), transmission spectra of a cigarette–Figure 6(B) and transmission spectra of a stick-Figure 6(C). So, having the

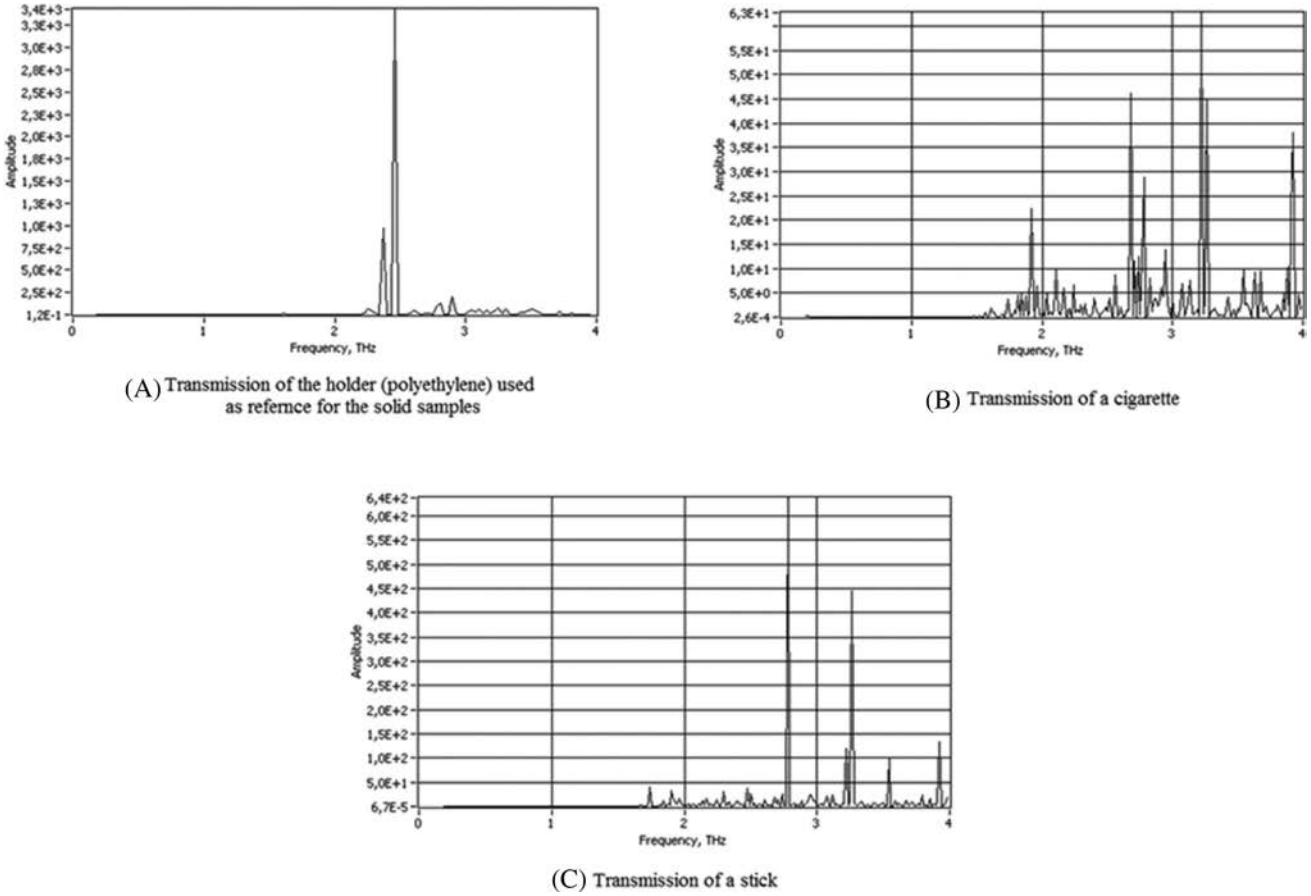


FIGURE 6 Transmission spectra for: (A) holder, (B) cigarette (TC), and (C) tobacco heating device (THD) stick.

transmission spectrum of the holder as a reference, we can identify from the transmission spectra of TC and THD stick the transmission of tobacco, which shows a maximum at 2.8 THz. The direction that the laser beam takes to finally attain electromagnetic radiation in the THz range was showed in Figure 6.

3.2 | Noninvasive breath analysis of ethylene

A total of seven regular smoking volunteer participants were involved in this study. The participants were male with ages between 35 and 42 years old and they have no medical problems and have not tried to quit smoking. Detailed breath collection instructions were provided to the participants with the requirement not to smoke 12 h before tests. The subjects were asked to smoke TC, EC, and THD with the specification to use only one product in a day. Each product administration consisted of a first session of 4 min smoking, which was followed by an identical second session after a 60 min pause. The data analysis was conducted for three consecutive days at the same intervals of time every day (between 9:00 and 11:00), and the breath samples were collected immediately after the final puff of each cigarette. At the beginning of the study, the volunteers were provided with inform consent on the procedures involved in collecting the breath samples, as well as information on the design, purpose of the study and the importance of the results. Information about the subjects and exhaled breath procedure is presented in Table 1.

The exhaled breath collection was realized in two sessions. The first session starts at 9:00 with a break of about 50 min and then starts the second session. The baseline mean value of breath ethylene for participants was 26.74 ± 6.23 ppb (the breath sample was collected in the morning before the exposure to cigarettes). According to our previous studies [24] a nonsmoker healthy subject has an exhaled breath ethylene level of 6 ppb.

In the case of TC inhalation, the mean ethylene level increased from 645 ppb after Session 1 to 687 ppb after Session 2. After EC inhalation the mean ethylene level was about 47 ppb in Session 1, and increased slightly in Session 2 till 56 ppb. Using THD the mean ethylene level was about

TABLE 1 The data obtained from multiple measurements of exhaled breath samples using the CO_2 LPAS system.

	Day 1: Breath ethylene concentration after smoking TC (ppb)		Day 2: Breath ethylene concentration after smoking EC (ppb)		Day 3: Breath ethylene concentration after THD (ppb)	
Participants ages	**S1**	**S2**	**S1**	**S2**	**S1**	**S2**
42	658	693	45	57	34	36
35	483	549	32	40	26	30
38	598	665	39	46	28	32
42	764	776	67	73	47	48
38	645	684	40	49	39	41
40	623	676	44	60	36	37
36	746	768	63	68	42	45

46 ppb in Session 1 and very small differences were observed in Session 2 where mean ethylene level was about 48 ppb. Data were reported as mean ± SD for seven analyses as follows, in session 1 (S1) for TC–645.29 ± 94.31 ppb, EC–47.14 ± 12.15 ppb, and for THD–36.43 ± 7.93 ppb, and in session 2 (S2) for TC 687.28 ± 75.47 ppb, EC–56.14 ± 11.33 ppb, and for THD 39.29 ± 6.36 ppb.

Figure 7 illustrates the box chart for ethylene concentration before smoking, and after smoking in session 1 and in session 2. The box is determined by the 25th and 75th percentiles, including the minimum, mean and maximum value for breath ethylene concentration.

As shown in Figure 7, there is a difference between the concentration of ethylene issued by subjects of TC smokers compared to EC and THD smokers.

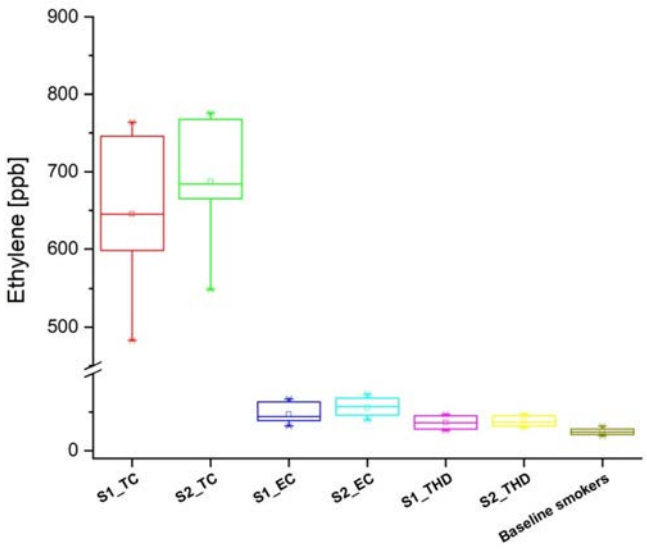


FIGURE 7 Graphical representation for ethylene concentration after smoking TC, EC, and THD in 2 sessions.

3.2.1 | Statistical analysis

The data reported was obtained from multiple measurements of exhaled breath samples. The experimental results obtained using the CO_2 LPAS system by measuring ethylene concentrations from the exhaled breath of smokers before and after smoking TC, EC, and THD were analyzed by multivariate methods using JMP from SAS.

In the upper part of Figure 8 is presented the parametric correlation between ethylene concentration in subjects before and after smoking in the two sessions. The variables with blue color are highly correlated while the variable with red color is uncorrelated with the others.

In the second part of Figure 8 is presented the scatter plot matrix which shows that the variables diagonally oriented are correlated. This means that the results obtained from participants after smoking in the two sessions are positively correlated with each other. Also, the values before smoking are randomly distributed, which means that this variable is not correlated with the other variables, that is, not those obtained after smoking in the two sessions.

This section may be divided by subheadings. It should provide a concise and precise description of the experimental results, their interpretation, as well as the experimental conclusions that can be drawn.

4 | DISCUSSION

In this study, a very sensitive gas detection tool was used to examine the effects of different smoking devices on the human body. We measured breath ethylene, an important biomarker of inflammatory response. Active

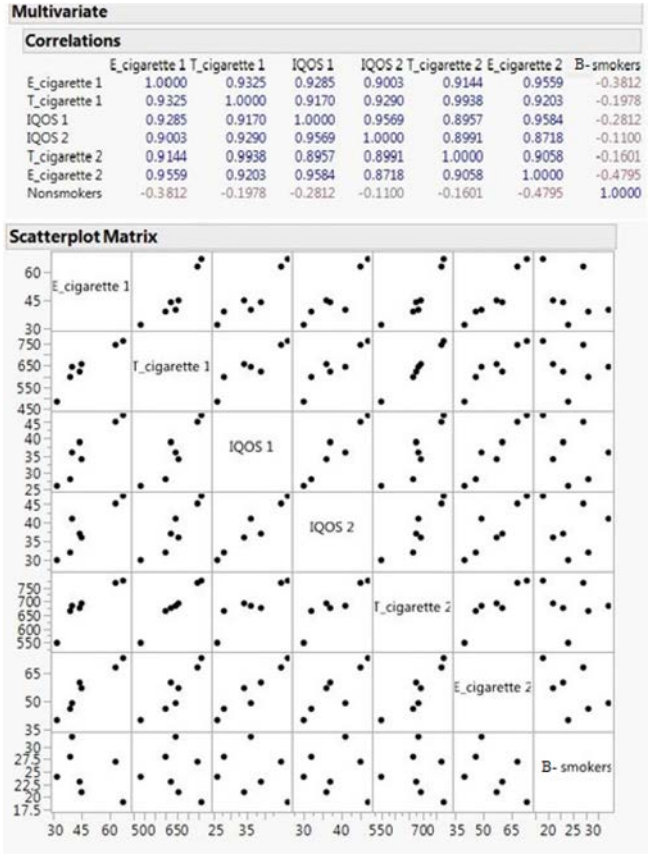


FIGURE 8 Correlation report of the exhaled breath concentration when using TC, EC, and THD.

smoking produces oxidative damages in the body and ethylene is released in that specific moment of biological stress.

As the main component present in tobacco and most smoking products, nicotine is responsible for their addictive nature. Limited and contradictory studies were reported regarding the effects of nicotine on oxidative stress. Qiao et al. [25] pointed out that nicotine administration can generate reactive oxygen species in the peripheral and central nervous systems causing oxidative stress. Barr et al. [26] demonstrated that nicotine induces oxidative stress leading to activation of the stress-dependent NF-κB pathway in mesencephalic cells. On the other hand, Newman et al. [27] discuss the antioxidant properties of nicotine by activating nicotinic receptors or by binding to iron. Recent studies have shown that nicotine may be a potential protective agent for neurological diseases [28, 29]. According to Guan et al. [29, 30] reasonable low concentration of nicotine may act as an antioxidant and contribute significantly as a neuroprotective agent, while a high dose of nicotine may generate oxidative stress inducing neurotoxicity.

Increased oxidative stress and smoking-related diseases have been attributed to the complex mixture of chemicals in tobacco smoke [30, 31]. It was demonstrated that smoking TCs is addictive and poses a high risk to the cardiovascular and pulmonary systems leading to several cancers [32]. The ECs are presented as an alternative to conventional cigarettes and experienced a rapid expansion around the world. Studies on ECs concluded that vaping presents substantially less health risk than smoking [33, 34]. Even still, current studies demonstrated that chemicals delivered during EC use, notably nicotine, oxidants, and particulates, may present damage to the cardiovascular system [35–37]. THD products are considered the closer experience to smoking cigarettes compared to other alternatives. THDs are considered safer because the toxic constituents in smoke have been found in smaller amounts than those in combustible materials. The current impact of THD on human health is not yet fully known. Research in this direction has shared on the one hand the view that aerosols released by THDs are less toxic [38–40] and on the other hand others have confirmed that emit substantially high levels of carbonyls [41]. Moreover, exposure to THD can cause inflammation and immunomodulation in the airways [42, 43].

Our results show that THD and EC emissions exhibit lower toxicity compared with TC. By comparing ethylene concentrations, we try to highlight the relationship between the body's exposure to three different tobacco products and expired ethylene in response to oxidative stress. It can be noticed that EC and THD have the potential to increase the oxidative stress of users of these devices in a manner very similar to cigarette smoke but at a lower level. Even if there is a difference between the concentrations of ethylene emitted by TC smokers and those who use EC and THD, statistical analysis shows that there is a positive correlation of data obtained using the three types of cigarettes and a negative correlation when not smoking.

Based on literature data [44–47] and correlated with our dates, THDs and ECs contain reduced harmful chemicals. The data presented have shown the relative effects of short-time exposure to three different tobacco products and that further research is needed to determine long-time exposure effects on health.

Smoking devices comprise a complex mixture of chemicals and natural ingredients, including several volatile and semivolatile organic substances in trace amounts. Since smoking is harmful and has adverse health effects it is important to investigate the presence of constituents of such samples. THz-TDS was used as a non-invasive method to investigate the chemicals before a smoking product is used. Liu et al. [48] using THz-TDS have detected the signal for both capsule and no capsule filter cigarette at 35 ps, since they wanted to demonstrate that from the transmission

time domain waveform, the THz signal of the capsule is much weaker than the tobacco filter without capsule. It shows high THz response contrast between with and without filter capsule filer. Also, regarding nicotine detection, Jibon et al. [49] have concluded that in the range from 1 THz to 2 THz and the optimum level for detecting nicotine is pointed at 1.5 THz, although they proposed a Photonic Crystal Fiber method for sensing nicotine of cigarette smoke in THz operating region. With our method, we have found a good transmission for nicotine in a similar regime (1–3 THz), at 1.9 THz, using this spectroscopic technique.

Content of TC, THD stick, and e-Liquid was studied using this THz-TDS. The transmission spectrum for each substance was realized considering the reference the holder for the solid samples and absorbent paper for the liquids. The tobacco signature was identified for both TC and THD stick at 2.8 THz.

For nicotine the transmission line was identified at 1.9 THz. In the case of EC we used glycerin and nicotine in a liquid state, which means a mixture of ethylene glycol and other types of polymers that are almost transparent to THz radiation, so the transmission in those cases is much higher than in solid state substances, where is significantly attenuated. That is why the transmission of nicotine has a higher maximum in liquid form than in solid ones.

Moreover, following Figures 5 and 6 it can be seen that TC have higher transmission in the THz region for more additional harmful constituents compared with e-Liquid and THD sticks. In THD sticks, the tobacco line is more visible than other additives (or at least do not have a relevant signature in the THz region). This finding can be linked to the results from breath analysis and we can say that in the case of TC we found the higher transmission of harmful constituents and the higher concentration of breath ethylene.

5 | CONCLUSIONS

This study had two aims: the first to study the content of TC, EC, and THDs smoking devices and second to determine the effect of smoking these devices on the body by evaluating the concentration of breath ethylene, to observe the link between dangerous constituents and the production of ethylene in the body as a result of oxidative stress. The content of elements in nicotine-related devices is observed in the THz region and the breath ethylene was evaluated using CO_2 laser PA spectroscopy.

The results indicate that the harmful constituents in nicotine-delivery devices showed higher transmission in the THz region for TC, and ethylene breath level after smoking THD and EC was lower than when smoking TC. Following these results, a connection can be made between the content of cigarettes and their effect on the body, demonstrating that the more toxic constituents the products contain, the greater the oxidative stress produced on the body.

TCs remain, according to this study the most dangerous ones.

Elucidating the relationship between content of smoking devices and the effects of smoking on the body is important from a health perspective for understanding the health risk attributed and informing public and responsive public policies. As a future goal, we are willing to investigate the potential long-term effects of the use of various nicotine-related devices.

AUTHOR CONTRIBUTIONS

Equal contribution and first authorship: the main authors Ana-Maria Bratu (first author) and Mioara Petrus, Cristina Popa (the last two authors) contributed equally to this work and share first authorship. Mihaela Bojan contributed with terahertz spectroscopy methodology and analysis. Stefan Banita contributed with resources and prepared figures. All authors reviewed the manuscript. All authors have read and agreed to the published version of the manuscript.

FUNDING INFORMATION

This research was funded by Romanian Ministry of Research, Innovation and Digitalization under Romanian National Nucleu Program LAPLAS VII––contract no. 30 N/2023, and project number PN-III-P1-1.1-TE-2021-0717 (Human respiration in wavelengths).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available upon reasonable request from the authors.

INFORMED CONSENT STATEMENT

The participants read and signed the informed consent and agreed to participate in this study which ensures the confidentiality of the participants.

ORCID

Ana-Maria Bratu https://orcid.org/0000-0002-4407-0292
Mihaela Bojan https://orcid.org/0000-0003-0511-6152
Stefan Banita https://orcid.org/0000-0001-9675-2132
Mioara Petrus https://orcid.org/0000-0001-5880-2477
Cristina Popa https://orcid.org/0000-0003-3881-6956

REFERENCES

[1] J. A. Miller, *Drug Metab. Dispos.* **1994**, *26*, 1.
[2] V. Margaritis, E. Mamai-Homata, *Oral Health Prev Dent* **2010**, *8*, 33.
[3] International Agency for Research on Cancer, *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Vol. 83, IARC, Lyon, France **2004**, p. 53.
[4] S. S. Hecht, *Act. Nicotine Tob Res.* **2012**, *14*, 18.
[5] H. Yin, L. Xu, N. A. Porter, *Chem. Rev.* **2011**, *111*, 5944.
[6] T. P. Devasagayam, J. C. Tilak, K. K. Boloor, K. S. Sane, S. S. Ghaskadbi, R. D. Lele, *J Assoc Physicians India.* **2004** Oct, *52*, 794 PMID: 15909857.
[7] M. Lieberman, P. Hochstein, *Science* **1966**, *152*, 213.
[8] E. E. Dumelin, A. L. Tappel, *Lipids* **1997**, *12*, 894.
[9] F. J. M. Harren, R. Berkelmans, K. Kuiper, S. t. L. Hekkert, P. Scheepers, R. Dekhuijzen, P. Hollander, D. H. Parker, *Appl. Phys. Lett.* **1999**, *74*, 1761.
[10] S. M. Cristescu, R. Kiss, S. Hekkert, et al., *Am. J. Physiol. Lung Cell Mol. Physiol.* **2014**, *307*, 509.
[11] G. Giubileo, L. De Dominicis, C. C. Lombardi, C. Mancini, A. Antonini, D. C. Dumitras, *Proc. SPIE* **2003**, *5147*, 219.
[12] E. Simonavicius, A. McNeill, L. Shahab, L. S. Brose, *Tob. Control* **2018**, *28*, 1.
[13] D. C. Dumitras, D. C. Dutu, C. Matei, A. M. Magureanu, M. Petrus, C. Popa, M. Patachia, *Rom. Rep. Phys.* **2008**, *60*, 593.
[14] C. Popa, S. Banita, M. Patachia, C. Matei, A. M. Bratu, M. Patachia, M. Petrus, D. C. Dumitras, *Rom. Rep. Phys.* **2015**, *67*, 946.
[15] N. Fens, M. P. van der Schee, P. Brinkman, P. J. Sterk, *Clin. Exp. Allergy* **2013**, *43*, 705.
[16] N. Labows et al., *J. Clin. Microbiol.* **1980**, *12*, 521.
[17] C. Lourenço, C. Turner, *Metabolites* **2014**, *4*, 465 2218-1989.
[18] V. Saasa, M. Thomas, B. Mervyn, M. Matlou, L. Chaun-Pu, M. Bonex, *Diagnostics* **2018**, *8*, 1.
[19] D. C. Dumitras, D. C. Dutu, C. Matei, A. M. Magureanu, M. Petrus, C. Popa, *J. Opt. Adv.Mat.* **2007**, *9*, 3655.
[20] D. C. Dumitras, S. Banita, A. M. Bratu, R. Cernat, D. C. A. Dutu, C. Matei, M. Patachia, M. Petrus, C. Popa, *Infrared Phys. Tehnol.* **2010**, *53*, 308.
[21] F. Xiaojian, L. Yujie, C. Qi, F. Yuan, C. T. Jun, *Front. Phys.* **2022**, *10*, 1. https://doi.org/10.3389/fphy.2022.869537
[22] M. Bojan, V. Damian, C. Fleaca, T. Vasile, Terahertz spectroscopic investigations of hazardous substances, Proc. SPIE 10010, *Adv Topics Optoelectron Microelectron Nanotechnol VIII* **2016**, *10010*, 1001010. https://doi.org/10.1117/12.2243285
[23] A. M. Bratu, C. Popa, C. Matei, S. Banita, D. C. A. Dutu, D. C. Dumitras, *J. Optoelectron. Adv. Mater.* **2011**, *13*, 1045.
[24] C. Popa, *J. Biomed. Opt.* **2015**, *20*, 051003.
[25] D. Qiao, F. Seidler, T. Slotkin, *Toxicol. Appl. Pharmacol.* **2005**, *206*, 17.
[26] J. Barr, C. S. Sharma, S. Sarkar, K. Wise, L. Dong, A. Periyakaruppan, G. T. Ramesh, *Mol. Cell. Biochem.* **2007**, *297*, 93.
[27] M. Quik, X. A. Perez, T. Bordia, *Mov Disord.* **2012** Jul, *27*, 947 Epub 2012 Jun 12. PMID: 22693036; PMCID: PMC3685410.
[28] B. Getachew, A. B. Csoka, M. Aschner, Y. Tizabi, *Neurochem. Int.* **2019**, *124*, 19.
[29] B.-L. Gao, A. F. T. Adam, Jr., *Med. Chem. Lett.* **2014**, *24*, 1472.
[30] Z. Z. Guan, W. F. Yu, A. Nordberg, *Neurochem. Int.* **2003** Aug, *43*, 243 PMID: 12689604.
[31] A. W. Caliri, S. Tommasi, A. Besaratinia, *Mutat. Res., Rev. Mutat. Res.* **2021**, *787*, 108365.
[32] U.S. Department of Health and Human Services, *National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health*, Centers for Disease Control and Prevention, Atlanta, GA, USA **2014**, p. 1.
[33] K. E. Farsalinos, R. Polosa, *Ther Adv Drug Saf.* **2014**, *5*, 67.
[34] M. A. Nides, S. J. Leischow, M. Bhatter, M. Simmons, *Am J Health Behav.* **2014**, *38*, 265.
[35] R. Putzhammer, C. Doppler, T. Jakschitz, K. Heinz, J. Förste, K. Danzl, B. Messner, D. Bernhard, *PLoS One* **2016**, *11*, e0157337.
[36] R. Carnevale, S. Sciarretta, F. Violi, C. Nocella, L. Loffredo, L. Perri, M. Peruzzi, A. G. M. Marullo, E. de Falco, I. Chimenti, V. Valenti, G. Biondi-Zoccai, G. Frati, *Chest.* **2016**, *150*, 606.
[37] P. Nabavizadeh, J. Liu, C. M. Havel, S. Ibrahim, R. Derakhshandeh, P. Jacob Iii, M. L. Springer, *Tob Control.* **2018**, *27*, s13.
[38] J.-P. Schaller, D. Keller, L. Poget, et al., *Regul. Toxicol. Pharmacol.* **2016**, *81*, 27.
[39] M. P. Ibañez, D. Martin, A. G. Gonzálvez, H. H. Telle, Á. G. Ureña, *Am. J. Anal. Chem.* **2019**, *10*, 76.
[40] K. E. Farsalinos, N. Yannovits, T. Sarri, V. Voudris, K. Poulas, S. J. Leischow, *Addiction* **2018**, *113*, 2099.
[41] F. Guerra, N. Guaragnella, A. A. Arbini, C. Bucci, S. Giannattasio, L. Moro, *Front. Oncol.* **2017**, *7*, 295.
[42] F. Moazed, L. Chun, M. A. Matthay, C. S. Calfee, J. Gotts, *Tob Control.* **2018**, *27*, s20.
[43] K. Adriaens, D. Van Gucht, P. Declerk, F. Baeyens, *Int. J. Environ. Res. Public Health* **2014**, *11*, 11220.
[44] K. Adriaens, D. V. Gucht, F. Baeyens, *Int. J. Environ. Res. Public Health* **2018**, *15*, E2902.
[45] A. McNeill, L. S. Brose, R. Calder, L. Bauld, D. Robson, *Evidence Review of E-Cigarettes and Heated Tobacco Products*; A report commissioned by, Public Health England London; Public Health England, London, UK **2018**.
[46] M. D. Litt, V. Duffy, C. Oncken, *Tob. Control* **2016**, *25*, 67.
[47] X. Liu, A. Lugo, L. Spizzichino, T. Tabuchi, R. Pacifici, S. Gallus, *Tob. Control* **2019**, *28*, 113.
[48] L. Liu, G. He, L. Wu, C. Zheng, S. Wang, Y. Zhang, L. Liang, J. Xie, J. Yao, *2021 46th International Conference on Infrared, Millimeter and Terahertz Waves (IRMMW-THz)*, Institute of Electrical and Electronics Engineers, Chengdu, China **2021**, p. 1. https://doi.org/10.1109/IRMMW-THz50926.2021.9567182
[49] R. H. Jibon, M. Ahmed, M. E. Rahaman, M. K. Hasan, M. M. Shaikh, T. A. Nicotine, *2nd International Conference on Robotics, Electrical and Signal Processing Techniques (ICREST)*, DHAKA, Bangladesh **2021**, p. 2021334. https://doi.org/10.1109/ICREST51555.2021.9331009

How to cite this article: A.-M. Bratu, M. Bojan, S. Banita, M. Petrus, C. Popa, *J. Biophotonics* **2023**, e202300120. https://doi.org/10.1002/jbio.202300120