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Исследование содержания карбонильных соединений и специфических нитрозаминов табака в сигаретном дыме и в аэрозоле системы нагревания табака

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Abstract. Investigation of some toxic compounds concentrations in aerosol of new class of tobacco products - tobacco heating systems and comparing their levels with regular cigarettes aerosol is an important step in understanding whether these products are low-risk, as some manufacturers claim. Three popular in Russia cigarette brands, reference cigarette 3R4F and new heated tobacco products (HTP) were tested for levels of emissions of some harmful and potentially harmful constituents (HPHC). Aerosols of these products were collected under the ISO intense smoking regime and quantified for levels of N'-nitrosonornicotine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, acrolein, acetaldehyde, formaldehyde. Levels of above mentioned HPHCs were measured by the high-performance liquid chromatography / mass spectrometry (HPLC/MS-MS). The results demonstrate that highest levels of measured HPHCs are obtained for reference cigarette 3R4F. As for popular in Russia cigarette brands their levels vary greatly and for some compounds can be very close to levels of 3R4F aerosol. Levels of all measured HPHCs in aerosol of HTP were significantly lower compared to all cigarettes. This can be explained by specific mechanism of HTPs aerosol formation without pyrolytic and pyrosynthetic reactions which are typical to all combustive tobacco products due to their high temperature of the process.

Keywords: innovative tobacco product, heated tobacco, electric tobacco heating system, stick, aerosol, toxic components, specific nitrosamines, nitrosonornicotine, acetaldehyde, acrolein

Introduction

Cigarette smoking is an established cause of serious health diseases including cardiovascular diseases, chronic obstructive pulmonary diseases (COPD), and cancer. Although smoking prevalence has declined over the last decade, tobacco products continue to be consumed on a global scale [1]. The actual worldwide policy of tobacco harm reduction recommends the necessity to put in place less harmful products available to smokers who would otherwise continue smoking. This strategy is promoted by various stakeholders, including regulators, public health organizations, healthcare professionals, and tobacco industry [2]. Increasing alternatives to tobacco products have been introduced by various industry players in the global market. These products include Electronic Nicotine Delivery Systems (ENDS, also called e-cigarettes) that heats a nicotine-containing solution [3] and electronically Heat-not-Burn (HNB) products also referred as Heated Tobacco Products (HTPs) which heats a tobacco mixture without combustion or burning process [4].

These new classes of products are gaining popularity among smokers who are looking for alternatives to quit smoking or to potentially reduce harms caused by toxicants emitted by conventional cigarettes [5]. Philip Morris International launched iQOS as a novel HTP. Other tobacco companies launched similar HTPs and HTP hybrids products British American Tobacco (BAT) and Japan Tobacco Inc. (JTI) marketed Glo, Glo iFuse and Ploom Tech [6].

Unlike cigarettes, where combustion is the principle of operation leading to smoke generation, ENDS and HTPs form an aerosol without combustion [7]. This is achieved by heating a substrate – either a tobacco mixture or a liquid, to evaporate aerosol forming compounds such as glycerine and propylene glycol, along with nicotine and flavour compounds. The condensation of the aerosol formers leads to an aerosol capable of reaching the consumers' lungs, which is necessary to achieve nicotine pharmacokinetic profiles similar to those of cigarettes [8, 9]. When comparing of components in the HTP's mainstream aerosol with standard tobacco reference cigarette (3R4F) smoke, the tobacco industry stated that levels of HPHCs in HTPs

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accounted to about 10% to what is found in conventional cigarettes [10]. This 90% reduction is related to the device mode of operation which heats the tobacco substrate to a relatively low temperature (200–350 °C) [11]. The iQOS device, for example, heats the tobacco unit to a maximum temperature of 350 °C via an electronically controlled heating blade. This temperature zone prevents tobacco from combustion process which occurs generally at temperatures reaching 900 °C [12]. Combustion process in conventional cigarettes results in complex chemical reactions – combination of burning, pyrolysis, pyrosynthesis, distillation, sublimation, and condensation processes [12]. As a consequence, more than 7000 chemical compounds of various classes are released into tobacco smoke [13] many of which are present in insignificant amounts. About 150 of them are considered toxic and pose a health hazard. About half of the Hoffmann list [14] of substances is present directly in tobacco; other compounds are formed during combustion processes.

The positioning of HTPs as a promising alternative to continued tobacco smoking determines the need for independent studies comparing the composition of aerosol inhaled by consumers of these products to cigarette smoke. The first consideration when evaluating the health and safety of tobacco-containing products is the presence of toxic and harmful compounds and their relative concentrations [15].

Materials and methods

Test products samples: tobacco heating system iQOS from Philip Morris Products S.A.; tobacco heating system Glo from British American Tobacco; The University of Kentucky 3R4F cigarettes (standard reference cigarette), designed and manufactured in accordance with ISO 16055:2012 (Tobacco and Tobacco Products, Monitor Test Sample, Requirements and Use) were used as a reference samples for research, method validation, comparative tests, monitoring the correctness of the tests during routine analyses; three commercially available cigarettes from the Russian market were used for comparison.

Test subjects (tobacco sticks and conventional cigarettes) were conditioned according to ISO 3402. Smoking of all cigarette samples and heated tobacco sticks was carried out using a 5-channel Cerulean SM 405 linear smoking machine. For the analysis of TSNAs the cigarette mainstream smoke and HTP aerosol was trapped on Cambridge filter pads. For the analysis of carbonyls, the smoke and aerosol were trapped in 2 consecutive impingers containing a dinitrophenyl hydrazine solution.

The ISO 20778:2018 intense smoking regime (55 ml puff volume, 2 s puff duration, 30 s puff interval, bell-shaped puff profile and 100% ventilation blocking) was applied to generate cigarette smoke and HTP aerosol.

A high performance liquid chromatograph coupled with tandem mass spectrometer (HPLC-MS/MS) TSQ Quantiva (Thermo Scientific, USA) was used to quantify N-nitrosonornicotine (NNN) and 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK). The same instrument was used for the determination of formaldehyde, acetaldehyde, and acrolein. Descriptive statistics was performed using Microsoft Office Excel software.

Results and discussions

A wealth of literature discusses prioritization of toxicants in cigarette smoke. In particular, the World Health Organization (WHO) proposed a list of priority toxicants that adversely affect human health due to high toxicity [16].

This list includes carbonyls such as formaldehyde, acetaldehyde and acrolein, and TSNAs. Formaldehyde is a very toxic compound, hazard class 2 (highly hazardous). Acetaldehyde is a carcinogen that can cause mutations and damage DNA. Acrolein is a strong lacrimator that irritates the mucous membranes of the eyes and upper respiratory tract, and has a general toxic effect. TSNAs are present in both the tobacco and cigarette smoke in contrast with several HPHCs. The most abundant TSNAs are N-nitrosonornicotine (NNN), 4-(methyl-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK), N-nitrosoanabasine (NAB) and N-nitrosoanatabine (NAT). They are formed from tobacco alkaloids and transferred to the mainstream smoke in the particulate phase of tobacco smoke from a combination of direct distillation, pyrosynthesis and pyrolysis.

There are a number of published analytical methods for the constituents selected in the present study. Various approaches in assessing these constituents in tobacco – and nicotine-containing products exist and each of them has methodological difficulties. In an analytical review of available scientific data evaluating chemicals in electronic cigarettes and in their aerosols [17], it was noted that inconsistent levels of aerosols compounds were associated with the absence of standardized methodologies for the generation of aerosols and the subsequent quantification of those compounds. The amount of carbonyl compounds in e-cigarette aerosols varied from trace amounts to very high levels, due, at least in part, to different aerosol generation conditions on the analytical smoking machine [18].

Analysis of the existing methods applied by ISO, CORESTA, various tobacco manufacturers, and independent laboratories for the determination of TSNAs and/or carbonyl compounds (formaldehyde, acetaldehyde, and acrolein) in cigarette mainstream smoke and heated tobacco products aerosol showed both similarities and differences.

The purpose of this work is to provide an independent analysis of the levels of priority toxicants in aerosol of novel tobacco products, as it is an important and necessary step to establish criteria for product differentiation, and to support regulatory and standardization activities. Smokers and nonsmokers need accurate information about products' emissions from independent sources beyond tobacco industry. The selected compounds are part of existing list of priority constituents in cigarette mainstream smoke [16].

Products' physical characteristics, such as product length, filter length; product diameter and net tobacco weight are summarized in table 1.

Table 1.

Physical characteristics of tobacco sticks and cigarettes

Parameter	Tobacco sticks				Cigarettes			
	iQOS		Glo		sample1	sample 2	sample 3	3R4F
	sample 1	sample 2	sample 1	sample 2				
Product length, mm	45	45	83	83	98	83	83	84
Filter length, mm	33	33	41	41	27	27	27	27
Product diameter, mm	7,18	7,26	5,44	5,42	6,80	7,82	6,68	7,95
Net tobacco weight, g	0,291	0,299	0,269	0,262	0,588	0,602	0,535	0,746

Table 2.

Levels of analytes in the HTP aerosol, the smoke of 3R4F and commercial cigarettes

Test sample	Content of aerosol components									
	NNN ng/pc		NNK ng/pc		Formaldehyde µg/pc		Acetaldehyde µg/pc		Acrolein µg/pc	
	mean	SD	mean	SD	mean	SD	mean	SD	mean	SD
Tobacco sticks (iQOS)										
Sample 1	10,8	0,47	13,9	0,67	2,05	0,40	149,9	2,51	9,2	0,69
Sample 2	7,2	0,34	10,2	0,46	2,58	0,44	169,6	2,24	12,8	0,61
Tobacco sticks (Glo)										
Sample 1	16,98	0,71	5,71	0,61	8,96	0,66	102,1	2,67	3,70	0,36
Sample 2	16,01	0,79	5,67	0,62	6,61	0,62	79,4	2,74	3,06	0,11
Cigarettes										
3R4F	292,86	14,37	226,31	13,52	66,57	6,54	1509,91	26,38	170,14	3,49
Sample 1	110.86	4.51	61.89	3.36	63.28	3.88	885.19	10, 13	116.51	13.48
Sample 2	171.11	10.20	150.75	6.08	65.61	2.33	1 139.68	51.03	134.02	5.57
Sample 3	86.51	5.97	44.37	3.05	66.86	1.01	791.36	29.29	97.69	7.04
SD – standard deviation										

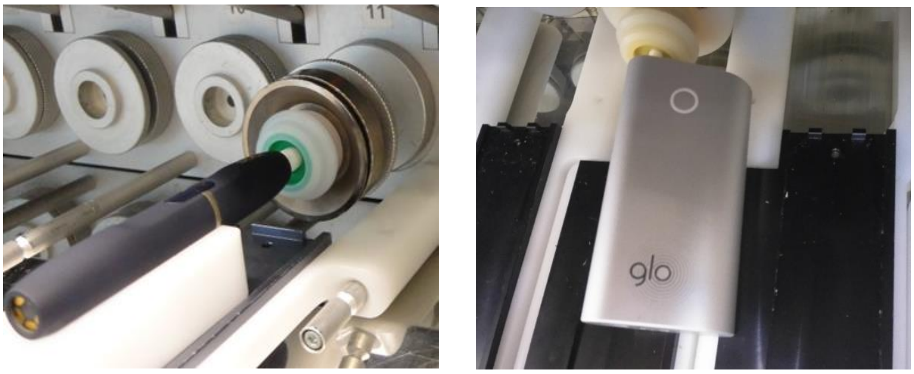

Figure 1. Collecting aerosol EHTP

In this study, we analyzed the levels of carbonyls (formaldehyde, acetaldehyde and acrolein) and two major TSNAs (NNN and NNK) in the aerosol of a reference cigarette 3R4F, 2 varieties of iQOS tobacco sticks, 2 varieties of Glo tobacco sticks and 3 varieties of commercial cigarettes (ISO Intense) [19].

The figure 1 shows the collection of aerosol of tobacco heating system iQOS / Glo.

The yields of analytes in the smoke of 3R4F, commercial cigarettes, and in the iQOS / Glo aerosol are summarized in Table 2 (Mean values ± SD are provided).

The results demonstrate that highest levels of measured HPHCs are obtained for reference cigarette 3R4F. As for popular in Russia cigarette brands their levels vary greatly and for some compounds can be very close to levels of 3R4F aerosol.

Statistical processing of the results (number of replicates n = 4), also presented in Table 2, indicate slight dispersion of single determinations.

It is evident that the levels of tobacco specific nitrosamines and carbonyl compounds in the HTP aerosol were significantly lower as compared to the levels in the smoke of 3R4F and commercial cigarettes. This can be explained by specific mechanism of HTPs aerosol formation without pyrolytic and pyrosynthetic reactions which are typical to all combustive tobacco products due to their high temperature of the process.

Heated tobacco products substantially differ from traditional tobacco products since they do not produce smoke, but a nicotine-containing aerosol, that was claimed by the manufacturers to contain significantly lower levels of harmful and potentially harmful constituents [10, 20]. This reduction was confirmed by several independent laboratories for selected compounds [15, 21]. TSNA and carbonyl yields found in the present study are in line with the results of studies by tobacco industry and independent laboratories. We observe significant reductions (87% and more) of yields of the five analyzed compounds (NNN, NNK, formaldehyde, acetaldehyde and acrolein) in HTP aerosol compared to 3R4F cigarette smoke and similar magnitude of reductions when compared to commercial cigarettes.

Conclusion

Chemical composition of aerosol of novel tobacco – and nicotine-containing products requires a systematic study, being a starting point in assessing the level of risk to consumers. Carbonyl compounds and tobacco-specific nitrosamines are included in the lists of priority tobacco smoke toxicants by WHO and various public health organizations, so their quantification in aerosols of novel products is an important step in determining both the absolute and relative (compared to cigarette smoking) product risk, taking into account mode of consumption and design features of these products. The results of the present study demonstrate that the levels of formaldehyde, acetaldehyde, acrolein, N'-nitrosonornicotine (NNN), and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in the aerosol of the tested samples of heated tobacco product are significantly lower than in 3R4F cigarette smoke, as well as compared to commercially available cigarettes. The applied analytical methods demonstrated good intra-laboratory reproducibility, and the obtained results are in line with findings from the studies conducted by product manufacturers and independent laboratories.

References

1 US Department of Health and Human Services et al. Reducing tobacco use: a report of the Surgeon General. 2000.

2 Shapiro H. No fire, no smoke: the global state of tobacco harm reduction 2018. London: Knowledge-Action // Change. 2018. Available at: https://gsthr.org/report/full-report

3 McNeill A., Brose L.S., Calder R. et al. E-cigarettes: an evidence update. A report commissioned by Public Health England // Public Health England. 2015. V. 111. P. 14-15. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/733022

4 Simonavicius E., McNeill A., Shahab L. et al. Heat-not-burn tobacco products: a systematic literature review // Tobacco control. 2019. V. 28. №. 5. P. 582-594. doi: 10.1136/tobaccocontrol-2018–054419

5 Farsalinos K.E., Le Houezec J. Regulation in the face of uncertainty: the evidence on electronic nicotine delivery systems (e-cigarettes) // Risk Manag Health Policy. 2015. V. 8. P. 157–167. doi:10.2147/RMHP.S62116

6 Mirgorodskaya A.G., Shkidyuk M.V. et al. Research toxic components: carbonyls compounds and tsna in cigarette smoke and in aerosol nicotine delivery systems. Global studies of tobacco, tobacco products, and innovative nicotine-containing products: status and perspectives: collection of scientific papers International scientific conference (November 17, 2020). Krasnodar: Enlightenment-South, 2020. 78 p. Available at: http://www.vniitti.ru/conf/conf2020/Conf_2020.pdf

7 Gnuchih E.V., Shkiduk M.V., Mirgorodskaya A.G., et al. Modern methods for regulation nicotine containing products // Proceedings of VSUET. 2019. V. 81. № 2. P. 196–201. doi: 10.20914/2310–1202–2019–2–196–201 (in Russian).

8 Fearon I.M., Eldridge A.C., Gale N. et al. Nicotine pharmacokinetics of electronic cigarettes: A review of the literature // Regul Toxicol Pharmacol. 2018. V. 100. P. 25–34. doi: 10.1016/j.yrtph.2018.09.004

9 Brossard P., Weitkunat R., Poux V. et al. Nicotine pharmacokinetic profiles of the Tobacco Heating System 2.2, cigarettes and nicotine gum in Japanese smokers // Regul Toxicol Pharmacol. 2017. V. 89. P. 193–199. doi: 10.1016/j.yrtph.2017.07.032

10 Schaller J.P., Keller D., Poget L. et al. Evaluation of the Tobacco Heating System 2.2. Part 2: Chemical composition, genotoxicity, cytotoxicity, and physical properties of the aerosol // Regul Toxicol Pharmacol. 2016. V. 81. № 2: P. 27–47. doi: 10.1016/j.yrtph.2016.10.001

11 Eaton D., Jakaj B., Forster M. et al. Assessment of tobacco heating product THP1.0. Part 2: Product design, operation and thermophysical characterization // Regul Toxicol Pharmacol. 2018. V. 93. P. 4–13. doi: 10.1016/j.yrtph.2017.09.009

12 Smith M.R., Clark B., Lüdicke F. et al. Evaluation of the Tobacco Heating System 2.2. Part 1: Description of the system and the scientific assessment program // Regul Toxicol Pharmacol. 2016. V. 81. № 2. P. 17–26. doi: 10.1016/j.yrtph.2016.07.006

13 Rodgman A., Green C.R. Toxic chemicals in cigarette mainstream smoke – hazard and hoopla // Beitr Tabakforschung/Int Contrib Tob Res. 2014. V. 20. № 8. P. 481–545. doi: 10.2478/cttr-2013–0764

14 Hoffmann D., Hoffmann I. The changing cigarette, 1950–1995 // Journal of Toxicology and Environmental Health. 1997. V. 50. № 4. P. 307–364. doi: 10.1080/009841097160393

15 Mallock N., Böss L., Burk R. et al. Levels of selected analytes in the emissions of "heat not burn" tobacco products that are relevant to assess human health risks // Archives of Toxicology. 2018. V. 92. P. 2145–2149. doi: 10.1007/s00204–018–2215-y

16 World Health Organization. WHO study group on tobacco product regulation: report on the scientific basis of tobacco product regulation: fifth report of a WHO study group. World Health Organization, 2015. V. 989.

17 Cheng T. Chemical evaluation of electronic cigarettes // Tobacco Control. 2014. V. 23. № 2. P. 11–17. doi: 10.1136/tobaccocontrol-2013–051482

18 Gnuchikh E.V., Shkidyuk M.V., Mirgorodskaya A.G. Studies of innovative product – electronic system for nicotine delivery // Proceedings of VSUET. 2018. V. 80. № 3. P. 265–271. doi: 10.20914/2310–1202–2018–3–265–271 (in Russian).

19 Results of scientific work «Preparation of proposals and recommendations for the establishment of safety requirements for nicotine-containing products circulated on the territory of the Eurasian Union» Available at: http://www.eurasiancommission.org/ru/

20 Forster M., Fiebelkorn S., Yurteri C. et al. Assessment of novel tobacco heating product THP1.0. Part 3: Comprehensive chemical characterisation of harmful and potentially harmful aerosol emissions // Regul Toxicol Pharmacol, 2018. V. 93. P. 14–33. doi: 10.1016/j.yrtph.2017.10.006

21 Salman R., Talih S., El-Hage R. et al. Free-Base and Total Nicotine, Reactive Oxygen Species, and Carbonyl Emissions From IQOS, a Heated Tobacco Product // Nicotine Tob Res. 2018. doi: 10.1093/ntr/nty235

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Contribution

All authors were equally involved in writing the manuscript and are responsible for plagiarism

Conflict of interest

The authors declare no conflict of interest.

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