ABSTRACT BOOK

5th Scientific Summit

Tobacco Harm Reduction: Novel products, Research & Policy

by SOHRE

21-22 SEPTEMBER 2022 I ATHENS

STAVROS NIARCHOS FOUNDATION CULTURAL CENTER

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Tobacco Harm Reduction:
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STAVROS NIARCHOS FOUNDATION CULTURAL CENTER

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ABSTRACT BOOK

SURVEY OF SMOKING BEHAVIOR, PERCEPTION AND GENERAL KNOWLEDGE REGARDING E-CIGARETTE AMONG MEDICAL STUDENTS IN THAILAND

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ABSTRACT BOOK

EVOLUTION OF SMOKING PREVALENCE IN JAPAN FOLLOWING THE INTRODUCTION OF HEATED TOBACCO PRODUCTS

Ondrej Koumal

Philip Morris International

OP 02

Since 2014, heated tobacco products have become increasingly popular in a number of countries, including Japan. As other researchers showed using sales volume data, the introduction of heated tobacco products in Japan coincided with an accelerated decline in cigarette sales. We examined the evolution of smoking prevalence in Japan before and after the introduction of heated tobacco products using data from the National Health and Nutrition Survey (from 2010 to 2019), as well as more recent (2016 to 2021) data from repeated, nationally representative, cross-sectional population surveys conducted by Philip Morris International. The results from both surveys show similar temporal trends: overall tobacco use moderately declined following the introduction of heated tobacco products, with the share of tobacco users who smoke declining at an accelerated pace while the prevalence of heated tobacco product use simultaneously increased. These trends indicate that heated tobacco products are successfully replacing combusted tobacco products in Japan and have likely contributed to a decline in the prevalence of cigarette smoking. While the prevalence of cigarette smoking had plateaued at 19-20% before 2015, the introduction and uptake of heated tobacco products coincided with a decrease of smoking prevalence to 13%.

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TWO-THIRDS OF THE DAILY USERS OF E-CIGARETTES AND HEATED TOBACCO ARE PEOPLE WHO PREVIOUSLY SMOKED TRADITIONAL CIGARETTES BUT CURRENTLY DO NOT SMOKE

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OP 03

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Background: The prevalence of tobacco use is a dynamic phenomenon, influenced by a number of socio-economic and health factors. In each population, it is important to know the scale of the phenomenon, as well as to understand its characteristics. The aim of the study was to determine the frequency of smoking traditional cigarettes and using e-cigarettes and heated tobacco (HnB, heat-not-burn) in the adult population of Poland and to determine whether new products (e-cigarettes, HnB) are used together with traditional cigarettes.

Material and Methods: A survey was conducted on a representative sample of 5000 Polish residents aged over 18. The survey was carried out from March to May 2022 using the Computer-Assisted Telephone Interviewing (CATI) method.

Results: Out of the total number of respondents (n=5000), 21.1% of the respondents currently smoke traditional cigarettes (25.5% among men and 17% among women; p<0.001); 3.3% of respondents use e-cigarettes, and 3.5% of respondents use heated tobacco. There were no gender differences in using e-cigarettes or HnB products.

Out of the total number of respondents, 21.4% (95% CI: 20.3-22.6) currently use only one of the three analyzed products (traditional cigarettes, e-cigarettes, and heated tobacco). Two products were used by 2.6% (95% CI: 2.2-3.0) and three by 0.4% (95% CI: 0.3-0.6) of the study participants.

Among people who use e-cigarettes every day, 5.4% (95% CI: 2.0-10.8) are the ones who have never smoked conventional cigarettes, and 65.7% (95% CI: 55.5-74.2) are former smokers. Among occasional e-cigarette users it was 3.1% (95% CI: 0.6-9.2) and 32.2%, respectively.

Of those who use heated tobacco daily, 2.1% (95% CI: 0.5-6.9) are people who have never smoked conventional cigarettes and 64.2% (95% CI: 54.7-74.1) are former smokers. Among occasional users of heated tobacco, the percentages were 6.4% (95% CI: 2.4-12.8) and 38.8% (95% CI: 29.0-49.8), respectively.

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Nicotine containing product that was declared as a first ever tried in life, regardless of age group, was traditional cigarette (93.8%), then e-cigarette (5.6%) and heated tobacco product (0.6%). In the group of 18-24 years old, e-cigarettes were declared by 22% of respondents which was more frequent than in other age groups.

Conclusions: In Poland, smoking traditional cigarettes is still common (one in five adults smoke every day). Currently, the percentage of users of e-cigarettes and heated tobacco is at a similar level (just over 3% of the adult population). In the case of e-cigarettes and HnB, two-thirds of everyday users are people who previously smoked traditional cigarettes but currently do not smoke. The nicotine containing product declared as the first one ever used is traditional cigarette.

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EPIDEMIOLOGY & SOCIAL ISSUES

TEMPORAL CHANGES IN A NOVEL HEATED TOBACCO PRODUCT'S (IQOS™) RISK PERCEPTION: EVIDENCE FROM JAPAN'S ROLLING POST MARKET CROSS-SECTIONAL (PMX) SURVEYS

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OP 04

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Background: Risk perception (RP) is a key factor influencing current adult smokers' decision to switch to smoke-free tobacco and nicotine products (TNP). This study assesses changes in health RP of a novel smoke-free heated tobacco product (IQOS™) relative to cigarettes, among current IQOS™ users.

Material and Methods: The analyses included data from four repeated cross-sectional surveys conducted in Japan (n=6881, years 2016-17, 2017-18, 2018-19, and 2020-21) among current adult IQOS™ users recruited from PMI's IQOS Owners Database. The health RPs of cigarettes and IQOS™ were assessed using the Health Risk scale of the ABOUT™ - Perceived Risk instrument. The score ranged from zero, indicating no perceived risk, to 100, indicating very high perceived risk. Relative RP of IQOS™ to cigarettes ($RP_{Cigarettes-IQOS}$) was computed as the difference in absolute RP scores of cigarettes minus IQOS™.

Results: In Japan, RP of cigarettes has remained stable over the years while RP of IQOS™ has increased over time from 44.0 (95% CI: 43.1-45.0) to 49.4 (95% CI: 48.5-50.3). The change was reflected in relative RP of IQOS™'s gradual decline from 19.5 (95% CI: 18.5-20.5) to 12.7 (95% CI: 11.9-13.4). IQOS™'s relative RP was higher among exclusive IQOS users compared to dual users, and increased with the number of HEETS™ used and length of IQOS™ ownership.

Conclusions: IQOS™'s relative RP decreased over time, driven by an increase in IQOS™'s RP, in agreement with epidemiological studies indicating a temporal reduction in smoke-free TNPs' relative RP. Regular surveillance of the RP of novel smoke-free TNPs is warranted to inform TNP risk communications and ensure that current adult smokers who would otherwise continue to smoke receive adequate communications on novel TNPs' relative risks.

PERCEPTIONS AND ATTITUDES OF PATIENTS WITH MENTAL ILLNESS TOWARDS SMOKING IN GREECE

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OP 05

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Background: Smoking is endemic among people with mental health disorders, with prevalence remaining high despite the significant decline in the general population in recent years. The impact of smoking-attributable morbidity on life expectancy is significant as people with severe mental disorders have a 15–20-year reduction in life expectancy compared to the general population.

Material and Methods: A cross-sectional study was conducted among 1015 people with mental health disorders through a personal interview. Patients were recruited from the outpatient department, community care accommodations and inpatient facilities of the Psychiatric Hospital of Attica. The questionnaire was designed to examine knowledge, perceptions and attitudes of these patients toward smoking. Statistical analysis was performed using SPSS 24.0.

Results: The prevalence of current smoking was 68.2% (n=692), while 12.2% (n=124) were former smokers. Most current smokers (85.3%) smoked their first cigarette within 30 minutes of waking up, and 60.1% found it difficult not to smoke in non-smoking areas. Former smokers' main motive to quit smoking was for health reasons (84.7%), and almost all of them (97.6%) had quit without using any smoking cessation aid. Only 11.4% of participants believe that health professionals inform smokers about smoking cessation programs and harm reduction strategies. Moreover, only 53% of participants believe that health professionals inform patients about the harmful health effects of tobacco. Non-smoking patients had fewer psychiatric readmissions than smoking patients. Males, divorced patients, outpatients and patients with past history of hospitalization in a psychiatric clinic were more likely to be current smokers. Patients living in community care accommodations were less likely to be current smokers.

Conclusions: High prevalence of current smoking and smoking dependence is observed among patients with mental health disorders. Healthcare professionals need to step up their efforts in discussing with patients about their smoking habit and in providing guidance about relevant cessation programs and harm reduction strategies.

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EPIDEMIOLOGY & SOCIAL ISSUES

PERCEIVED REDUCED FORMATION OF HARMFUL CHEMICALS AND PERCEIVED REDUCED RISK OF HARM IMPACT EXCLUSIVE USE OF THE HEATED TOBACCO PRODUCT IQOS™: A PROSPECTIVE CONSUMER COHORT STUDY IN FOUR CULTURALLY AND SOCIO-ECONOMICALLY DIFFERENT COUNTRIES

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Funding: Philip Morris International is the sole source of funding and sponsor of this research.

Declaration of Interest: K.F., S.R., and P.M. are employees of Philip Morris International. A.S. and M.C. are employees of Smartech s.r.l., a scientific market research consulting company commissioned by Philip Morris International.

Background: Perceived reduced formation of harmful chemicals (RF) or reduced risk of harm (RH) of smoke-free tobacco products (TP) relative to combustible TPs may influence their acceptance and use patterns among current adult cigarette smokers and therefore impact public health. We analyzed whether and how perceived RF and/or RH of Philip Morris International (PMI)'s heated TP (HTP) IQOS™ impacted "exclusive" (100%) IQOS use in Japan, Italy, Germany, and Russia.

Material and Methods: Between 2016 and 2020, adult participants from longitudinal IQOS Owner consumer cohorts in Japan (N=6257), Italy (N=8137), Germany (N=8474), and Russia (N=7231) repeatedly indicated the reasons for using IQOS, including reasons referring to RF and RH, during their 48 weeks of follow-up. Logistic regression was used to analyze the relationships between RF and/or RH indications for using IQOS and exclusive IQOS use.

Results: At week 48, exclusive IQOS use in Japan (odds ratio [OR]: 1.89), Italy (OR: 3.35), Germany (OR: 3.48), and Russia (OR: 3.05) was more likely for the highest versus lowest category of number of RF and/or RH indications. Similar results were observed for overall HTP use in Japan, where other HTPs were also available. In Japan, where RF and RH could be indicated separately as reasons for using IQOS, indicating RH (OR: 2.92) versus RF (OR: 1.81) resulted in a greater likelihood of exclusive IQOS use within the highest category of RF or RH indications.

Conclusions: The perceived RF and/or RH of IQOS, especially when indicated with certainty, have a significant impact on users switching from cigarette smoking to exclusive IQOS use. This also seems to be true for the overall HTP category. Moreover, perceived RH of IQOS was a stronger driver for exclusive IQOS use than perceived RF.

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THE EFFECT OF SMOKING ON EXHALED CARBON MONOXIDE AND ARTERIAL ELASTICITY DURING PROLONGED SURGICAL MASK USE IN THE COVID-19 ERA

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OP 07

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Background: During the COVID-19 era, the use of surgical face mask hampers the spread of COVID infection. The impact of smoking while wearing a surgical face mask on exhaled CO and vascular function in smokers has not been investigated.

Material and Methods: We studied 40 smokers of conventional cigarettes (ConCig), 40 exclusive heat-non-burn cigarettes (HNBC) users and 40 non-smokers with similar age and sex ($p>0.05$ [45.1±10.8 years, 34 (28.3%) male]). We measured exhaled CO (parts per million [ppm]), pulse wave velocity (PWV) and central systolic blood pressure (cSBP).

Results: A significant interaction was found between CO at baseline and at the end of an 8h period with and without wearing a mask and the use of tobacco products vs no-smoking ($F=46.58$, p for interaction <0.001). Exhaled CO was higher in ConCig smokers compared to HNBC and non-smokers throughout the study ($p<0.05$).

Compared to baseline, the percent increase of CO was greater after smoking ConCig with than without wearing a mask for 8h (141.79% [95% confidence interval (CI): 116.16-167.42] vs 56.99% [95% CI: 44.80-69.18], $p<0.001$). Similarly, the percent increase of CO was greater after smoking HNBC with than without wearing a mask for 8h (103.84% [95% CI: 70.50-137.18] vs 30.76% [95% CI: 15.61-45.92], $p<0.001$). Among non-smokers, the use of mask did not alter exhaled CO ($p>0.05$).

In both ConCig and HNBC users, all vascular markers were increased at the end of each one of two study assessments, compared to baseline ($p<0.05$). In non-smokers, the use of a mask had a neutral effect on vascular markers ($p>0.05$).

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Compared to baseline, the percent increase of PWV was greater after smoking ConCig with than without wearing a mask for 8h (16.54% [95% CI: 9.13-23.95] vs 4.36% [95% CI: 1.41-7.31], p=0.001).

Compared to baseline, the percent increase of PWV was greater after smoking HNBC with than without wearing a mask for 8h (9.71% [95% CI: 4.57-14.84] vs 2.73% [95% CI: 0.12-5.35], p=0.003).

Conclusions: This study demonstrates that smoking of any tobacco product (conventional tobacco or HNBC) during a prolonged use of a surgical face mask may further compromise vascular function. Thus, quitting both conventional and HNBC cigarettes is imperative for a better health in the COVID-19 pandemic.

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SMOKING BEHAVIORS AND OPINIONS OF ADULT STUDENTS FROM GREEK PUBLIC IEK

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OP 08

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Introduction: Nowadays, the smoking rates in Greece are extremely high and a huge part of smokers, especially when it comes to young adults, are looking for more healthy smoking options, such as the electronic cigarette.

Material and Methods: A two-part questionnaire was shared to 550 students in Public Schools of various specialties. The first part included socio-demographic characteristics, such as the gender, age and the students' smoking habit. The second part included questions that had to do with the effectiveness of electronic cigarette.

Results: Out of 550 students, 42% of them had begun smoking in the age group of 16-19 years old ($p<0.05$), 59% of total students are not smoking nowadays and 67% of smokers do not want to stop smoking. Furthermore, 53% of the students that participated in the survey consider the e-cigarette as a healthier option for smoking ($p<0.05$).

Conclusions: More and more students are trying to adapt to a healthier lifestyle and choose alternative and healthier smoking options, such as e-cigarette, instead of the conventional cigarettes.

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HARM REDUCTION ASSOCIATION IN KAZAKHSTAN

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OP 09

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Generally recognized harm reduction promotion has experienced a significant rise in Kazakhstan over the last years. Following years of research, experience, opinion exchanges and reports, in 2020 industry leaders, healthcare professionals and other respective experts came together and formed Harm Reduction Association of Kazakhstan. The association is now the main holder of harm reduction concept development in the state. The vision is to disseminate and educate the public on harm reduction with real world research results and science-based international reports through the prism of factors of non-infectious diseases and consumers' rights. The association was the first non-governmental organization that brought drug replacement therapy to Kazakhstan back in 2014 under a pilot project which after being proved effective has evolved into a state program funded by the government. The members' list of the association has expanded since its formation and its experts have completed numerous studies, organized impactful events and drawn communication reports to government bodies. This recently created organization aspires to further continue developing harm reduction mindset among the public leveraging various forms of research, educational events and publicly available reports.

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SMOKING IN THE RUSSIAN FEDERATION AND POINTS OF REVIEWING THE PREVENTION STRATEGY FOR SMOKING ASSOCIATED DISEASES

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OP 10

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Background: The purpose of this study was to evaluate the status of smoking in the Russian Federation (RF), and to develop proposals for changing the strategy for primary and secondary prevention of smoking associated diseases in terms of motivation to quit smoking.

Material and Methods: The Russian Public Opinion Research Centre (VCIOM) presented the data of a monitoring survey on the smoking problems in the Russian Federation. The survey was posted on the website httpps://wciom.ru on July 12, 2022. Based on the obtained results, suggestions to change the strategy of primary and secondary prevention among smokers in terms of motivation to quit smoking were formulated.

Results: The share of smokers in the Russian Federation has remained unchanged for the last 5 years - 33%.

Since 2013, warning labels and ugly drawings have been added to cigarette packs. The share of smokers has decreased (2013 - 41%, 2022 - 33%). The proportion of people who quit smoking is also growing (2013 - 10%; 2022 - 17%). Among smokers, there is 20% of "heavy" smokers (a pack per day or more) and the proportion of occasional smokers (several cigarettes per day / week) has decreased from 20% to 13% since 2009. The portrait of a smoking Russian is as follows:

- Smoking is primarily a male habit (47% vs 21% among women).
- The proportion of smokers is higher among 25-59 year olds (37%-42%).
- Half of Russians with secondary education smoke (50%), while among people with higher education 24% smoke.

A typical heavy smoker is a man aged 35-44, living in a village (36% vs 28% among residents of both capitals), having a poor financial situation (43%).

The profile of a smoker has changed since 2009. If 13 years ago the group of 18-44 years old (48-50%) was the most smoking part of the population, today it is filled with 25-59 year olds (38-42%), that is, those who smoked 13 years ago and didn't give up habit. This allows us to predict that young people aged 18-24 will become the driver of a new model of "non-

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smoking behavior". In 2009 22% of 18-24 year olds smoked a pack per day, compared to 12% in 2022; the total share of smokers aged 18-24 decreased by 1.7 times from 48% to 29%. However, the proportion of people aged 18-24 who use devices to smoke (vape, electronic cigarette or tobacco heating system) hasn't been studied separately, and therefore smoking may be underreported. The awareness of this category of people about the dangers of smoking also hasn't been studied, and separate studies are required. 62% of Russians who smoke want to kick the habit. The share of those who don't want to give up cigarettes increased 1.5 times from 19% to 31%. Moreover, smoking cessation is perceived as a forced measure: in 2017, many people had a strong desire, today health problems influence the decision to quit smoking to the same extent. Only 4% of smokers will be able to stop the growth in the cost of cigarettes, although among 18-24 year olds this option is mentioned by every third.

Conclusions: Thus, with respect to the decreasing proportion of people who want to quit smoking and the high percentage of heavy smokers, it is necessary to revise the approaches to motivate smokers to quit smoking, as well as develop a comprehensive harm reduction approach for those who don't intend to quit smoking. The concept of harm reduction in this aspect is designed to reduce the harmful effects of smoking on the body due to the heating of tobacco and the absence of combustion, which can affect the reduction in the incidence of cardiovascular, bronchopulmonary and oncological diseases. Also, in the strategy of primary and secondary prevention of diseases associated with smoking, it is necessary to develop personalized recommendations for quitting smoking, depending on the patient's gender and age status, taking into account the degree of tobacco dependence and motivation to quit smoking; develop and implement harm reduction principles for those who do not intend to quit tobacco use and create conditions for this, including the opportunity to receive information about scientifically proven less harmful alternatives to traditional cigarettes.

ABSTRACT BOOK

A SYSTEMATIC REVIEW AND META-ANALYSIS ON THE EFFECT OF HEATED TOBACCO PRODUCTS VS TRADITIONAL TOBACCO CIGARETTES ON HEART RATE, BLOOD PRESSURE AND OTHER PREDICTORS OF CARDIOVASCULAR RISK AMONG ADULT SMOKERS

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OP 11

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Background: Over the last decades, a large body of evidence has already demonstrated the association between traditional tobacco cigarette smoking and cardiovascular events. Through the years, products have been developed with the goal of providing 'relatively safer' or 'less harmful' alternatives to traditional tobacco cigarettes (TTCs). More recently, modified-risk tobacco products such as heated tobacco products (HTPs) have been introduced, to potentially reduce exposure to harmful constituents in cigarette smoke and ultimately reduce the health burden of smoking-related diseases such as cardiovascular disease. This meta-analysis was done to determine the association of TTC and HTP smoking on known cardiovascular risk factors and find evidence of this benefit as claimed.

Material and Methods: Randomized controlled trials comparing TTCs and HTPs with outcomes on blood pressure (BP), heart rate, flow mediated dilatation (FMD), pulse wave velocity (PWV), and products of lipid metabolism -high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides and total cholesterol- were searched through PubMed, Google Scholar and Cochrane database. A total of 11 studies were included in the meta-analysis.

Results: Pooled analysis of studies on adult smokers showed that HTP use showed significant difference compared to traditional tobacco cigarettes on heart rate (MD -3.16 with 95% CI of -15.41 to -0.91), FMD (MD 2.53 with 95% CI of 0.17 to 4.89) and HDL (MD 2.52 with 95% CI of 1.41 to 3.64). No significant differences were noted on systolic BP (MD -1.56 with 95% CI of -3.87 to 0.76), diastolic BP (MD -1.59 with 95% CI of -3.37 to 0.20), LDL (MD -2.24 with 95% CI of -6.26 to 1.78), triglycerides (MD 10.31 with 95% CI of -5.90 to 26.51) and total cholesterol (MD 10.31 with 95% CI of -5.90 to 26.51). Only 1 study had a complete report of outcomes on PWV also showing no significant difference.

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Conclusions: The present study evaluated the effects of the use of HTPs compared to TTC on the outcomes of blood pressure, heart rate and other predictors of cardiovascular risk. The results have shown that HTP use, compared to TTC use showed benefits on heart rate, high density lipoprotein, and flow mediated dilatation, but no significant difference on the other cardiovascular risk factors analysed. Larger and long term studies are still needed to support the cardiovascular benefits of alternative tobacco products such as HTPs.

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ARE HEATED TOBACCO PRODUCTS A PRAGMATIC MIDDLE GROUND FOR RECALCITRANT SMOKERS? REVISITING THE PROBLEM IN THE CONTEXT OF THE CURRENT PANDEMIC

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Recalcitrant smokers managed for their cardiovascular problems pose a serious challenge to practicing physicians in their efforts to effectively reduce cardiovascular and overall health risk in these patients. This problem has been magnified during the current pandemic, when the already increased health risk of active smokers is aggravated further in the event that they develop coronavirus disease 2019 (COVID-19). Active smoking increases the risk of developing severe COVID-19 by around two folds, and those with chronic obstructive pulmonary disease (COPD) -which many recalcitrant smokers are likely to have already- have a fourfold increase in risk translating to much poorer clinical outcomes. This is aggravated by the delay in diagnosis since the symptomatology in COPD with acute exacerbation and COVID-19 may significantly overlap.

This predicament with recalcitrant smokers during this pandemic has prompted us to reconsider our previous policy to give up on them after six months of making them quit smoking totally. The current pandemic highlighted the need to explore alternatives that could at least mitigate the cardiovascular and COVID-19 risk of recalcitrant smokers. Based on the potential to reduce health risk and also on patient feedback, we have allowed the use of heated tobacco products (HTPs) in our recalcitrant smokers who really could not attain total smoking cessation despite all known smoking cessation measures. Quite different from electronic cigarettes, HTPs produce aerosols, still containing nicotine, using a battery-powered heating system device. Based on studies, the amount of toxic substances a smoker gets is up to 95 percent less, compared to traditional tobacco smoking. Though HTPs may be considered a pragmatic middle ground for recalcitrant smokers, there is still some degree of addiction; hence, legislative and regulatory control measures are imperative, so as to prevent the youth and nonsmokers to be "seduced" into trying them. However, these regulatory measures should not be more stringent than what are currently imposed on tobacco smoking since it would defeat the purpose of getting current smokers out of this deadly vice.

ABSTRACT BOOK

THE INCIDENCE OF POST-COVID BRONCHO-OBSTRUCTIVE SYNDROME (BOC) IN PATIENTS WITH A NEW CORONAVIRUS INFECTION DEPENDING ON SMOKING STATUS

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OP 13

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Background: The purpose of the study was to determine the incidence of BOS in the post-COVID period based on a comprehensive assessment of clinical, laboratory and functional parameters, as well as taking into account the existing risk factors for the development of BOS.

Material and Methods: The study was conducted on the basis of the respiratory rehabilitation center of LLC Medical Association New Hospital in Yekaterinburg from July 2020 to December 2021. The study was approved by local ethical committee of OOO Medical Association New Hospital. Each patient signed an informed consent.

Inclusion Criteria: Adult patients 2-4 weeks after the end of treatment for COVID-19 of varying severity regardless of the % of lung involvement (according to CT scan). During the follow-up period 10,456 patients were examined, mean age 48.1±7.6 yo, including 6,259 women (59.8%). First-time detected BOS was registered in 7,506 patients (71.8%).

The patients were divided into 3 groups:

1. Group 1: patients who smoke or use alternative sources of nicotine delivery at the time of inclusion in the study, n=4135, of which
    a. group 1.1 = 2150 using cigarettes,
    b. group 1.2 = 1985 using THS
2. Group 2: never smokers, n=3001
3. Group 3: patients who quit smoking more than 12 months ago, n=3320

Patients of all groups were examined according to the protocol for managing patients with in the post-Covid period: laboratory, functional (spirometry with bronchodilator test, peak flowmetry) and clinical (need for short-acting β2-agonists, cough, shortness of breath, sputum discharge) parameters were studied.

For statistical processing "Statistica 12" was used.

Results: BOS was diagnosed in 71.8% of patients within 2 to 8 weeks after suffering COVID-19. In severe COVID-19 the incidence of BOS is significantly higher by 19.5%, than in mild cases. The frequency of development of virus-induced BOS was significantly higher in groups 1 and 3. In the 1st group the development of BOS was recorded in 56.4%, and in the 3rd group in 41.1%. In subgroup 1.1 the incidence of BOS was significantly higher by 15% compared with group 1.2. The relationship between the development of BOS in the post-COVID period and the presence of atopy, frequent acute respiratory viral infections in history before COVID-19, the number of peripheral blood eosinophils, the severity of the acute phase of COVID-19 and the presence of smoking at the time of inclusion in the study and in history was established. Moreover, using THS leads to a significantly lower incidence of BOS compared to smoking combustible cigarettes.

Conclusions: Smoking increases the risk of developing BOS and worsens the prognosis. The use of tobacco heating systems in those patients who do not quit smoking may lead to a lower risk of developing BOS.

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BIOMARKERS OF EXPOSURE AND POTENTIAL HARM IN EXCLUSIVE USERS OF ELECTRONIC CIGARETTES AND CURRENT, FORMER AND NEVER-SMOKERS: A CROSS-SECTIONAL CLINICAL STUDY PROTOCOL

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Despite public health efforts to reduce the health burden of cigarettes by encouraging smoking cessation, a proportion of smokers remain unwilling to quit. A shift from smoking cessation to tobacco harm reduction, based on smokers switching completely to potentially less harmful products such as electronic cigarettes (ECs), has been proposed as an alternative strategy. This is a single-centre, cross-sectional confinement study, involving healthy exclusive Vuse EC users and current, former, or never-smokers. Exclusive EC use and smoking status will be confirmed by urinary cotinine and exhaled carbon monoxide levels. Participants will be confined for 24 hours, during which they will use their usual product (EC or cigarette) as normal. Biomarkers of exposure and potential harm will be analysed in 24-hour urine and blood and compliance will be measured using N-(2-cyanoethyl)valine. The primary objective is to quantitatively assess differences between EC users and current smokers in urinary total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and 8-epi-prostaglandin $F_{2\alpha}$ Type III, exhaled nitric oxide, and carboxyhaemoglobin, white blood cell count, soluble intercellular adhesion molecule-1, and high-density lipoprotein. The secondary objectives are to quantitatively assess differences between EC users and current smokers in selected urinary biomarkers of tobacco exposure, 11-dehydrothromboxane B2, forced expiratory volume in 1 second as a percentage of predicted, carotid intima-media thickness and a quality-of-life questionnaire. Endpoints will also be compared between EC users and former and never-smokers. The results of this study are anticipated to add to the current knowledge about the role of ECs in tobacco harm reduction.

ABSTRACT BOOK

THE RELATIONSHIP OF MULTIFOCAL ATHEROSCLEROSIS, GENDER AND LIPID PROFILE PARAMETERS IN ACTIVE SMOKERS COMPARED TO PATIENTS WHO USED THS

Elizaveta G. Skorodumova

OP 15

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Background: According to modern data, "multifocal atherosclerosis" (MFA) is a hemodynamically significant atherosclerotic damage of arteries. To assess the MFA, the patient was assessed on three scales: Diamond-Forrester, Duke model, SADC2. The Duke model had the maximum efficiency in predicting atherosclerotic damage (92.5±3.43%), while Diamond-Forrester was in second place (84.2±2.2%), and CADC2 was in third place (64.2±4.4%). All presented scales had a limitation - they were developed to assess stenosing atherosclerosis of the coronary arteries and could only theoretically serve as a guideline for MFA screening. The purpose of the study was to assess the effect of smoking on lipid profile parameters and the development of multifocal atherosclerosis in active smokers compared to patients who used THS.

Material and Methods: The study included 102 patients with stable angina [62 male (60.8%) and 40 female (39.2%)]. Mean age was 64.2±12.7 years, mean smoking history 10.2±3.4. 52 patients had multifocal atherosclerosis, which corresponded to the minimum level of statistical significance $p<0.05$ according to the method of K.A. Otdelnova. The basis for the MFA detection scale was taken from the Diamond-Forrester, Duke, CADC models for assessing the risk of coronary artery stenosis, as well as the SMART scale, since endpoint predictors should be associated with atherosclerosis, however, such a relationship was statistically significant only for total cholesterol (TC) ($r=0.519$; $p<0.001$), low-density lipoproteins (LDL) ($r=0.586$; $p<0.001$), gender ($r=0.195$; $p=0.049$). The atherogenic coefficient (CA), not included in these scales, had a fairly high correlation coefficient $r=0.384$ ($p=0.048$). The sample of patients was divided into two subgroups: 1. Patients who smoked traditional cigarettes (n=70), and 2. Patients who used tobacco heating systems (n=32).

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Results: The development of MFA had an effect 6.77 times higher on the blood's level of TC, compared with the opposite situation, and the same holds true for LDL (4.94 times). The degree of mutual influence of factors and multifocal atherosclerosis looked as follows. For total cholesterol, the influence of the factor on the development of multifocal atherosclerosis was 3.549 at $p=0.040$, while the reverse situation was 24.012 at $p<0.001$; thus leading to a ratio of 1:6.77; the same pattern is typical for LDL - Factor → MFA - 3.593 at $p=0.032$, while MFA → factor 17.744 at $p<0.001$. The same pattern was observed for KA: 4.318 at $p=0.048$ and 4.165 at $p=0.023$. The CA level had a mutual influence of 1:1.04.

The level of high density lipoproteins did not affect the development of MFA ($F=1.80$, $p=0.19$). In patients with MFA, the male predominated ($F=3.960$, $p=0.049$). This model was tested using ROC analysis: the area under the curve was 0.798, which corresponded to a "good" score on the area under the curve scale.

As a result, various degrees of severity of multifocal atherosclerosis in patients were revealed. In a sample of cigarette smokers, the number of patients with severe multifocal atherosclerosis was statistically significantly higher than with alternative methods of nicotine delivery: 54 (77.1%) cases versus 145 (43.8%) cases.

Conclusions: 1) Multifocal atherosclerosis is a factor that increases the blood content of TC (6.77:1) and LDL (4.94:1). 2) In male the risk of developing MFA is higher than in female (1.037:1). 3) The use of tobacco heating systems in patients who are not motivated to quit smoking may reduce the risk of developing multifocal atherosclerosis and the associated increase in cholesterol and LDL.

ABSTRACT BOOK

HEAD AND NECK SQUAMOUS CELL CARCINOMA BY ANALYSIS OF TUMOR MICROENVIRONMENT

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OP 16

Background: Head and neck squamous cell carcinomas (HNSCCs) are particularly aggressive epithelial tumors that affect more than half a million patients worldwide each year. They represent a multi-factorial group of tumors caused by: alcohol, tobacco, and human papillomavirus (HPV) infections.

Discussion: Over the last ten years the overall 5-year survival rate of HNSCCs remained ~40-50%, in spite of significant improvement in clinical outcome of many tumor types. There are recent data that claim how some of these cells fulfill a suppressive role in the antitumor immune response. It is interesting that new clinical studies demonstrated that HPV (+) HNSCCs were among tumors with the highest immune infiltrates, while HPV (-) presented a reduced number of immune infiltrating cells.

Conclusions: Recent researches prove that tumor microenvironment of HNSCC has an important role in tumor progression, aggressivity, metastasis process, in addition to genetic aberrations and molecular alterations of cancer cells. New researches in stromal composition of the HNSCC may be useful in understanding of mechanisms of different responses to therapy, also can be used as a target for therapeutic purposes. Cancer-associated fibroblasts and immune cells, as well as their products found in neck squamous cell carcinoma significantly influence the biological properties of this tumor. Quitting is hard – even for people with cancer. Smokers diagnosed with cancer continue to smoke. Promoting smoking cessation should become an essential contributor to the treatment of cancer in all oncologic pathologies. In cases when patients can't quit smoking completely within the shortest possible period of time, doctors should focus on harm reduction strategies – tobacco harm reduction.

ABSTRACT BOOK

FAVOURABLE CHANGES IN BIOMARKERS OF POTENTIAL HARM WHEN SWITCHING FROM CIGARETTE SMOKING TO USING A TOBACCO HEATING PRODUCT FOR 12-MONTHS

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OP 17

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Compared to conventional cigarette smoke, tobacco heating products (THPs) generate lower levels of toxicants. In two 5-day, confined clinical studies and a 6-month, ambulatory clinical study, the glo THP has been shown to expose users to lower levels of particulate matter and harmful and potentially harmful compounds compared with smoking cigarettes. However, it is not known whether such exposure reductions lead to changes in biomarkers of potential harm (BoPH).

This controlled, randomised study investigated whether BoPH are modified when smokers switch from smoking cigarettes to using the glo THP in a real-world setting. Control groups consisted of never smokers and smokers who, after enrolment, abstained from cigarette smoking. Levels of the haemoglobin adduct N-(2-cyanoethyl)valine (CEVal) were used to determine compliance with smoking restrictions. Various BoPH related to oxidative stress, cancer, cardiovascular and respiratory diseases were assessed at a baseline study visit and here we report findings for these BoPH after 12-months.

By 12-months, favourable changes in the BoPH 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, 8-epi-Prostaglandin F2α type III, white blood cell count and fractional concentration of exhaled nitric oxide were observed in smokers switching to using glo when compared with those who continued smoking. Levels of 11-dehydrothromboxane B2 were also reduced compared with continued smoking and, whilst not statistically assessed, favourable trends directionally consistent with beneficial changes in health effects were observed in soluble intercellular adhesion molecule-1 and high-density lipoprotein with unfavourable trends seen in continuing smokers. For several of these BoPH, the changes were comparable to those experienced by smokers who abstained from cigarette smoking for the same twelve-month period.

Our findings, alongside chemical and toxicological studies undertaken on the THP used in this study, lead to the conclusion that smokers who would have otherwise continued to smoke and instead switch entirely to the use of this THP, will reduce their exposure to tobacco smoke toxicants and as a consequence are reasonably likely to reduce disease risks compared to those continuing to smoke.

CREATING CONFUSION: MISREPRESENTING SCIENTIFIC EVIDENCE JEOPARDIZES PUBLIC HEALTH

Carrie Wade, Markus Nordlund

OP 18

Philip Morris International

A recent review, "Should IQOS™ Emissions Be Considered as Smoke and Harmful to Health? A Review of the Chemical Evidence", by Uguna and Snape suggested that IQOS emissions fit the definition of both aerosol and smoke. Furthermore, the authors suggest that Harmful and Potentially Harmful Constituent (HPHC) levels in the IQOS aerosol are underestimated without considering how the product is actually used. In this review, the authors misinterpreted or misrepresented the data from some of the referenced publications while omitting publications that are relevant to the topic which leads to an incorrect conclusion. They rely on data that were generated using incorrect methodologies, misrepresent the findings from an air quality study as evidence for the existence of black carbon in IQOS emission, and compare IQOS aerosol to cigarette smoke using data sets generated from two separate studies. In fact, smoke from a cigarette contains approximately 5,000 chemicals above 100 ng per stick and carbon-based solid particles generated during tobacco combustion, while IQOS aerosol contains substantially fewer chemicals and no carbon-based solid particles – an aerosol chemistry study identified only 532 compounds at levels above 100 ng per stick for one variant of HeatSticks™. Moreover, with regard to estimations of HPHCs present in IQOS aerosol, the product design and product use data indicate that a 1:1 comparison between cigarettes and HeatSticks™ is appropriate when estimating the relative reduction in HPHC emissions. It is vital that scientific studies and reviews are comprehensive, accurate, and provide a complete understanding of the subject matter. This extends past maintaining scientific integrity and impacts people who rely on accurate information to make decisions. Publications that misinterpret, misrepresent, or do not consider the totality of scientific evidence add to the confusion surrounding smoke-free products, and may jeopardize public health by discouraging adult smokers from switching to non-combustible alternatives.

ABSTRACT BOOK

TOXICOLOGY AND AEROSOL CHEMISTRY

COMPARATIVE ASSESSMENT OF ELECTRONIC NICOTINE DELIVERY SYSTEMS AEROSOL AND CIGARETTE SMOKE ON ENDOTHELIAL CELL MIGRATION: THE REPLICA PROJECT

Massimo Caruso[1,2], Rosalia Emma[1], Alfio Distefano[1], Sonja Rust[3], Konstantinos Poulas[4,5], Antonio Giordano[6], Vladislav Volarevic[7], Konstantinos Mesiakaris[4,5], Silvia Boffo[6], Aleksandar Arsenijevic[7], Georgios Karanasios[4,5], Roberta Pulvirenti[1], Aleksandar Ilic[7], Angelo Canciello[6], Pietro Zuccarello[8], Margherita Ferrante[8], Riccardo Polosa[2,3,9], Giovanni Li Volti[1,2] (Replica Project Group)

OP 19

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Cigarette smoking is associated with impairment of repair mechanisms essential for vascular endothelium homeostasis. Reducing the exposure to smoke toxicants may result in the mitigation of the harmful effect on the endothelium and cardiovascular disease development. Previous investigations performed by the tobacco industries evaluated in vitro the effect of electronic cigarette (e-cig) compared to cigarette smoke demonstrating a significant reduction in endothelial cell migration inhibition following e-cig aerosol exposure. In the present study, we replicated one of these studies, evaluating the effects of cigarette smoke on endothelial cell migration compared to an e-cig, adding to the comparison two heated tobacco products (THPs). We performed an in vitro scratch wound assay on endothelial cells with a multi-center approach (ring-study) to verify the robustness and reliability of the results obtained in the replicated study. Consistently with the original study, we observed a substantial reduction of the effects of e-cig on endothelial cell migration compared to cigarette smoke. This reduction was observed with the exposure of endothelial cells to the extracts from THPs. Cigarette smoking reduced endothelial wound healing capability already at low concentrations (12.5%) and in a concentration-dependent manner, e-cig and HTPs aerosol showed no effect on endothelial cells until 80% -100% concentration. In conclusion, our study further confirms the importance of e-cig and THPs as a possible harm reduction strategy for cardiovascular diseases development in smokers.

ABSTRACT BOOK

HEALTH RISK PROFILE COMPARISON OF TOBACCO HEATING SYSTEM (THS) PRODUCTS VERSUS INDONESIAN "KRETEK" CIGARETTE

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OP 20

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Tobacco heating system (THS) products are intended to be a substitution product for conventional cigarette for smokers attempting to quit smoking. Tobacco products health risks are strongly correlated with the presence of harmful and potentially harmful constituents (HPHCs) within the product. The work was conducted following common steps in the risk assessment of chemicals, which includes hazard identification, hazard characterization, exposure assessment, and risk characterization. However, all hazard identification and characterization data, as well as quantification data of HPHCs in THS aerosol, were based on the literature study, whereas quantification data of HPHCs in kretek cigarette were based on our results. By comparing the HPHCs concentration and their hazard characterization in both the generated aerosol of THS product and smoke of kretek cigarette, as well as their exposure to consumer, health risk profile comparison of the two products is possible. Our results revealed that THS product showed lower health risk profile compared to kretek cigarette.

ABSTRACT BOOK

BIOMARKERS' EVALUATION IN ANIMAL OR HUMAN STUDIES

COMPARISON OF BIOMARKERS OF EXPOSURE TO NICOTINE, VOLATILE ORGANIC COMPOUNDS, AND HEAVY METALS IN US ADULT SMOKERS, EXCLUSIVE USERS OF ELECTRONIC NICOTINE DELIVERY SYSTEMS, AND DUAL USERS, PATH WAVE 5

Nathan M. Holt[1], Saul Shiffman[2], Ryan A. Black[1], Nicholas I. Goldenson[1], Mark A. Sembower[2], Michael J. Oldham[1]

OP 21

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Disclosures: The analysis was sponsored by Juul Labs, Inc. Authors Holt, Black, Goldenson, and Oldham are employed by Juul Labs, Inc. Through Pinney Associates, authors Shiffman and Sembower provide consulting on tobacco harm reduction to Juul Labs, Inc. on an exclusive basis.

The harm caused by cigarette smoking is overwhelmingly due to inhalation of products of combustion. For that reason, Electronic Nicotine Delivery Systems (ENDS), which deliver nicotine, but without combustion, are considered an important tool for tobacco harm reduction. Exposure to smoking-related toxicants can be measured using biomarkers of exposure (BOEs). This analysis uses biomarker data from wave 5 of the PATH Study of US adults (2018-19), analyzing creatinine-adjusted urinary BOEs for nicotine, 3 heavy metals, and 14 smoking-related volatile organic compounds (VOCs) (e.g., mandelic acid, a marker of styrene exposure, related to cancer; HPMA, a marker of exposure to acrolein, a respiratory and cardiovascular toxicant). Analyses compared BOE levels in 151 exclusive ENDS users to those in 1,341 exclusive cigarette smokers and in 1,846 past 30-day non-users of tobacco; BOEs in 115 dual users (cigarettes and ENDS) were also compared to smokers. As expected, markers of nicotine exposure in ENDS users and dual users did not differ from those in smokers. Except for one (PMA, a marker for benzene exposure) all other BOEs were significantly higher in smokers vs non-users, making them potentially informative. All of these BOEs, representing 13 VOCs and 3 heavy metals, were significantly lower in ENDS users than in smokers. On 11 of these BOEs, levels in ENDS users were also not significantly different than those in non-tobacco users. Dual users, who reported smoking an average of 10.3 [95% CI: 8.5,12.2] cigarettes per day, showed BOE levels intermediate between smokers' and ENDS users', consistently lower than smokers', significantly so for 6 of the BOEs. These findings in a real-world representative US population confirm and extend findings from other studies showing that use of ENDS is associated with exposure to much lower levels of many harmful and potentially harmful chemicals associated with smoking-related disease. This further reinforces the potential of ENDS for tobacco harm reduction among smokers.

ABSTRACT BOOK

NICOTINE EFFECTS ON ANXIETY BEHAVIOR AND BRAIN BIOCHEMICAL MARKERS IN ADULT MALE MICE

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OP 22

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Nicotine has been described as the main component of cigarette which is responsible for a wide variety of neurochemical and behavioral effects. The aims of the present study were to investigate the effects of nicotine intake on behavior parameters (anxiety-like behavior, mobility) acetylcholinesterase's (AChE) isoforms (G1, G4) activity on specific brain regions (cerebral hemispheres, cerebellum) of adult male mice.

Mice were divided into 4 groups: control, 1 cigarette', 2 cigarettes' and Tobacco Heating System 2.2 (THS2.2') smoke/aerosol exposed groups. The exposure was carried out in a unique smoking device with whole body exposure in smoke. The behavioral analysis was assessed by using the open field test (measurements at 2 time point: 5min and 10min). The activity of G1 and G4 AChE's isoforms was determined by using Ellman's colorimetric method.

The results show that no change has been found in both anxiety and mobility after smoke exposure of 1 cigarette.Mice exposed to smoke of 2 cigarettes exhibited increased anxiety levels and decreased mobility at the 10min time point. Moreover, mice exposed to THS2.2 aerosol exhibited decreased anxiety levels only at 5min time point and increased mobility in both time points. Furthermore, all the exposures reduce AChE's activity (both isoforms) in cerebral hemispheres. The exposure of 2 cigarette and THS2.2' aerosol caused reduction of G1 isoform's activity and the exposure of 1 and 2 cigarette smoke caused reduction of activity of G4 isoform in cerebellum.

ABSTRACT BOOK

IN VITRO MUTAGENICITY POTENTIAL OF A POD-BASED E-CIGARETTE AEROSOL COMPARED TO CIGARETTE SMOKE: THE REPLICA PROJECT

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OP 23

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Global scientific communities and government agencies recognized the Ames assay as an initial screen for the assessment of mutagenicity, therefore it is used to determine the mutagenic potential of chemical products, including cigarette smoke and modified risk products (MRPs) vapor. MRPs indicate the alternative products to cigarette smoke, able to deliver nicotine without smoke, such as electronic cigarette (e-cig) and tobacco heating products (THPs). Unlike conventional cigarettes, MRPs seem to exhibit reduced health risks and can help smokers to quit smoking. Previous studies on mutagenic effect of MRPs by the tobacco industries showed reduced mutagenicity compared to cigarette smoke. In the present study, we replicated one of these studies, assessing the mutagenicity effect of Myblu e-cig vapor on TA98 and TA100 Salmonella typhimurium strains with and without S9 enzymatic activation. 1R6F cigarette whole smoke (from 1 to 5 cigarettes, 9 puffs each, following HCI regime) and Myblu whole aerosol (from 60 to 300 puffs following CRM81 regime) were bubbled through 10 ml of PBS bacterial suspensions. Bubbling with filtered room air was used as negative control. Dose response curve of 1R6F smoke and Myblu aerosol mutagenic activities were calculated with fold changes in the number of revertants on the treated plates and the untreated controls, and tested for significance. Consistently with the original study, we observed significant dose-depended increase of revertant number for both TA98 and TA100 after exposure to 1R6F whole smoke, either with or without S9 enzymatic activation. Instead, the Myblu e-cig aerosol (up to 300 puffs) did not increase the number of revertants compared with the Air negative control in either strains with and without S9 enzymatic activation. In conclusion, we confirmed the reduced mutagenicity of e-cig aerosol compared to cigarette smoke, confirming that e-cigs can be a valuable tool for the harm reduction strategies in smokers.

ABSTRACT BOOK

SMOKING CESSATION

THE VALUE OF FAGERSTROM SCORE IN PREDICTING RECURRENCY OF SMOKING SIX MONTHS AFTER AN ACUTE MYOCARDIAL INFRACTION

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OP 24

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Background: Fagerstrom score is a validated marker of nicotine addiction in smokers.

Material and Methods: In a prospective study, we investigated a) the predictive value of Fagerstrom score for the smoking status in patients early after acute myocardial infarction (AMI) and b) the effectiveness of medically assisted smoking cessation programs in the prevention of relapsing to smoking post discharge. In 103 smokers (58±12 years, 79.6% males), we assessed Fagerstrom score during hospitalization for AMI. Patients filled a dedicated questionnaire including data on family, marital and educational status, habits related to smoking and were followed-up at 3 and 6 months after discharge.

Results: Twenty-eight patients (27.2%) did not quit smoking throughout the 6-months follow-up period (Fagerstrom score: 8.1±1.6), 39 patients (37.8%) ceased smoking at 3 months but relapsed to smoking at 6 months (score: 6.8±2.1), and only 34 patients (33%) had ceased smoking for 6 consecutive months (score: 5.2±2, $p<0.05$ for all comparisons between subgroups). By multivariate analysis, Fagerstrom score remained a significant predictor of smoking cessation at 6 months (OR: 0.72, 95% CI: 0.60-0.86, $p<0.001$). Out of 73 patients who abstained from smoking for the first 3 months post-AMI, those who participated in a smoking cessation program displayed lower rate of relapsing to smoking compared with those who opted to cease smoking without any support (33.3% vs 61.8%, $p=0.012$).

Conclusions: Fagerstrom score is a useful predictor of smoking cessation 6 months post-AMI. Patients participating in a smoking cessation program display lower relapse rates post-discharge suggesting the need of well-organized smoking cessation clinics for secondary prevention of heart disease.

5th Scientific Summit

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Novel products, Research & Policy

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POSTER PRESENTATIONS

ABSTRACT BOOK

EPIDEMIOLOGY & SOCIAL ISSUES

HOLISTIC APPROACH FOR TOBACCO HARM REDUCTION STRATEGY IN INDONESIA

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PP 25

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Indonesia ranks third in the number of smokers in the world after China and India. The number of smokers in Indonesia reaches 66 million (25.09%) of the total population of 263 million. Attempts in reducing the number of smokers have been continued yet still ineffective even in the last 10 years, and the number of smokers has continued to increase, especially among young people. From the medical aspect, smoking has a negative impact on health, including yellow teeth, neck cancer, lung disease, etc. The main problem that arises is that it is difficult to stop the smoking habit directly even though it has been through various efforts. This research aimed to identify and analyze the factors that caused a person to smoke, and which strategies were the most appropriate of tobacco harm reduction according to the real condition. The method used was the combination of inductive and deductive approaches. The inductive approach used the descriptive and inferential statistical analysis, based on the empirical data obtained from the respondents through questionnaires, while the deductive approach used the discussion by experts. The analysis methods used were SAST (Strategic Assumption Surfacing and Testing) and ECM (Exponential Comparison Method). The analysis results of 930 respondents and discussions by experts, involving health experts, policy makers, business actors, as well as active and passive smokers, academics and associations, showed that the main factors that cause people to become smokers were just wanted to try, and being invited by their friends, and soon after feeling good, then they got used to it. There were three factors that made them willing to quit smoking: health, economic reasons, and also family encouragement. The development of other low-risk products was an alternative to tobacco harm reduction for those who found it difficult to quit immediately (cold turkey). The most appropriate strategy to adopt tobacco harm reduction was government affirmative policy, as well as correct and complete education regarding the risks of smoking, based on scientific evidence through segmented communication by building Penta Helix collaboration and synergy involving business actors, academics, government, society, and the media.

ABSTRACT BOOK

PREVALENCE PATTERNS OF COMBUSTIBLE TOBACCO PRODUCTS AND NON-COMBUSTIBLE ALTERNATIVES IN THE GREEK POPULATION

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PP 26

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Background: Up-to-date monitoring of combustible and non-combustible nicotine products is important for public health planning according to WHO recommendations (WHO, 2021). We aimed to assess the prevalence in the use of these products and the perceptions concerning non-combustible alternatives to cigarettes in the adult Greek population in 2022.

Material and Methods: A cross-sectional survey was conducted throughout Greece in June 2022. Random digit dialing and proportional quota sampling was used to recruit respondents, with quotas based on the NUTS I regions of Greece (N=2,004). We defined smokers, users of e-cigarettes and users of heated tobacco products (HTPs) as those who had smoked at least 100 cigarettes, used e-cigarettes at least 100 times and used at least 100 sticks in their entire lifetime, respectively. Current use was defined as use in the past 30 days.

Results: The prevalence of use of any tobacco/nicotine product in the past 30 days was 32.7% (boxed/hand-rolled cigarettes: 28.3%, cigars/cigarillos/pipes: 2.0%, e-cigarettes: 3.2%, HTPs: 4.0%). Current daily users constituted 25.4% (boxed/hand-rolled cigarettes), 0.8% (cigars/cigarillos/pipes), 2.4% (e-cigarettes) and 3.4% (HTPs) of the sample. Exclusive use of boxed/hand-rolled cigarettes, cigars/cigarillos/pipes, e-cigarettes and HTPs was reported by 24.2%, 0.4%, 1.4% and 2.3% of the participants, respectively. In the sample, 93.7% had heard about e-cigarettes and 55.9% about HTPs before the interview. Of those, 31.7% and 40.4% believed that the use of e-cigarettes and of HTPs, respectively, is less harmful than cigarettes.

Conclusions: The prevalence of cigarette smoking in 2022 in Greece was higher compared to the prevalence in 2020 in the European region (28.3% vs. 23.0%) (WHO, 2021). Boxed/hand-rolled cigarettes remain the most used form of tobacco products and a small proportion report daily or exclusive use of alternative products.

ABSTRACT BOOK

MODELING THE POPULATION HEALTH IMPACT OF A MODIFIED RISK CLAIM ON AN EXISTING ENDS PRODUCT

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PP 27

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The US FDA Modified Risk Tobacco Product Application (MRTPA) process provides a regulatory pathway by which reduced exposure or modified risk claims for a specific tobacco product can be communicated to consumers. An MRTPA must show that promulgating such communication would benefit the population as a whole, taking into account both users and non-users of tobacco products. Building on the population health impact model (PHIM) of Wissmann et al. (2021), we estimate the impact on mortality from reduced-exposure messaging for JUUL ENDS. This agent-based PHIM was used to model transitions among nine tobacco use states (e.g., smokers switching to ENDS use, never-smokers initiating with ENDS). It compared a Base Case where ENDS were already available to a Modified Case where a reduced exposure claim applied to ENDS was additionally made. Tobacco use transition rates were drawn from Wissmann et al. (2021) and based on data from PATH, NHIS/CISNET, and published studies on JUUL users. The effect of the claim on transitions was estimated from a randomized experiment assessing behavioral intentions with and without the claim. The mortality risks of tobacco use behaviors were estimated from the NHIS Linked Mortality File. The model projects a robust net population benefit over 100 years, averting tens of thousands of premature deaths and more than a quarter million life-years lost as a result of making the reduced exposure claim. Sensitivity and tipping point analyses suggest that dissemination of the reduced-exposure claim yields a population benefit under a wide array of scenarios, and only results in population harm under grossly unrealistic assumptions about its effects on initiation and switching.

ABSTRACT BOOK

GINGIVAL RESPONSE IN VAPERS DURING EXPERIMENTAL GINGIVITIS: A PRELIMINARY STUDY

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PP 28

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Background: Smokers expressed less gingival inflammation and less gingival bleeding than non-smokers did. It is difficult to define a good clinical diagnosis and prompt treatment, when the symptoms are hidden in smokers. In experimental gingivitis, smokers displayed a less pronounced gingival inflammatory reaction compared to non-smokers. Today, e-cigarette or vape has become the most popular alternative tobacco product and has been said as less harmful than combustible tobacco, but no studies have been carried out to observe the gingival response of vapers during an experimental gingivitis.

Objective: To evaluate gingival response as assessed by gingival inflammation index and bleeding index during an experimental gingivitis in vapers, in comparison with smokers and non-smokers.

Material and Methods: Fifteen participants were divided into 3 groups, namely non-smokers, smokers, and vapers. Before the trial, dental cleaning was performed to reach zero plaque accumulation for each participant. Acrylic stents were custom-made to cover an area in lower jaw's teeth. Participants were instructed to wear the stent when brushing their teeth, throughout the duration of the experimental gingivitis phase (21 days), in order to avoid brushing of the lower jaw's teeth. Assessments performed were Plaque Index (Loe et al. 1967), Gingival Index (Loe et al. 1967), Angulated Bleeding Index (Van der Weijden et al. 1994) at the beginning of the study (H0), at 14 days (H14), and 21 days (H21) of the experimental gingivitis period. Salivary cotinine levels were confirmed by Salimetrics, ELISA at H0 and H21.

Results: During experimental gingivitis, bacterial plaque accumulated in all groups. Despite the similar amount of bacterial plaque accumulation, gingival and bleeding index of non-smokers and vapers were higher compared to smokers, while salivary cotinine levels of smokers and vapers were higher than these of non-smokers.

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Conclusions: There was an obvious increase in gingival bleeding and inflammation after 21 days of experimental gingivitis in vapers who consumed e-liquid with nicotine as confirmed by salivary cotinine levels and in non-smokers, contradicting the claim from previous studies that gingival vasoconstriction by nicotine component is the cause of reduced bleeding and inflammation. Under the limitations of the present study, we observed that vapers have similar gingival responses as non-smokers, during 21 days of experimental gingivitis.

ABSTRACT BOOK

THE EFFECT OF SHIFTING TO HEATED TOBACCO PRODUCTS ON METABOLIC SYNDROME IN LONG-TERM CIGARETTE SMOKERS: PRELIMINARY RESULTS OF A THREE-YEAR FOLLOW-UP

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Background: Cigarette smoking has been established as a risk factor for developing metabolic syndrome (MetS), which is a common condition in Kazakhstan affecting up to a quarter of the population. The aim of this study was to analyze the long-term effects of shifting to heated tobacco products (HTP) use on the prevalence of metabolic syndrome compared to continued combustible cigarettes (CC) use in long-term smokers.

Material and Methods: A cohort of 1200 participants (400 HTP and 800 CC) aged 40-59 years with a minimum of 10 pack-year smoking history were recruited and followed for 36 months. Data on demographic, medical history, smoking habits, etc. was collected. International Diabetes Federation was used as MetS definition. Specifically, subjects were considered to have MetS if they had had central obesity [waist circumference (WC) >94 cm in males and >80 cm in females for Caucasian; >90 cm in males and >80 cm in females for Asians] plus two and more of the following criteria: (1) hypertriglyceridemia, ≥150 mg/dL; (2) reduced HDL cholesterol, <40 mg/dL in males and <50 mg/dL in females; (3) high blood pressure, ≥130/85 mm Hg; (4) raised fasting plasma glucose, ≥100 mg/dL. Chi-squared test were used to compare the frequency of MetS between visits (baseline, 12-, 24-, and 36-months).

Results: The prevalence of MetS was 35% in CC and HTP users at baseline. Over the observed period (36-months) the prevalence of MetS significantly decreased for HTP users from 35% to 28% (P=0.03), compared to 35% to 30% (P=0.32) decrease in CC users. The prevalence of reduced HDL cholesterol and raised fasting plasma glucose components decreased for both CC and HTP users, whereas central obesity and high blood pressure components significantly decreased for HTP users only (P=0.003 and P=0.03 respectively).

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Conclusions: This study demonstrated that while both CC and HTP users experienced decrease in the prevalence of MetS components, HTP users experienced decreases in a larger number of MetS components. The results of this study suggest that HTP might be a less deleterious alternative compared to CC in people with long history of CC use and who cannot quit smoking.

ABSTRACT BOOK

BIOMARKERS OF EXPOSURE AND POTENTIAL HARM IN EXCLUSIVE USERS OF NICOTINE POUCHES AND CURRENT, FORMER, AND NEVER SMOKERS: A PROTOCOL FOR A CROSS-SECTIONAL CLINICAL STUDY

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Background: Tobacco harm reduction (THR) aims to reduce the health burden of cigarettes by encouraging smokers to switch to using alternative tobacco or nicotine products. Nicotine pouches (NPs) are smokeless, tobacco-free, oral products that may be beneficial as part of a THR strategy.

Objective: This 2-center, cross-sectional confinement study conducted in Denmark and Sweden aimed to determine whether biomarkers of exposure (BoEs) to tobacco toxicants and biomarkers of potential harm (BoPHs) in exclusive users of NPs show favorable differences compared with current smokers.

Methods: Participants were healthy NP users (target n=100) and current, former, or never smokers (target n=40 each), as confirmed by urinary cotinine and exhaled carbon monoxide concentrations. During a 24-hour confinement period, participants were asked to use their usual product (NP or cigarette) as normal, and BoEs/BoPHs were measured in blood and 24-hour urine samples, with compliance determined using anabasine, anatabine, and N-(2-cyanoethyl)valine. BoEs/BoPHs were compared between NP users and current, former, and never smokers. Urinary total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (BoE to nicotine-derived nitrosamine ketone) and urinary 8-epi-prostaglandin F2α type III, exhaled nitric oxide, blood carboxyhemoglobin, white blood cell count, soluble intercellular adhesion molecule-1, and high-density lipoprotein cholesterol (BoPHs) were evaluated as primary outcomes. Other measures include urinary 11-dehydrothromboxane B2, forced expiratory volume, carotid intima-media thickness, self-reported quality of life, and oral health.

Results: The results of this study were received mid-2022 and will be published late 2022 to early 2023.

Conclusions: The results of this study will provide information on toxicant exposure and biomarkers associated with the development of smoking-related diseases among users of NPs compared with smokers, as well as on the potential role of NPs in THR.

ABSTRACT BOOK

WHAT HAPPENS WHEN YOU HEAT NICOTINE MOLECULE IN DIFFERENT ATMOSPHERES – A MOLECULAR MODELLING PERSPECTIVE

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The fate of nicotine molecule, when heated at different temperatures in different surroundings (i.e. atmospheres) is of fundamental importance to harm reduction when inhaling the aerosols of different tobacco products. In the present study, we tackle this issue from the viewpoint of molecular modelling. Series of *ab initio* molecular dynamics simulations of free nicotine molecule as well as of nicotine molecule in the presence of oxygen molecules at series of different temperatures ranging from 600 to 1200 K are performed with the atom-centered density matrix propagation scheme (ADMP). Simulations are performed at different levels of theory. The possible degradation pathways implied by the generated molecular dynamics trajectories are related to the products detected in the smoke of conventional cigarettes and aerosols generated by electronic devices for controlled heating of tobacco.

ABSTRACT BOOK

CANCER RISK ASSESSMENT OF HEATED TOBACCO PRODUCTS AEROSOL BASED ON DIFFERENT METHODOLOGIES COMPARISON

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Background: Heated tobacco products (HTPs) are becoming more and more popular during the last decades among smokers. HTPs recent innovative non-combusted products due to heating of tobacco up to 350°C (lower than 600°C as in conventional cigarettes). Unfortunately, combustible cigarette smoking is the most important preventable cause of cancer. Therefore, strict standards and requirements have been developed and applied to these products. Thus, HTPs offer alternatives to combustible cigarettes and have partially replaced combustible cigarettes. Moreover, the HTPs use is rising, but potential health risk in the result of long-term use has not been studied completely. The aim of the study is to analyze and compare the different methodologies based on evaluation of the cancer risk associated with the use of HTPs.

Material and Methods: Advanced bibliographic study of 35 bibliographic sources from databases: Medline, Scopus, HINARI, PubMed, and Cochrane Electronic.

Results: The cancer risk assessment using different methodologies were analyzed and compared. The first method was based on the change in cumulative exposure (CCE) of the compounds emitted. Another was focused on margin of exposure (MOE) determination, which represented as the ratio between the toxicological thresholds of the compound to the estimated human expose (with a higher MOE indicating a lower risk). The next one attempted to estimate the cancer potencies of various product types using levels of chemical constituents found in the aerosols of each product type and their associated inhalation unit risks.

Conclusions: Three modelling cancer risk assessments estimated that the heated tobacco product under performed investigations had a lower cancer potency (compared to that of conventional cigarettes).

ABSTRACT BOOK

JUUL IN VITRO TOXICOLOGY, A COMPARATIVE ASSESSMENT BETWEEN LUNG AND BRONCHIAL CELL LINES

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E-cigarette devices that youth prefer have evolved substantially over time, from early-generation cigar like ECs, to more advanced modifiable tank-style ECs, to the recent emergence of a sophisticated, sleekly designed, discreet high-tech device called JUUL. JUUL is an electronic cigarette which uses nicotine salts, prefilled with a high concentration in pods, rather than free-base nicotine. Due to its popularity among young ages, concerns have been voiced and public health officials have pressed the FDA to step in. E-liquids contain various combinations of nicotine, flavors, and carriers. These factors affect nicotine delivery, appeal, and ease of product use and underscore the degree to which individual preferences may play a role in use patterns. Cartridge nicotine solution in ECs seems to exacerbate asthmatic symptoms by elevating infiltration of inflammatory cells including eosinophils into airways and promotion of oxidative stress.

The aim of this study is to evaluate the effects of JUUL on human alveolar cell lines of upper respiratory and bronchial epithelium, besides with conventional cigarette exposure, on cell toxicity and oxidative stress. AqE extracts from JUUL different flavors were created in different concentrations with Borgwaldt LM4E vaping machine, to determine the concentration that exhibits toxicity. 1R6F reference cigarette was used as control and the condensates prepared with Borgwaldt LM1 smoking machine. A549 human alveolar cell line and NCI-H292 bronchial epithelial cells were tested. Cell toxicity was monitored with MTT assay for cell viability and Superoxide Dismutase Assay was performed as indicator of ROS activity. The results indicate a loss of viability only in high puff volumes, in high concentrated AqEs, with small differences between different flavors in 24h treatment. In 48h treatment differences were observed between flavors toxicity. SOD induction observed in different flavors between the two cell lines.

ABSTRACT BOOK

1R6F WHOLE SMOKE VS VAPOR PHASE CELL TOXICITY: ESTABLISHING AN AIR-LIQUID INTERFACE EXPOSURE SYSTEM

Konstantinos Mesiakaris[1,2], Marilena Kaperoni[1,2], Konstantinos Poulas[1,2]

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There are several different methods that have been used to investigate and assess the biological effects of cigarette smoke, with a range at the design of an inhalation machine. Smoking Machines are designed to fulfill the requirements of in vitro experiments as well as of various other research tasks. Many old studies used hand-made smoking delivery machines and it was difficult to transfer the knowledge and maintain strict conditions on the experiments. Newest studies use experimental set-ups with automated methods, that can follow experimental regimes such as Health Canada Intense (HCI), ISO and CRM and control the experimental parameters strictly, such as puff volume, puff duration, puff profile etc. Several in vitro techniques have been reported, which involve the exposure of submerged cellular cultures to either total particulate matter (TPM) or aqueous cigarette smoke extracts.

The aim of the present study was to set-up LM4E vaping and LM1 smoking machines by Borgwaldt and the use of Air liquid Interface (ALI) technique for experimentation. Cell cultures performed at the air-liquid interface facilitate the establishment of stable and functional 3D models of the respiratory tract. In these models, the basal side of the cells is in contact with the culture medium, and the apical side is in contact with the air. For that purpose, 1R6F cigarette was tested on NCI-H292 cells, in two ways, as whole smoke and vapor phase, following ISO and HCI regimes. Cell viability was measured using NRU assay.

ABSTRACT BOOK

CAN B-ESCIN MAKE CIGARETTE SMOKERS HEALTHIER? THE USE OF HORSE CHESTNUT SEED EXTRACT IN TOBACCO HARM REDUCTION

Malwina Sołtysiak, Magdalena Paplińska-Goryca, Paulina Misiukiewicz-Stępień, Paulina Wójtowicz, Rafał Krenke, **Katarzyna Koziak**

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Among chemicals found in cigarette smoke, World Health Organization Study Group on Tobacco Product Regulation (WHO TobReg) identified six volatile aldehydes regarded as priority toxicants. An estimation of exposure to aldehyde from cigarette smoke and risk assessment studies show that due to their pervasiveness and documented toxicity, acrolein, acetaldehyde, formaldehyde, propionaldehyde, crotonaldehyde, and butyraldehyde have particularly detrimental effects on human health. While mandatory lowering aldehyde levels in cigarette smoke is a part of regulatory strategy for reducing exposure of smokers to toxicants, pharmacological approaches mitigating their health impact are also considered. For example, aldehyde-related damage can be mitigated by boosting endogenous aldehyde dehydrogenase (ALDH) activity. ALDH is a superfamily of 19 enzymes that catalyze oxidation of aldehydes to carboxylic acids. This enzymatic activity prevents the accumulation of aldehydes derived *i.a.* from exogenous exposures and represents a major cytoprotective mechanism of the ALDH family members.

A recent study revealed that β-escin, a mixture of triterpenoid saponins extracted from the seed of horse chestnut tree (*Aesculus hippocastanum* L), is a strong activator of ALDH activity. Here we report the effect of β-escin on ALDH activity and gene expression in primary human nasal epithelial cells exposed to cigarette smoke extract (CSE). We revealed that while both β-escin (1μM) and CSE (5%) stimulated ALDH activity, their combination evoked much more pronounced response (at 24h: 132% and 137% vs 174%, respectively). The observed increase in the enzyme activity correlated with an increased expression of ALDH1A3, ALDH3A2, ALDH3B1 and ALDH18A and was significantly higher in the cells treated with the combination of β-escin and CSE. Importantly, β-escin reversed CSE-induced inhibition of ALDH1A1 and ALDH2 expression.

These results suggest that increasing the ALDH gene expression and enzyme activity by β-escin may facilitate aldehyde removal and thus be useful in reducing cigarette smoke toxicity. Such approach might be a part of harm reduction strategy which should be applied for smokers that are unwilling to quit or failed to quit smoking conventional cigarettes.

ABSTRACT BOOK

EFFECT ON BEHAVIOR AND BIOCHEMICAL MARKERS AFTER VAPING AND ORAL ADMINISTRATION OF GRAPE STEMS EXTRACT

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Background: Electronic cigarettes (ECigs) use has increased substantially in recent years. ECigs have been proposed as a potentially effective smoking cessation tool, they deliver nicotine, thus dealing with the chemical part of the addiction, and, at the same time, they provide sensory and motor stimuli like smoking. In addition, the flavored liquid ECigs from plant extracts have been widely used as potentially beneficial due to plant properties.

The winemaking procedure results in the production of stems, by-products that are not environmentally friendly. However, grape stems are rich in polyphenols and, therefore, they are putatively beneficial for human health.

The aim of the present study is to investigate the effect of the grape stems extract on behavior, redox status (liver and brain regions) adult male mice and its possible use in e-liquids maintaining its antioxidant and anxiolytic properties.

Material and Methods: The grape stem extract was derived from a native Greek vine, namely Mavrodaphne and was rich in polyphenols (205.2 mg/g extract). LM4E Vaping Machine by Borgwaldt was used to create an aquatic extract enriched with vaping constituents of the E-liquid (VG/nicotine) enriched with grape stems aquatic extracts (AqE).

The stem extract was administrated in two different ways a) intraperitoneally (IP) (AqE that contains nicotine, VG, stem extract and saline) and b) orally (gavage) (stem extract) for 28 days (long-term). Behavior analysis was assessed by using the open-field test, followed by video-tracking software (Any-maze 6.3) analysis. Antioxidant analysis was performed by determining the SOD activity.

Conclusions: Anxiolytic-like behavior was observed after the stem extract and aqueous extract administration. Stem extract treatments also showed antioxidant effect. In conclusion, long term administration of grape stem extract, rich in polyphenols, appears to have anxiolytic, antioxidant activity.

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