

Scientific paper

The limits of ‘Generally Recognized As Safe’ classification for inhaled compounds in Electronic Nicotine Delivery Systems

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Abstract

Electronic Nicotine Delivery Systems (ENDS) liquids contain compounds deemed safe for ingestion “Generally Recognized As Safe” (GRAS), yet lack inhalation safety data, posing risks, especially to adolescents. This study analysed chemical discrepancies in ENDS via gas chromatography–mass spectrometry and surveyed Slovenian secondary students on nicotine use. Analysis revealed cytotoxic substances when inhaled and unlisted solvents, exposing a mismatch between labelled and actual content. Most adolescents who used ENDS focused only on nicotine percentage and largely ignored product composition, despite knowing nicotine is harmful. Findings stress the need for toxicological evaluation, clearer labelling, stricter regulation, and targeted youth education.

Keywords: Electronic Nicotine Delivery Systems (ENDS), vapes, chemical analysis, questionnaire, school students, nicotine use patterns.

1. Introduction

Despite regulatory measures, the global ENDS (Electronic Nicotine Delivery Systems) market continues to grow. In 2024, it was valued at approximately \$4.6 billion, and it is projected to reach \$7 billion by 2032, with the annual growth rate of around 4.9%. Key drivers include the search for alternatives to traditional smoking habits and technological innovations (e.g. pod systems, adjustable devices).¹ The Tobacco Products Directive in EU (TPD, 2014/40/EU)² and The Family Smoking Prevention and Tobacco Control in USA (FDA, Public Law 111-31 [H.R. 1256])³ enforce strict guidelines on tobacco manufacturers to create a controlled environment, reducing health risks and promoting informed consumer choices. Lately, in 2024 in EU, the extension of TPD to »EU tobacco traceability system« is including all tobacco products other than cigarettes and roll-your-own tobacco for achieving a uniform identifier for all products.⁴

In a complex system of tobacco products regulations, which can still vary by country, state or region, common

requirements for e-cigarette packaging labels include: nicotine content (mg/mL or as a percentage); health warnings; product and manufacturer information and most importantly ingredient list with appropriate toxic substance warnings.^{5,6} The ingredient list on e-cigarette packaging typically includes two common solvents: propylene glycol (PG) and glycerine (G) (for a smoother inhalation and as flavour carriers), and generally named flavourings and additives. The late two categories include "natural and artificial flavourings" or specific individual aromatic compounds and additives which should be listed by their specific names, if they are included in the e-liquid.

For the EU market, the ingredient list is expected to follow Table 4 of the TPD (article 20, named: »Description of ingredients contained in the product«),² where each chemical used in the product should have the following listed variables: CAS number, IUPAC identification, function, REACH (Registration, Evaluation, Authorization and Restriction of Chemicals), CLP (Classification, Labeling and Packaging), toxicity, etc. For the USA market, the

ingredients list established in 2012 by the U.S. Food and Drug Administration (FDA 2012)⁷ contain 93 harmful and potentially harmful constituents (HPHCs) to be followed. These regulations targeted only four tobacco product types (cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco). Legislative loopholes allow e-cigarette and ENDS manufacturers to overpass gaps in regulations, attracting young users with a wide variety of flavours and creative branding. Although FDA regulations ban most flavours in tank and cartridge-based e-cigarettes, disposable e-cigarettes, which are popular among youth, remain largely unregulated due to ambiguities in defining what a cartridge is.⁶ However, knowledge gaps exist regarding whether certain HPHCs are present in ENDS e-liquids and aerosols and whether all possible components could ever be included in such a list.⁸

Inhalation of e-cigarette aerosol exposes lung tissue to various chemicals, including nicotine, propylene glycol (PG), glycerine (G), and flavourants.⁹ These flavouring chemicals are evaluated under the GRAS ("Generally Recognized As Safe") safety criteria, which are intended for food additives, not for inhaled substances. Some e-cigarette companies claim their ingredients are safe based on GRAS, but this designation applies only to oral consumption, not inhalation.¹⁰ Besides the list of added chemicals, attention should also be given to the nicotine form (free-base or monoprotonated nicotine, etc.). Moreover, the type and amount of organic acids, alcohols, esters, and ketones (intended as solvent use) should be analysed, because their breakdown products have different toxicity profiles than their parent compounds found initially in conventional e-cigarettes and liquids.¹¹ The variability in e-liquid formulations, device designs, nicotine forms, and usage behaviours complicates the quantification of HPHCs in ENDS, making it different from tobacco products.

Amid these scientific gaps, disposable e-cigarettes have emerged as the most widespread and least regulated ENDS category, aggressively marketed to youth through social media, influencers, and sleek designs. According to the World Health Organization, 88 countries lack minimum age restrictions and 74 have no regulations in place, fostering a global landscape where youth vaping continues to escalate.¹² Epidemiological observations suggest that a significant proportion of young individuals have tried these products at least once, although comprehensive data on regular use patterns and addiction outcomes are still lacking.

According to National Institute of Public Health of the Republic of Slovenia (NIJZ) data presented by Koprivnikar, 30% of Slovenian secondary school students reported using e-cigarettes in 2023 (2,089 13-year-olds, 2,151 15-year-olds, and 2,309 17-year-olds).¹³ Among individuals aged 35 to 44 who have ever smoked, 63% began smoking before the age of 18, 95% started by the age of 21, and 99% initiated use before the age of 25.¹³ These findings highlight that tobacco and e-cigarette initiation is concen-

trated in adolescence and early adulthood, with almost no onset of smoking after age 25. This underscores the importance of preventive strategies targeting youth. One potential factor is participation in sport and physical activity, which has been suggested as a protective influence against e-cigarette use. However, evidence remains limited and largely qualitative. Given the lack of comparable data for Slovenia, our study aims to explore whether sport habits correlate with consumer awareness and vaping behaviour among young people. Although some preventive strategies show promise, more evidence and focused interventions are necessary to support long-term success.¹⁴

The main goal was to examine discrepancies between the declared and actual composition of flavoured vape products available on the Slovenian market, focusing on disposable e-cigarettes. Additionally, the study aimed to identify the most prevalent compounds permitted under GRAS standards and assess potential health risks associated with their inhalation. Besides these, the study aimed to gain some insight into young users' behaviors and usage patterns by examining youth nicotine use and perceptions through a closed-ended questionnaire, analysing consumption habits, and attitudes toward various nicotine products in Slovenia.

2. Experimental

2.1 ENDS - Vape specifications

Vapes (9 types of disposable e-cigarettes, specified in the Supplemental Tables) purchased in the local market in the winter 2023/2024 in the capital city of Slovenia, Ljubljana, were analysed for differences between labelled (Table S1) and measured compounds (Table S2). The names in Table S1 are reproduced exactly as they appear on the labels of the original packaging of disposable vapes from five different producers (available upon request to the corresponding author), each of them with a distinct flavour. The maximal content of nicotine or nicotine salt in all vape samples was labelled to be less than 20 mg/mL (except in PI4, 10 mg/mL), within a 2 mL load (offering 550–600 puffs), placed in the cartridge fill. The general instructions included a 5-second wait until the cartridge blinked 4 times, after which the user could inhale the content, described to be 0.02 mg of nicotine per inhalation.

2.1.1 Compound analyses by gas chromatography mass spectrometry (GC-MS)

The vape liquid was diluted 1:100 with hexane and analysed in triplicates by gas chromatograph with a mass-selective detector Agilent 6890 Series GC System with Agilent 5973 Mass Selective Detector (GC-MS, Agilent Technologies, Santa Clara, California, USA). Volatiles were separated on a 15 m × 0.25 mm × 0.25 µm Rxi-35 Sil MS (Restek, USA) capillary column.

The temperature program used was: initial temperature 50 °C (2 min), gradient 10 °C min⁻¹ to 270 °C. The mass spectrometer was operated in the electron ionization mode at 70 eV, the temperature of the MS Quad was set at 150 °C, the interface 270 °C and the ion source at 230 °C (50–550 amu; scan mode 10 000 amu s⁻¹). Compounds were identified by comparing the experimental mass spectra with the mass spectral library (NIST02, Gaithersburg, Maryland, USA). The peak area for quantification was measured in the total ion current (TIC) chromatogram. The volatiles listed in Table S2 represent compounds whose peak area accounts for more than 0.1% of the total area of all measured peaks and are calibrated against a free nicotine standard; therefore, they are expressed as nicotine concentration equivalents.

2.1.2 Questionnaire

An online survey with 13 items was conducted to assess trends in adolescent nicotine product use, their attention to ENDS labelling, and the influence of sports participation on such behaviour. The survey used an open-source web application system for student evaluation of educational work at the University of Ljubljana (UL) (www.1ka.si; 1KA - One Click Survey). The 1KA platform prohibits collecting personal data without prior knowledge and consent, and complies with the Personal Data Protection Act and EU Regulation 2016/679 (GDPR), ensuring strict adherence to data privacy standards. Data were collected anonymously and participants signed consent forms after the research protocol was explained to them and could withdraw at any time. Ethical research guidelines were followed at all the stages. This study was reviewed and approved by the Ethics Commission of the Faculty of Education of the University of Ljubljana (No. 13/2023) on August 25, 2023.

The questionnaire items are presented in Supplement Tables (Table S3, Table S4, Table S5, Table S6). They included closed-ended multiple-choice questions and several items rated on a 4-point Likert scale. The survey gathered demographic data (grade level, gender, sports involvement), information on nicotine use (frequency, product types, reasons), and insights into participants' attitudes, risk perceptions, and views on product harmfulness. A total of 80 secondary school students participated in the

survey (mean age = 15 years). The sample was purposive and not representative, intended to provide a rapid and simple overview of nicotine product use among adolescents rather than to generalise results to the entire population. Given the non-probability sampling design, confidence intervals and measures of population representativeness were not calculated.

3. Results and discussion

3.1 Listed and identified compounds in vapes

Lately, Nottage and co-workers⁹ examined more than 100 ENDS (48 disposable vapes and 60 e-liquids) from England, Canada, and the United State and found them of variable compliance with regulations and inconsistent in labelling. While most products met basic health warning requirements, compliance with rules on flavours and marketing elements was lacking. A considerable discrepancy (Table 1), was observed between the reported number of ingredients (Table S1) and those actually quantified (Table S2) in our study, as well.

Using GC-MS provided a direct measurement of volatile compounds. The identified compounds were compared to the chemicals listed on the original packaging, and the proportion of identified compounds that matched the listed ones ranged from 75% to 29%, with an average match of 51%. All listed chemicals are volatiles, so their absence led us to two possible reasons: either the labelling uses a template, or the listed compounds were present at lower concentrations and thus not detected under our procedure, given the 0.1% of the total area (0.03 mg/mL nicotine equivalents) threshold.

As illustrated in Fig. 1, the market offers a wide variety of vape flavours, resulting in distinct chemical profiles. Some formulations exhibit a high concentration of esters (e.g., W1, SW9, GI3), while others are characterized by pronounced aromatic compounds such as terpenes and related substances (e.g., TA8, MI7, WI1). Despite these compositional differences, all products consistently contained the common solvents propylene glycol (PG) and vegetable glycerine (VG).

Nicotine, in terms of molecular structure, is a dibasic compound composed of a pyridine ring linked to a hydrogenated pyrrole ring.¹⁵ Upon interaction with acidic com-

Table 1. Analysis of discrepancies between listed and GC-MS-identified chemicals, and their matches, per vape product.

	A6 (18 mg/mL)	AS5 (20 mg/mL)	GI3 (20 mg/mL)	MI7 (20 mg/mL)	TA8 (20 mg/mL)	PI4 (10 mg/mL)	WI2 (20 mg/mL)	SW9 (20 mg/mL)	WI1 (20 mg/mL)
Number of listed chemical	4	6	19	14	12	5	12	17	20
Number of identified chemicals	40	19	12	7	19	15	33	27	21
Number of matched chemicals (identified and listed)	3	4	7	4	6	2	7	10	9
% of matched vs. listed chemicals	75	67	37	29	50	40	58	59	45

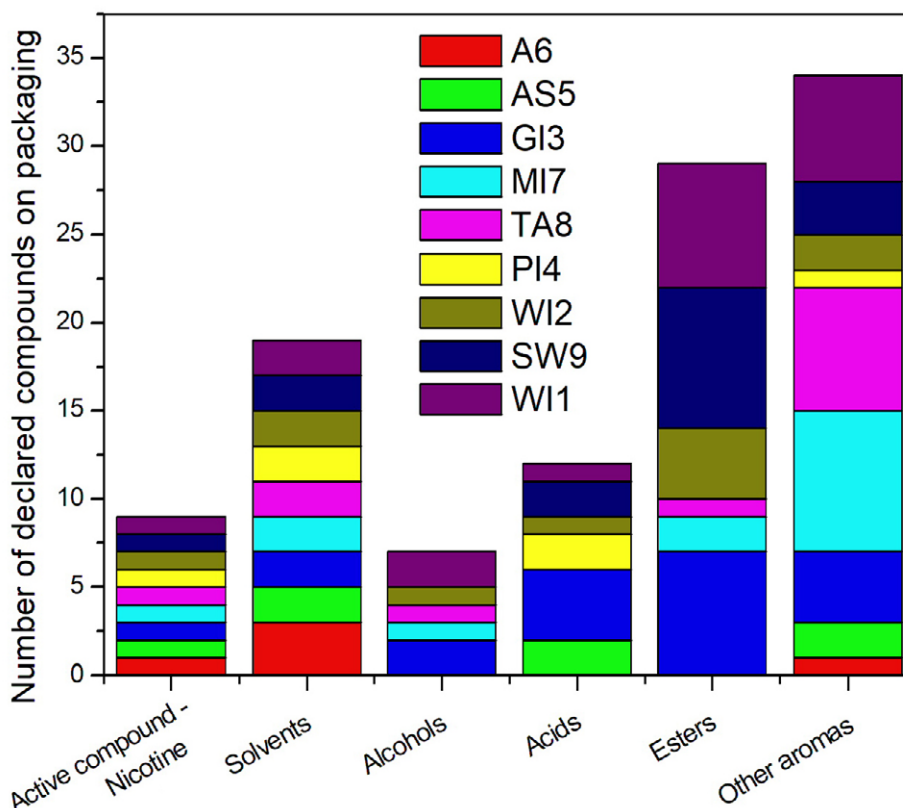


Fig. 1 Distribution of labelled chemical compounds in tested vape samples, grouped by primary chemical classes. Compound profiles, which vary across producers, are detailed in Table S1.

ponents, nicotine can bind up to two protons, thereby forming a salt. Consequently, nicotine may exist in three distinct states: the free molecular form, the single-protonated form, or the double-protonated form.¹⁵ In our analysis, the free molecular form was taken as the standard. Since certain ENDS products reported nicotine content in the form of nicotine salts, the quantified nicotine (Table S2) corresponds to the free form. Dilution with organic solvents such as cyclohexane and hexane allowed direct measurement of free nicotine with high analytical accuracy and precision. This explains why the experimentally determined values were consistently lower than those declared on the labelling of the analysed vaping products.

While glycerine and propylene glycol are well-characterized ingredients in ENDS, earlier studies suggested that standard glycerine levels in tobacco did not increase smoke toxicity or biological activity and might even reduce certain harmful compounds.¹⁶ However, more recent research indicates notable toxicological effects. Propylene glycol (PG) and vegetable glycerine (VG) aerosols have been linked to epithelial inflammation and immune responses,^{17,18} as well as cardiovascular risks due to thermal degradation products, such as formaldehyde and acetaldehyde, which contribute to endothelial dysfunction.¹⁹ Both PG and VG were consistently reported as constituents in the tested vape products, occurring in substantial quanti-

ties across varied PG/VG ratios ranging from: a) PG $\leq 30\%$ /VG $\geq 70\%$, b) $30\% < \text{PG} < 50\%$ / $50\% < \text{VG} < 70\%$, to c) PG $\geq 50\%$ /VG $\leq 50\%$.²⁰

3.2 Toxicity of inhaled flavour chemicals designated as "Generally Regarded As Safe" (GRAS)

Although flavour chemicals in e-cigarettes are designated as "Generally Regarded As Safe" (GRAS) for ingestion, they are not endorsed for inhalation by the Flavour Extract Manufacturers Association (FEMA).²¹ Certain flavours in e-liquids or e-cigarette aerosols have been shown to trigger toxic responses in various organ systems, including the respiratory and cardiovascular systems.²² Cinnamaldehyde was the most frequently reported cytotoxic flavouring agent, followed by vanillin, menthol, ethyl maltol, ethyl vanillin, benzaldehyde, and linalool, all of which were found in our experiment. Additional concerns arise from the fact, that all these complex chemicals can interact with each other at elevated temperatures. It is already known that vanillin, ethyl vanillin (vanilla), and benzaldehyde (almond-like scent) undergo reactions with the e-liquid solvent, propylene glycol, to form acetals that efficiently transfer to e-cigarette aerosols and may be more toxic than their parent aldehydes.²²

The absence of data does not imply safety. Many chemicals considered safe for ingestion or topical use may pose risks when inhaled. More emphasis was placed on the dominant flavouring compounds, which, as reported previously,^{21,23,24} exhibited concentrations exceeding 1 mg/mL in at least one of the analysed products. In our survey, the toxicity of volatiles exceeding 0.3 mg/mL (Figure 2, Table S2, expressed in nicotine equivalents) in vapes were analysed in detail. These compounds were: 5-methyl-2-propan-2-yl cyclohexan-1-ol (menthol), benzyl alcohol, 3-hydroxy-2-methylpyran-4-one (maltol); 2-ethyl-3-hydroxypyran-4-one (ethyl maltol); benzoic acid, 4-hydroxy-3-methoxy benzaldehyde (vanillin), 3-ethoxy-4-hydroxybenzaldehyde (ethyl vanillin), 1-ethyl-3-piperidinol, and (*Z*)-*N,N*-dimethylnon-7-enamide (Fig. 2).

3.3 Benzyl alcohol

Benzyl alcohol has historically been considered a compound with low toxicity under typical dermal and inhalation exposures. No Federal Occupational Safety and Health Administration Permissible Exposure Limit (OSHA PEL) currently exists for it, though serious toxicity was previously observed in neonates with immature hepatic function following parenteral exposure.²⁵ More recent findings, however, raise concerns about its inhalation risks, particularly in vaping contexts. Benzyl alcohol, used as a solvent and flavour enhancer, was detected in 42 of 65 e-liquids at concentrations up to 1687 mg/L and is recognized as a dermal sensitizer and allergen.²⁶ In our study it was found in levels 15-times higher in two cases (23.75 ± 0.79 mg/mL nicotine eq. in AS5, and 27.81 ± 2.19 mg/mL

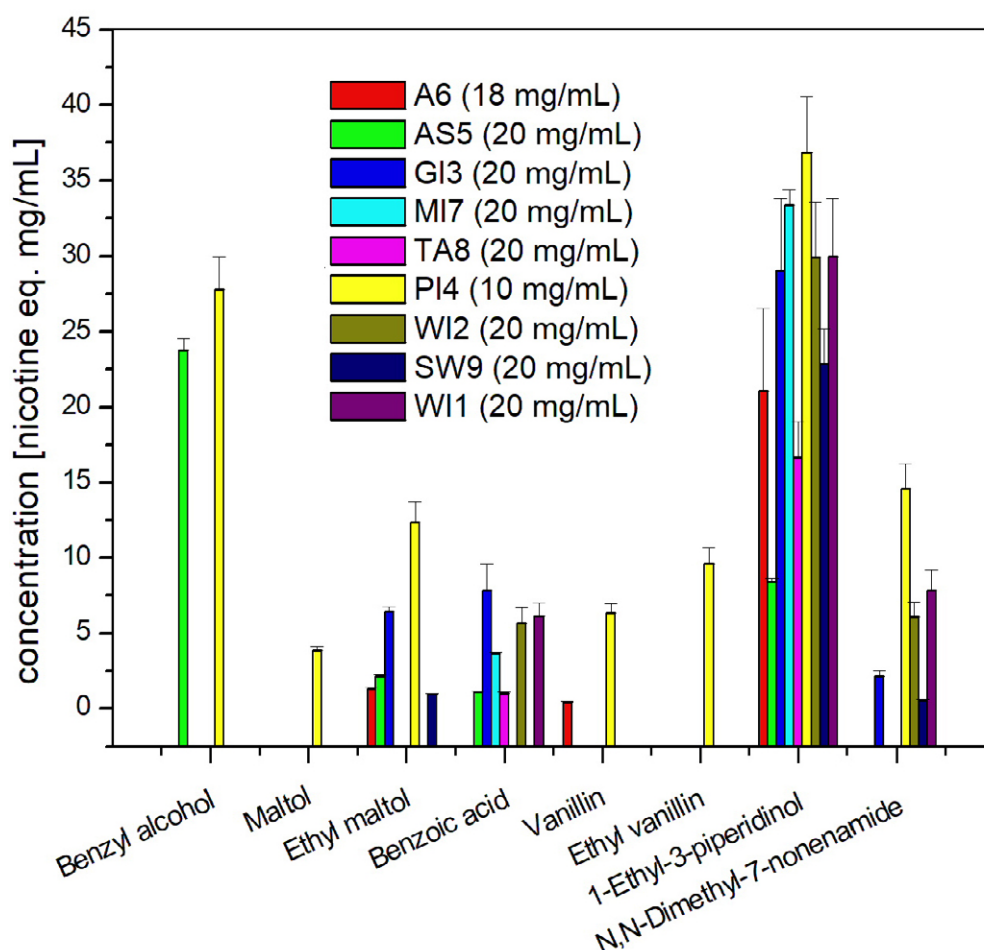


Fig. 2 Volatile compounds (≥ 0.3 mg/mL, expressed in nicotine equivalents) detected in vape samples, analysed by GC–MS and quantified using nicotine as the calibration standard.

Menthol, recognized as one of the most extensively utilized flavouring agents, is excluded from detailed analysis in this report. Nevertheless, its inclusion in e-liquids is authorized, provided that its concentration and labelling comply with the regulatory requirements outlined in the European Union's Tobacco Products Directive (TPD).

nicotine eq. in PI4). Inhalation of its vapors may cause drowsiness, dizziness, respiratory and eye irritation.²⁷ Studies have shown that benzyl alcohol can oxidize into harmful carbonyls such as benzaldehyde during vaping,²⁸ and controlled exposure trials revealed strong respiratory symptoms in most participants. An occupational exposure

limit (OEL-C) of 25 mg/m³ has been proposed to mitigate systemic effects, and it is classified as a Group 2 skin sensitizer based on human data.²⁹

3.4 Maltol and ethyl maltol

Both, ethyl maltol and ethyl vanillin contributed to increased free radical formation,²¹ to cytotoxic effects by increasing pro-inflammatory cytokines, such as interleukin-1 beta, a key pro-inflammatory cytokine that mediates immune response and fever (IL-1 β) and a tumor necrosis factor-alpha (TNF- α), which promotes systemic inflammation in macrophages.^{30,31} Given its prevalence in e-liquids (32% of 16,839 e-liquids contain ethyl maltol)³⁰ and its high concentrations – 85% of ENDS had flavour concentrations above 1000 ppm, with 37% exceeding 10,000 ppm,²³ further research into its potential pro-inflammatory and other health effects is needed.

In our study 1 mg/mL (nicotine eq., 1000 ppm) was exceeded in 5 vapes, with the highest concentration of 12.37 $\pm$ 1.32 mg/mL (nicotine eq., 12 370 ppm) found in one (PI4). Concentrations of ethyl maltol (>22 mg/mL) expressing cytotoxic effect²¹ were not found. However, before drawing safety conclusions, it is essential to study in detail the synergistic effects observed, such as the increased mRNA expression of IL-8 (Interleukin-8) in MucilAir cells (in vitro tissue model of the human upper airway epithelium cultured at the air liquid interface) exposed to a combination of nicotine and ethyl maltol in e-liquids, and the decreased expression of MCP-1. Monocyte chemoattractant protein-1 has a vital role in the attraction or enhancement of the expression of other inflammatory factors in cells exposed to nicotine alone.³²

Similarly, maltol demonstrated dose-dependent inflammatory responses in lung epithelium and fibroblasts³³ and it was present in 3.83 $\pm$ 0.28 mg/mL (nicotine eq., 3830 ppm) in one vape (PI4). In another study, maltol was found to be teratogenic. Holden et al. (2020) exposed zebrafish embryos to eight e-cigarette flavoured liquids, including maltol.³⁴ The results revealed various morphological changes, such as alterations in the yolk sac, pericardial edema, eye abnormalities, bent body axis, and jaw deformities at five days post-fertilization. The study also identified specific flavouring agents associated with these morphological changes, with the highest incidence of cranial and cardiac malformations observed in embryos exposed to flavours containing ethyl vanillin, maltol, and vanillin.

3.5 Benzoic acid

Weak organic acids, such as benzoic or salicylic acid, are commonly added to nicotine salt liquids to adjust the pH value to deliver higher nicotine concentrations deeper into lungs.³⁵ The presence of benzoic acid in ENDS is particularly concerning because it contributes to the forma-

tion of reactive oxygen species (ROS). ROS levels increase significantly with higher benzoic acid concentration (2% wt).³⁶ In our case, concentrations did not exceed 1%, with the highest measured at 7.84 $\pm$ 1.77 mg/mL nicotine equivalent (GI3). Additionally, the use of benzoic acid in nicotine salt liquids, can lead to increased benzene formation through the decarboxylation of benzoic acid during vaping.³⁷ Benzene, a major component of the volatile organic compounds (VOCs) group, is a known carcinogen that significantly increases cancer risk upon inhalation. Interestingly, the highest benzene emissions were observed when benzoic acid was added to PG.³⁸

3.6 Vanillin and ethyl vanillin

While generally recognized as safe (GRAS) for consumption, common flavourings like vanillin and ethyl vanillin, have raised concerns regarding their inhalation toxicity. Both exert cytotoxic effects on respiratory cells and cause disruptions in cellular and immune functions. Additionally, they possess addictive properties.³⁹ In our case, concentrations did not exceed 1%, with the highest measured at 6.32 $\pm$ 0.61 mg/mL nicotine equivalent (vanillin in PI4) and 9.59 $\pm$ 1.10 mg/mL nicotine equivalent (ethyl vanillin in PI4).

Another risk factor is the formation of potentially harmful chemicals due to reactions among substances mixed in e-liquids. In particular, carbonyl compounds can react with alcohols (mainly PG) to produce acetals, which are recognized as respiratory irritants. For widely used aldehyde flavours, such as benzaldehyde and vanillin, the conversion rates to acetals have been estimated to range from 15% to 30%.⁴⁰ Besides, the data showed that vanillin, ethyl vanillin, and ethyl maltol reduced HepG2 (*in vitro* model of immortal human liver cancer cell line) cell viability, with repeated exposure leading to greater cytotoxicity compared to single exposure. This supports the hypothesis that frequent vaping may contribute to hepatotoxicity.⁴¹

3.7 1-Ethyl-3-piperidinol

One of the rare studies on 1-ethyl-3-piperidinol use dates back to 1971, when it was tested as a local anesthetic.⁴² It was present in all vapes at concentrations ranging from 0.8% to 3.7 % (with the highest concentration being 36.86 $\pm$ 3.69 mg/mL nicotine eq.). A recent study on this compound is the only one to report that higher acute exposure to second-hand vaping emissions, which could pose significant health risks to younger age groups, depends on the puff volume.⁴³

3.8 (Z)-N,N-dimethylnon-7-enamide

There are no reports available, meaning that in-depth toxicological studies, inhalation safety data, and en-

vironmental impact assessments for this compound are currently lacking. It was present in many vapes with the highest concentration being 14.60 ± 1.65 mg/mL nicotine equivalent.

3.9 Questionnaire on labelling, composition, and sport

The most notable finding from the questionnaire on adolescent nicotine use trends, consistent with our expectations, was that most respondents who used vapes and nicotine pouches at the same frequency (Table S3) reported paying attention only to the nicotine percentage (48%) and no attention to the composition (41) (Table 2). The second most important response was that the composition of the products is not important to them (only 15% reported paying attention to ingredients). These results are surprising, since despite being aware of the harmful effects of nicotine, they do not actively choose products that might be less damaging to their health.

Table 2. User awareness of product composition among ENDS consumers

Item	f	f%
Percentage of nicotine.	13	48%
I don't pay attention to the composition of the product I'm using.	11	41%
To the presence of other ingredients (e.g. flavourings...).	4	15%
Other	2	7%

Although 99% of participants rated the health risks of nicotine products as relatively high, almost 34% continue to use them (Table S4). This suggests that the perceived psychoactive benefits, namely stress relief, often outweigh the concerns about adverse health effects, as similarly found in the national survey by Koprivnikar and Farkaš Lainščak in 2023¹³. Moreover, both vapes and pouches are viewed as similarly harmful, revealing notable ambiguity among users regarding the comparative risk profiles of newer nicotine products. Despite general awareness of health-related consequences, habitual use persists, suggesting a cognitive dissonance between knowledge of harm and behavioural choices (Table S5).

The data also provide insight into the relationship between physical activity and nicotine use among adolescents. Although 85% of respondents reported participating in sports at least once a week, 32% of them still used nicotine products, contradicting the idea that sports team participation was associated with lower odds of nicotine use⁴⁴ (Table S6). Similar findings have been reported in Australia, where 30% of adolescents who participated in

sports reported using e-cigarettes, challenging the assumption that participation in physical activity serves as a protective factor against nicotine use.⁴⁵ In Italy, the results were slightly more encouraging; however, 23% of athletes still used nicotine.⁴⁶

Newer nicotine products like vapes and nicotine pouches are increasingly popular, with usage rates of 74% and 70% among users, while e-cigarettes were least used (only two participants, Table S3). Alarmingly, 89% of respondents use nicotine, mainly for stress relief, despite recognizing health risks (Table S5). These findings echo Yoong and co-workers,⁴⁷ who also identified stress as a key motivator for ENDS use among adolescents. Unlike their study, peer pressure and social conformity were not significant factors in our sample.

The primary limitation of the survey component of this study is the small sample size, which included only adolescents from lower secondary schools who completed the questionnaire. To obtain more generalisable findings on nicotine product use in the broader adolescent population, future research should employ a representative sample and extend the study population to include upper secondary school students up to 18 years of age.

4. Conclusions

Although many e-cigarette compounds are classified as 'Generally Regarded As Safe' (GRAS) for ingestion, several harmful substances associated with respiratory inflammation, cellular toxicity, and developmental hazards when inhaled were identified. These included benzyl alcohol, maltol, ethyl maltol, vanillin, benzoic acid, and lesser-known chemicals such as 1-ethyl-3-piperidinol and (Z)-N,N-dimethylnon-7-enamide. The formation of reactive byproducts such as ROS, carbonyls, acetals, and benzene further heightens health concerns. The disconnect between adolescents' awareness of these risks and their continued use underscores the urgent need for comprehensive toxicological assessments, stricter regulation of inhaled flavouring agents, and targeted public health interventions that integrate education, critical media literacy, and collaboration with healthcare professionals.

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Povzetek

Tekočine v elektronskih sistemih za dostavo nikotina (ENDS) vsebujejo spojine, ki veljajo za varne za zaužitje (»splošno priznane kot varne« oziroma GRAS), vendar primanjkuje podatkov o varnosti njihovega vdihavanja, kar predstavlja tveganje, zlasti za mladostnike. Ta študija je analizirala kemična odstopanja v ENDS s plinsko kromatografijo z masno spektrometrijo in anketirala slovenske srednješolce o uporabi nikotina. Analiza je razkrila citotoksične snovi pri vdihavanju in navedena topila, kar kaže na neskladje med označeno in dejansko vsebino. Večina mladostnikov, ki so uporabljali ENDS, se je osredotočala le na odstotek nikotina in v veliki meri zanemarjala sestavo izdelka, kljub vednosti, da je nikotin škodljiv. Ugotovitve poudarjajo potrebo po toksikološki oceni, jasnejšem označevanju, strožji regulaciji in ciljno usmerjenem izobraževanju mladih.



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