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Original research

E-liquids vs. cigarettes: mexican analysis

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ABSTRACT

Introduction: The combustion of tobacco produces thousands of toxic compounds, many of which are recognized carcinogens. In contrast, electronic cigarettes (ECs) heat e-liquids at lower temperatures without combustion, potentially reducing exposure. **Objetive**: This study aimed to assess the presence of five compounds of concern diacetyl, formaldehyde, acetaldehyde, benzaldehyde, and vitamin E acetate (VEA) in commercial e-liquids and to qualitatively compare their chemical profile with combustible cigarette smoke. **Methods:** Twenty e-liquids and one combustible cigarette brand were analyzed. E-liquids and Cigarette smoke were examined using Headspace Gas Chromatography with Flame Ionization Detection and Gas Chromatography–Mass Spectrometry (GC-MS). Identification was based on retention times and spectra compared with pure standards. Compounds were classified according to the Hazardous Substances Data Bank (HSDB) and the Globally Harmonized System (GHS). **Results:** None of the five target compounds were detected in e-liquids. A total of 24 compounds were identified, with 1.7% classified as carcinogenic and 5.5% as toxic. In contrast, cigarette smoke contained 27 compounds, with 10.2% carcinogenic and 12.7% toxic, dominated by aldehydes, ketones, and polycyclic aromatic hydrocarbons (PAHs) linked to tobacco pyrolysis. The lower operating temperatures of ECs (≤ 250 °C) and the absence of combustion likely explain the reduced toxic burden observed. **Conclusion:** Commercial e-liquids presented a less hazardous chemical profile compared to combustible cigarette smoke, supporting their potential as lower-risk alternatives. However, EC aerosols are not free of health risks. Further quantitative studies, simulations of realistic use, and long-term toxicological evaluations are warranted to assess residual risks and confirm their contribution to harm reduction strategies.

Key words: electronic cigarettes; e-liquids; gas chromatography; toxic compounds; harm reduction; diacetyl; formaldehyde.

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RESUMEN

Introducción: La combustión del tabaco produce miles de compuestos tóxicos, muchos de los cuales son carcinógenos reconocidos. En contraste, los cigarrillos electrónicos (ECs) funcionan calentando e-líquidos a temperaturas sustancialmente más bajas, lo que puede reducir la exposición de los usuarios a sustancias nocivas. **Objetivo:** Nuestro objetivo es evaluar la presencia de diacetilo, formaldehído, acetaldehído, benzaldehído y acetato de vitamina E en e-líquidos comerciales comparando su perfil químico con el del humo de cigarrillos combustibles. **Métodos:** Se analizaron veinte e-líquidos y una marca de cigarrillos combustibles. Los e-líquidos y el humo de cigarrillos fueron examinados cualitativamente utilizando cromatografía de gases por ionización de llama y espectrometría de masas. La identificación se basó en los tiempos de retención y los espectros comparados con estándares puros. Los compuestos fueron clasificados de acuerdo con el "*Hazardous Substances Data Bank*" y al "*Globally Harmonized System*". **Resultados:** Los compuestos objetivo en los e-líquidos no se detectaron. Se identificaron 24 compuestos, 1.7% carcinogénicos y 5.5% tóxicos. En los cigarrillos se identificaron 27 compuestos, 10.2% carcinogénicos y 12.7% tóxicos. Las temperaturas más bajas de operación de los ECs (≤ 250 °C) y la ausencia de combustión probablemente explican la menor carga tóxica observada en los e-liquidos. **Conclusión:** Los e-líquidos comerciales presentaron un perfil químico menos peligroso lo que respalda su potencial de menor riesgo. Sin embargo, los aerosoles en los ECs no están libres de riesgo. Se requieren estudios cuantitativos adicionales y evaluaciones toxicológicas de largo plazo para valorar riesgos residuales y confirmar su papel en la reducción de daños.

Palabras clave: cigarrillos electrónicos; e-líquidos; cromatografía de gases; compuestos tóxicos; reducción de daños; diacetilo; formaldehído.

INTRODUCTION

According to the World Health Organization (WHO), cigarette smoking remains one of the leading threats to global public health, accounting for more than 8 million deaths annually. Approximately 7 million of these deaths result from direct tobacco use, while an additional 1.3 million are attributed to second-hand smoke exposure.[1] Cigarettes contain numerous harmful substances, including nicotine, tar, ammonia, and carbon monoxide.[2] Moreover, tobacco comprises over 2,550 known chemical constituents, and tobacco smoke contains more than 4,000 compounds; among them, 43 have been confirmed as carcinogens.[3] The adverse health effects of smoking have been well documented since at least 1977, with widespread awareness of its systemic risks.[4] In recent decades, the landscape of nicotine consumption has undergone a significant transformation, as the reduction or elimination of toxicants is increasingly seen as a viable strategy for disease prevention.[5] The long-standing dominance of conventional combustible cigarettes —shaped by cultural, social, and historical forces— is now being gradually displaced by emerging technologies that offer alternative inhalation-based nicotine delivery systems, most notably electronic cigarettes (ECs).[4] Also referred to as vapes or electronic nicotine delivery systems (ENDS), these devices have gained considerable popularity, largely due to discourse framing them as less harmful substitutes for traditional tobacco smoking.[4]

E-liquids used in ECs primarily consist of glycerin, propylene glycol, flavorings (which vary by product), and may or may not contain nicotine. Some formulations also may or may not contain potentially harmful carbonyls such as diacetyl, formaldehyde, acetaldehyde, and benzaldehyde -all of which are compounds of interest in this study. In recent years, heavy metals (e.g., nickel, cadmium, chromium) and organic chemicals such as pesticides, aromatic hydrocarbons, and carbonyl groups have also been detected in these products.[6] *In vitro* studies exposing human cell lines to flavored e-liquids have demonstrated oxidative stress, inflammatory responses, and disruption of pulmonary barrier function, including reduced cell viability and cell count, alterations in pro-inflammatory biomarkers, and increased cytokine release.

Diacetyl, widely used as a flavoring agent, has been linked to bronchiolitis obliterans, a severe and irreversible pulmonary condition.[2,7] Formaldehyde and acetaldehyde are known respiratory irritants and potential carcinogens. Benzaldehyde, though a common flavoring compound, has demonstrated cytotoxicity depending on dose and route of exposure. Furthermore, vitamin E acetate (VEA) has been implicated in severe lung injury when inhaled via vaping products (VPs).[8] VEA is typically found in unregulated THC-containing cartridges, where it is used as a thickening agent for THC oil.[9]

According to the National Youth Tobacco Survey from the Center for Disease Control and Prevention (CDC) the use

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of ECs among adolescents increased significantly between 2019 and 2020.[10] In response, a 2019 study analyzed 206 EC liquid samples, finding that 71% contained THC and 69% VEA.[11] This finding was central to the identification of EVALI (E-cigarette or Vaping Product Use-Associated Lung Injury) and the subsequent link to VEA-containing VPs. Symptoms of EVALI include dyspnea, cough, fever, constitutional symptoms, gastrointestinal disturbances, and hemoptysis.[9] Confirmed cases typically involved patients with a history of vaping within the previous 90 days, imaging findings (e.g., bilateral pulmonary infiltrates or ground-glass opacities on chest CT), and exclusion of infectious, neoplastic, or rheumatologic etiologies.[9] As of 2020, the CDC had reported 2,807 EVALI cases and 68 confirmed deaths, although these figures have not been updated at the time of this publication.[12]

Regardless of EVALI, expert opinions indicate that other potential health risks associated with ECs may arise from multiple sources, including the e-liquid itself, chemical reactions within the heating element, and the device's components. User behavior also influences exposure levels. The combination of these factors increases the risk of addiction, poisoning, and inhalation-related toxicity. Potential health effects may depend on specific chemical constituents or device characteristics, meaning that risks can vary across different EC products. Despite certain methodological limitations, current evidence suggests that ECs use by non-smokers especially youth is harmful, while for many major health outcomes, the overall effects of ECs remain uncertain.[13]

Methods that assess health risks based on individual component toxicity may misestimate exposure risks because interactions between components are not well studied.[14] To detect and quantify harmful compounds in ECs, several studies highlight the importance of advanced analytical techniques such as gas chromatography–mass spectrometry (GC-MS).[6] The concentration and toxicity of inhaled substances are closely related to both, the chemical formulation of the e-liquids and technical parameters involved in vaporization.[15,16] In contrast to conventional cigarettes, which combust tobacco via oxidative reactions at temperatures ranging from 600°C to 950°C, ECs heat liquids via an electrically powered coil without requiring combustion or oxygen.[17] This generates aerosols by evaporation, typically at temperatures below 250°C, thus reducing the formation of thermally degraded byproducts commonly found in cigarette smoke.[16-18]

The combustion of cigarettes produces a complex mixture of gases, free radicals, tar and solid particles through the pyrolysis of tobacco, paper and additives. In conditions of limited oxygen availability, incomplete combustion may result in the formation of hazardous substances, such as carbon monoxide (CO), polycyclic aromatic hydrocarbons (PAHs) and aldehydes.[17] Pyrolysis studies have shown that volatile compounds can be released at temperatures as low as 180°C, while PAHs and CO emerge between 300–650°C and above 600°C, respectively.[18]

Under conditions of low liquid volume or excessive power, ECs heating elements may exceed 300 °C, potentially producing irritant carbonyls such as formaldehyde and acrolein, thereby increasing the risk of chemical reactions that enhance toxicity.[14,18-20]

These differences in temperature, oxygen availability, and combustion explain the observed lower production of toxic species in ECs compared to conventional cigarettes, resulting in distinct emission profiles and toxicity levels.[16,19,20] In light of the growing use of EC products and their ever-changing chemical formulations, it is crucial to keep investigating their composition and behavior to inform regulatory frameworks and protect public health.

Despite existing regulations in some countries limiting nicotine concentrations in e-liquids, the lack of comprehensive standards for other potentially harmful substances remains a significant concern.[2,21]

In this context, it is imperative to conduct comparative investigations examining the chemical differences between combustible tobacco smoke and EC aerosols.[16] Only through rigorous scientific characterization the true risks of ECs can be elucidated and their role in harm reduction strategies be accurately assessed.[21]

METHODOLOGY

This study aimed to identify the presence of five target substances: diacetyl, benzaldehyde, acetaldehyde, formaldehyde, and VEA. Analyses were performed on 20 e-liquid samples and were categorized by compound type as follows: diacetyl analysis (20 samples), aldehyde analysis (benzaldehyde, acetaldehyde, formaldehyde; 20 samples), and vitamin E acetate analysis (20 samples). This study was approved for publication by the International School of Medicine within Universidad Anáhuac Cancún. The Research Committee of our School thoroughly reviewed the protocol, methodology, and content of the manuscript, determining that it meets the ethical and academic standards required. Consequently, the committee granted its approval and authorized the study's dissemination as part of the university's scientific output.

Analysis of Diacetyl and Aldehydes

Samples were prepared in 5 mL glass vials at different concentrations, sealed with PTFE-lined caps, and placed in 500 mL beakers containing water in a controlled-temperature water bath. The samples were heated to 80°C for 10 minutes to ensure temperature equilibration. Once stabilized, 0.6 mL aliquots were drawn using syringes and injected into the gas chromatography column. The compounds were analyzed using Headspace Gas Chromatography with Flame Ionization Detection (HS-GC-FID) and GC-MS, employing a Perkin Elmer Clarus 580 system with a Clarus SQ 8S mass spectrometer and a Perkin Elmer Autosystem GC with an FID detector. Volatile components were also extracted using a chloroform/water partitioning method, with diacetyl quantified from the aqueous phase. Flavor compounds were specifically analyzed via HS-GC-FID.

Identification Using Pure Standards

All sample preparations followed the same procedure, with identification of analytes based on retention time and molecular mass compared to pure analytical standards. For GC-MS analysis, 5 mL of each sample was subjected to liquid–liquid extraction using 10 mL of a water–chloromethane mixture (CH_3Cl, 1:1 v/v) in a separatory funnel, agitated three times for 10 minutes using a magnetic stir bar. The extracts were then dried in a vacuum oven at 40°C, concentrated to 1 mL, and a sample of 2 µL was injected into the GC-MS system.

Analysis of Vitamin E Acetate

For VEA analysis, 100 µL of each sample was combined with 2 mL of a pyridine–acetic anhydride solution (2:1 ratio) and left at room temperature for 24 hours until the reagents had fully evaporated. The dry residues were dissolved in 500 µL of chloroform, and 2 µL was injected into the GC-MS for analysis.

Analysis of Combustible Cigarette Smoke

A dual vacuum-trap system was assembled using two 125 mL flat-bottom round flasks connected by glass tubing. Each flask contained 30 mL of a methanol–dichloromethane solution (5:1 ratio) to adsorb smoke and volatile emissions from burning cigarettes.

Direct Analysis of 20 Combustible Cigarettes

Cigarettes were placed one by one into the manifold inlet and ignited; each was allowed to burn for 5 minutes while the resulting smoke passed through the vacuum-trap system. This process continued until all 20 cigarettes from a single pack were consumed. The trapping solvents were then evaporated, the residue was reconstituted in 1 mL of methanol–dichloromethane, and 5 µL was injected into the GC-MS for compound identification.

RESULTS

Four e-liquid samples (two domestic and two imported brands) were analyzed for the presence of five target compounds: diacetyl, formaldehyde, acetaldehyde, benzaldehyde, and VEA, in comparison with combustible cigarette smoke. A qualitative analysis was performed on each e-liquid using pure standards to screen for the presence of the target analytes. Based on molecular weight and retention time data, none of the analyzed e-liquids showed detectable traces of the target compounds when assessed via GC-MS. Specifically, diacetyl, formaldehyde, acetaldehyde, benzaldehyde, and VEA were not identified in any of the samples.

Table 1 exhibit the 27 most frequently identified compounds in combustible cigarette smoke, as detected through GC-MS following collection in a methanol–dichloromethane solution. The table includes compound names, CAS numbers, functional group classification, and toxicological classification (toxic and/or carcinogenic) according to the HSDB and the GHS. Chemically, the most prevalent compounds in cigarette smoke included aldehydes, ketones, aromatic hydrocarbons, and nitrogen-containing substances—byproducts characteristic of the pyrolysis of tobacco, paper, and additives. These compounds are largely generated through thermal degradation reactions, particularly at temperatures exceeding 600°C, where incomplete oxidation dominates.

As mentioned earlier, combustion in conventional cigarettes results in elevated levels of thermal degradation products such as formaldehyde, acrolein, acetone, benzene, naphthalene, and nitrogenated derivatives. From Table 1, it

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can be inferred that 10.2% of the compounds detected in cigarette smoke were classified as carcinogenic, including benzene, 1,3-butadiene, and several polycyclic aromatic hydrocarbons (PAHs), while 12.7% were classified as toxic, including respiratory irritants and sensitizing agents. Table 1 thus provides a critical reference point for toxicological comparison with compounds found in e-liquids. The higher prevalence of hazardous substances in combustible cigarette smoke supports the hypothesis that tobacco combustion is a major source of toxicant exposure relative to the aerosol emissions produced by vaporizers.

Table 1. Most Frequently Identified Compounds in Combustible Cigarette Smoke

TYPE	COMPOUNDS / DERIVATIVES	SYMPTOMS	CARCINOGENIC
Fatty Acids	Linoleic Acid	Irritation of respiratory tract, eyes, skin; nausea and vomiting.	✗
Fatty Acids	Nonadecanoic Acid	Skin irritation and gastrointestinal symptoms; cause of colorectal cancer.	✓
Fatty Acids	Alpha-Linolenic Acid	Respiratory mucosal irritation, blurred vision, cough, gastrointestinal symptoms.	✗
Alkaloid	Nicotine	Addictive substance; in the CNS it produces a feeling of well-being and relaxation. Severe intoxication causes gastrointestinal symptoms, respiratory secretions and bradycardia; teratogenic.	✗
Alcohol	Cyclopentanol	Irritation of respiratory mucosa, pulmonary edema, pneumonitis, hemorrhage; dehydration and dermatitis.	*
Alkyl Alcohol	5-Hexen-2-ol, 5-methyl	Irritation of respiratory mucosa, skin and gastrointestinal symptoms.	*
Fatty Alcohol	Behenyl Alcohol	Irritation of respiratory mucosa, CNS depression and low-grade hepatic effects.	✗
Terpenoid Alcohol	Geraniol	Allergic dermatitis, CNS depression, spastic paralysis and changes in liver weight.	✗
Terpenoid Aldehyde	Farnesal	Tearing, redness, swelling and blurred vision; allergic dermatitis and skin rash.	✗
Amides	N-Benzoyl-dl-alanine	Respiratory mucosal irritation, specific pulmonary toxicity.	*
Bromates	Carbromal	Mental confusion, ataxia, areflexia, loss of pupillary response, cyanosis, coma, pulmonary shock and disseminated intravascular coagulation defect.	✓
Aromatic Compound	Caryophyllene Oxide	Lung, brain, breast and liver neoplasms. (NOT LISTED BY IARC)	*
Polyprenyl Compounds	Vitamin E / Alpha-Tocopherol	Irritation of respiratory mucous membranes, nausea, headache and weakness.	✗
Saturated Alkane Hydrocarbon Ester	Octadecane, 1-(ethenyloxy)	Allergic dermatitis.	✗
Fatty Acid Esters	Ethyl Linoleate	Irritation of respiratory mucous membranes. Breast cancer.	✓
Fatty Acid Esters	Farnesyl Acetate	Irritation of respiratory mucous membranes.	✗
Steroid	α-Cholest-5-ene, 3-methoxy	Irritation of respiratory mucous membranes.	✗
Hydrazone (–C=N–NH_2)	4-Hydrazono-5-hydroxyimino-4,5,6,7-tetrahydrobenzofurazone	Irritation of respiratory, skin and eye mucous membranes; allergic reactions and gastrointestinal symptoms. Hepatocellular carcinoma, malignant bronchial and lung neoplasms.	✓
Benzenic Hydrocarbon	Cis-β-Caryophyllene	Acute myeloid leukemia. Irritation of respiratory mucous membranes.	✓
Saturated Alkane Hydrocarbon	Heptacosane	Irritation of respiratory mucous membranes. Squamous-cell carcinoma.	✓
Saturated Alkane Hydrocarbon	Tetratetracontane	Skin and eye irritation; gastrointestinal symptoms. Squamous-cell carcinoma.	✓
Alkyl Nitrates	Amyl Nitrate	Acute pulmonary edema, renal tubule alterations; inhalation causes convulsions, cyanosis, headache, methemoglobinemia and nausea.	*
Hydrocarbons	Benzenes	Leukemia; dizziness, excitement, pallor followed by flushing, weakness, headache, dyspnea, chest tightness, nausea and vomiting. Coma and possible death.	✓
Aldehydes	Formaldehyde	Respiratory irritation, cough, wheezing, asthma, pulmonary edema, lung and nasopharyngeal cancer, leukemia.	✓
Haloalkanes	Vinyl Chloride	Inhalation causes dizziness, CNS depression, hepatic cirrhosis, pulmonary irritation.	✓
Organochlorine Compounds	Dioxins	Eye irritation, allergic dermatitis, acne, gastrointestinal symptoms, teratogenic effects; possible hepatic and renal damage.	✓
Inorganic Acids	Sulfuric Acid	Respiratory tract irritation, tracheobronchitis, stomatitis, gastritis, gastric perforation, peritonitis, circulatory shock. Laryngeal and lung cancer.	✓
*	NOTE		
	No conclusive data indicate carcinogenicity; however, at high temperatures it may pose a potential toxic risk to pulmonary health.		

This table summarizes the 27 most frequently identified compounds found in the smoke of combustible cigarettes, based on gas chromatography–mass spectrometry (GC-MS) analysis. Compounds are classified by type, laboratory of origin, functional group, known health effects, and toxicological status according to the Hazardous Substances Data Bank (HSDB) and the Globally Harmonized System (GHS). The presence of a high proportion of carcinogenic and toxic substances in cigarette smoke highlights the significant health burden associated with tobacco combustion.

Table 2 lists the 24 most frequently identified compounds in the analyzed e-liquids, also determined by GC-MS. Each compound is detailed with its CAS number, functional group classification (e.g., aldehydes, ketones, esters), and toxicological classification as per HSDB and GHS criteria. From a chemical standpoint, Table 2 highlights the structural diversity of components present in commercial e-liquid formulations. Most of the compounds identified were low-molecular-weight volatile substances, many of which were esters and aldehydes derived from food-grade flavorings, along with fatty and nitrogenous compounds typically used as carriers (e.g., glycerin, propylene glycol) or to enhance sensory profiles.

Table 2. Most Frequently Identified Compounds in Analyzed E-Liquid Samples

TYPE	COMPOUNDS / DERIVATIVES	SAMPLE 1 - 0 MG	SAMPLE 1 - 3 MG	SAMPLE 1 - 6 MG	SAMPLE 2 - 3 MG	SAMPLE 3 - 3 MG	SAMPLE 4 - 0 MG	SAMPLE 4 - 3 MG	SAMPLE 5 - 0 MG	SAMPLE 5 - 3 MG	COMMON USES	SYMPTOMS	CARCINOGENIC
Esters	Ethyl citrate	✓	✓	✓	✓	✓	✓		✓	✓	In foods as a citrus-flavouring agent, solvent and surfactant.	Irritation and/or sensitivity of mucous membranes, cough, vomiting. Causes metastasis in stromal tumours.	✓
Esters	Ethyl acetate		✓			✓		✓	✓		Printing inks, paint thinners/solvents, textile cleaners, perfume manufacture, solvent for explosive compounds.	Headache, nausea, loss of consciousness.	✗
Esters	Nona-lactone (Coconut lactone)	✓	✓	✓							Coconut/fruit flavouring, cleaning products, cosmetics, perfumery.	Irritant effects on the respiratory tract.	✗
Carboxylic acids	Stearic acid, methyl ester	✓	✓	✓			✓				Stable base for lotions, creams and deodorants.	Respiratory-tract irritation, gastrointestinal disorders.	✗
Carboxylic acids	Palmitic acid, ethyl ester	✓		✓	✓					✓	Soaps, detergents and cosmetics.	Increased risk of cardiovascular disease and breast cancer in post-menopausal women.	✓
Carboxylic acids	Di-n-octyl phthalate						✓			✓	Production of resins, plastics, dyes, pharmaceuticals and fungicides.	Cough, dyspnea, wheezing, liver damage, systemic toxicity.	✗
Carboxylic acids	Adipic acid, diethyl ester			✓	✓		✓				Nylon production, manufacture of clothing, tires and carpets.	Cough, odynophagia.	✗
Carboxylic acids	2-Decenoic acid, methyl ester	✓	✓				✓				Food preservatives.	Headache, nasal mucosa irritation, liver and kidney involvement.	*
Aromatic aldehydes	4-Acetyloxy-3-methoxybenzaldehyde	✓		✓			✓	✓			Flavouring (anise/almond).	Cough, headache, nausea, vomiting.	*
Aromatic aldehydes	Isovanillin	✓		✓			✓	✓			Vanilla- or caramel-like flavouring.	Respiratory toxicity, irritation and pulmonary inflammation.	*
Aromatic aldehydes	Vanillin	✓	✓	✓			✓	✓			Cosmetics, perfumes, flavouring.	Not classified as toxic.	✗
Flavourings	Ethyl maltol	✓	✓	✓	✓		✓	✓	✓	✓	Food additive; enhances sweet caramel flavours.	Hepatic and renal damage. Oncogenic when combined with metals.	✓
Flavourings	Maltol	✓	✓	✓			✓				Flavour enhancer.	Eyes: tearing, swelling, redness, blurred vision. Respiratory: mucosal irritation.	*
Alcohols & polyols	Glycerin	✓	✓	✓	✓		✓		✓		Cosmetics, food preservative, sweetener.	Mucosal irritation, cough and wheezing.	*
Alcohols & polyols	Propylene glycol	✓	✓	✓	✓		✓		✓		Cosmetics, pharmaceuticals, antifreeze additive (cooling systems).	Headache, nasal mucosa irritation, liver and kidney damage.	*
Nitrogen compounds	1-Nitroso-azetidine		✓			✓		✓	✓		Chemical industry.	Tumorigenic agent affecting gastrointestinal system, liver and thorax.	✓
Nitrogen compounds	Methylamine				✓		✓	✓			Agrochemicals (herbicides, fungicides, insecticides, biocides, acaricides); fuel additive.	Irritation of nasal/oropharyngeal mucosa, cough, wheezing. Repeated exposure may cause bronchitis, breathing difficulty, liver effects.	*
Nitrogen compounds	Guanosine	✓	✓	✓			✓	✓	✓	✓	Manufacture of certain pharmaceuticals.	Vomiting, nausea.	✗

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Nitrogen compounds	Pyridine (3-[1-methyl-2-pyrrolidinyl]-, (S)-)	✓	✓	✓	✓	✓	✓	✓		✓	Solvent; manufacture of medicines, vitamins, food flavourings, pesticides, paints, dyes, rubber products, adhesives and waterproofing for fabrics.	Mucosal irritation, headache, nausea, respiratory difficulty, cardiovascular diseases.	✗
Others	Fluoxymesterone (synthetic steroid)									✓	Chemical & pharmaceutical industry (hormone-replacement therapy).	Acne, virilization, fluid retention, hyperkalemia; teratogenic in animals.	*
Others	Vulcanol (2,4,7,9-Tetramethyl-5-decyn-4,7-diol)	✓	✓	✓		✓		✓			Raw material for plastics, adhesives, construction materials, paints, solvents; low-emission fuel.	Dryness of nasal and oropharyngeal mucosa, epistaxis.	✗
Others	Triamcinolone acetonide (corticosteroid)									✓	Pharmaceutical industry to treat inflammatory, atopic and allergic conditions.	Pulmonary damage at uncontrolled doses; immune-system suppression.	*
Others	Alpha-carotene		✓	✓		✓			✓	✓	Pharmaceutical industry; adds yellow/orange colour.	Irritability, loss of appetite and weight, fever, pulmonary involvement (pneumoconiosis).	✗
Others	1,4-Dioxane (stabilising ether)		✓			✓		✓	✓		Chemical & pharmaceutical industry; solvent for cellulose acetate, resins, oils, waxes, dyes and other compounds.	Respiratory-tract mucosal irritation, cough, dyspnoea, dizziness, headache. Nasopharyngeal and hepatic cancer.	✓
*	NOTE												
	No conclusive data indicate carcinogenicity; however, at high temperatures it may pose a potential toxic risk to pulmonary health.												

This table presents the 24 most frequently identified compounds in commercial e-liquid formulations, analyzed via gas chromatography–mass spectrometry (GC-MS). Each compound is categorized by type, functional group, and known health effects, including toxicological classification according to the Hazardous Substances Data Bank (HSDB) and the Globally Harmonized System (GHS). While structurally diverse, the compounds detected in e-liquids showed a notably lower proportion of carcinogenic and toxic agents compared to those found in combustible cigarette smoke, reinforcing the hypothesis of reduced chemical risk in non-combustion nicotine delivery systems.

A key finding is that, despite the chemical complexity of the mixtures, only 1.7% of the compounds detected in e-liquids were classified as carcinogenic, and 5.5% as toxic, representing a considerably lower toxicological burden than that of combustible cigarette smoke. Among the substances with adverse toxicological classification were certain aldehydes with irritant potential and esters that may thermally degrade into hazardous byproducts. However, none of the most critical compounds —formaldehyde, acetaldehyde, or diacetyl— were identified in detectable concentrations.

Discussion

In the present study, we identified and characterized toxicologically relevant chemical compounds in selected domestic and international commercial e-liquids. Five key analytes were analyzed: diacetyl, formaldehyde, acetaldehyde, benzaldehyde and vitamin E acetate (VEA). Additionally, we compared the chemical composition of these e-liquids with that of combustible cigarette smoke. To ensure analytical reliability, we applied robust chromatographic techniques —HS-GC-FID and GC-MS— with standardized sample preparation and validation using pure standards. This methodological rigor enhanced confidence in compound identification.

As previously mentioned, across all 20 e-liquid samples analyzed, none showed detectable levels of diacetyl, formaldehyde, acetaldehyde, benzaldehyde, or VEA, based on the methods employed. However, while the number of total compounds detected in e-liquids was broad, the proportion

of hazardous substances was considerably lower than that found in combustible cigarette smoke: only 1.7% were classified as carcinogenic and 5.5% as toxic, according to the HSDB. Conversely, the analysis of combustible cigarette smoke under standardized conditions (absorption in a methanol–dichloromethane mixture and controlled evaporation) revealed the presence of compounds classified as potentially carcinogenic and toxic according to the GHS and HSDB. Specifically, 10.2% were identified as carcinogenic and 12.7% as toxic.

Both matrices —e-liquids and cigarette smoke— contained aldehydes, ketones, esters, nitrogenated compounds, and fatty acids. However, combustible cigarette smoke exhibited a greater proportion of thermal degradation products and byproducts of incomplete combustion, including free radicals and polycyclic aromatic hydrocarbons (PAHs), which are well-established contributors to tobacco-related toxicity.[22] The combination of HS-GC-FID and GC-MS techniques used in this study ensures high validity of these comparative results. As previously discussed, electronic devices operate at much lower temperatures (typically ~250°C) compared to lit cigarettes, which can reach peaks of up to 950°C.[23] These temperature differences, along with the absence of combustion and tobacco in e-cigarettes, are key factors in the substantially lower levels of toxicants in EC aerosols compared to cigarette smoke.[24]

The comparative findings from this study reinforce the well-established notion that, while not harmless, e-liquids and e-cigarette aerosols pose a lower overall toxicological burden than conventional tobacco smoke.[25] Other studies have similarly reported the presence of toxicants in e-cigarette vapors, though generally at levels 9 to 450 times lower than those found in combustible cigarette smoke, and often comparable to background or trace levels.[26]

This comparatively less hazardous chemical profile can be partly attributed to the absence of combustion processes in ECs, which restricts the formation of additional hazardous by-products. Additionally, many components are derived from the food industry and are generally recognized as safe (GRAS) for oral use. However, safety via inhalation does not necessarily equate to oral safety, which highlights the need for future studies in this field.

Table 2 provides a representative chemical characterization of commercial e-liquids and supports the hypothesis that, although not entirely risk-free, these products exhibit a significantly lower toxicological profile compared to tobacco combustion products.

Numerous researchers have analyzed the chemical compositions of e-liquids and aerosols, including commercial and prototype products, through systematic reviews aimed at understanding their potential health risks and benefits.[21] In April 2024, the Royal College of Physicians (UK) published a report based on a systematic review of studies exploring the relationship between vaping, toxicant exposure, and biomarkers of potential health damage. The report concluded that, compared to smokers, vapers are exposed to a much narrower and lower spectrum of toxicants (as shown in the present work), including reduced carbon monoxide levels. Moreover, it noted that nicotine vaping is not associated with a high frequency of adverse health outcomes, especially when adjusted for prior smoking history.[27]

In line with these findings, the methodological framework of this study, which included aqueous/organic phase separation for the detection and identification of volatile compounds based on molecular mass and retention time, provided a robust and reproducible basis for evaluating the chemical profiles of e-liquids and combustible cigarette smoke. The results support the hypothesis that the analyzed e-liquids may represent a lower-risk alternative to combustible cigarettes in the short to medium term.[25] However, this relative advantage should be interpreted with caution.

We argue that chronic inhalation of complex chemical mixtures, even in the absence of traditionally regulated substances, may pose long-term health risks that remain insufficiently understood and warrant further investigation. In our view, the findings presented here raise important concerns regarding formulation transparency and underscore the urgent need for regulatory standards on the composition and inhalation safety of these products.

Study Limitations

Although this study employed robust analytical techniques such as HS-GC-FID and GC-MS, several limitations must be considered when interpreting the findings:

Restricted scope of target compounds

The analysis was limited to five specific substances (diacetyl, formaldehyde, acetaldehyde, benzaldehyde, and VEA). While these compounds are well-documented for their toxicological relevance, the complex chemical composition of e-liquids suggests that additional contaminants or degradation products —potentially present— were not evaluated. The dynamic nature of commercial formulations also contributes to substantial variability in product composition across the market.

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Qualitative rather than quantitative analysis

The methodology focused on compound identification based on retention time and molecular mass relative to pure standards. However, no quantitative determination was performed using calibration curves or validated limits of detection (LOD) and quantification (LOQ), thereby limiting the precision of residual concentration assessments. Moreover, this methodological and qualitative approach prevented statistical comparison of the samples, as the broad list of compounds was obtained using different protocols and at different time points. To enable quantitative comparison, it would be necessary to prepare e-liquid samples from different brands using the same flavor and identical nicotine concentrations to ensure consistent experimental conditions. This type of analysis would be both interesting and necessary for future studies.

Limited sample representativeness

A total of 20 e-liquid samples (10 domestic, 10 international) and one brand of combustible cigarette were analyzed. While sufficient for preliminary comparison, this sample size does not fully represent the breadth of vaping products or the diversity of combustible tobacco brands available, limiting the generalizability of results.

Limited detection of thermally unstable or low-volatility compounds

HS-GC-FID is well-suited for detecting small, moderately volatile molecules such as aldehydes. However, it may fail to identify thermally labile, low-volatile, or highly polar compounds—including oxidized glycols, cannabinoids, pesticides, or high-molecular-weight components—commonly found in some e-liquids. These substances might remain undetected unless complemented with techniques such as LC-MS or non-volatile residue analysis.

Absence of aerosol analysis under real-use conditions

The study did not analyze aerosols generated during active inhalation or under realistic vaping conditions, which could yield different chemical profiles due to thermal transformation during use.

Lack of standardization in sensory and flavor profile characterization

No structured assessment of the flavoring and sensory components was included, despite their potential to influence user exposure and chemical reactivity during vaporization. Therefore, while this study provides a useful comparative chemical characterization between e-liquids and combustible cigarettes, additional research is required. This should include quantitative analyses, real-use simulations, broader sample populations, and complementary toxicological studies to achieve a more comprehensive risk assessment.

It is also important to note that laboratory vaporization settings do not fully replicate real-world user behavior. Variables such as device power output, coil temperature, puff volume, and usage frequency can dramatically influence the formation of thermal degradation products. While controlled temperatures were used in this study, they may not account for overheating scenarios commonly encountered during daily use.

CONCLUSION

Based on the number and classification of carcinogenic and potentially toxic compounds detected via gas chromatography, the findings of this study suggest that the chemical constituents of the analyzed e-liquids may pose a lower health risk compared to those of combustible cigarettes. Nevertheless, e-liquids are not free from health risks. Future research is needed to deepen our understanding of the health effects associated with vaporized e-liquids and to clarify their potential role in harm reduction strategies.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest related to this research. None of the participants have received financial, professional, academic, or personal benefits that could have influenced the results or interpretation of the study. Dr. Christian Heinrich-Henonin is an active medical writer and consultant for Philip Morris International (PMI); however, this affiliation did not influence the design, execution, analysis, or conclusions of the present study.

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