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Review Article
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HEALTH RISK ASSESSMENT AND TOXICITY ANALYSIS OF ELECTRONIC CIGARETTES

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Abstract
Electronic cigarettes (e-cigarettes) have emerged as widely used alternatives to conventional tobacco products, particularly among adolescents and young adults, due to perceptions of reduced harm, appealing flavours, and ease of access. This review critically examines the toxicological profile of electronic cigarettes, focusing on their chemical composition, biological effects, and public health implications. E-cigarette aerosols typically contain nicotine, propylene glycol, glycerol, flavouring agents, vitamin E derivatives, and trace metals such as nickel, chromium, lead, and tin. Thermal degradation of e-liquids during heating can generate toxic aldehydes, including formaldehyde, acetaldehyde, and acrolein, which pose respiratory and cardiovascular risks. Experimental, clinical, and epidemiological evidence indicates associations between e-cigarette use and adverse outcomes such as lung injury (EVALI), oxidative stress, inflammation, endothelial dysfunction, increased cardiovascular risk, and potential carcinogenic effects. While e-cigarettes may expose users to fewer toxicants than conventional cigarettes, their long-term health effects remain insufficiently understood, especially in vulnerable populations such as adolescents and individuals with pre-existing respiratory disease.

Keywords: *electronic cigarettes, nicotine, chemical flavours, smoking, vaping, cardiovascular, respiratory, toxicology.*

INTRODUCTION

In China, the e-cig is a product invented in 2003 as nicotine delivery products and has been developed to provide the smokers with the satisfaction of the usual tobacco cigarettes with no side effects on their health [1]. Since its introduction in the United States in 2007, the sales revenues of e-cigarettes have grown at a high rate in the world. The American Lung Association, American As sociation of Pediatrics, World Health Organization, and the US Centres for Disease Control and Prevention have all expressed concern over the healDisposable POD (d POD) e-cigarettes, which is the most up-to-date electronic nicotine delivery systems, which have widely spread in popularity and are now the most popular e-cigarettes on the market, especially amongst adolescent children [2,3].

Nicotine salts contain organic acids [4]. in e-liquids, which can potentially dissolve metals and metalloids such as nickel(Ni),chromium(Cr),antimony(Sb), and lead (Pb) in the aerosols of e-cigarettes containing d PODs tested[5-6], but to the best of our knowledge, none of the ELF Bars, Flum Pebbles or Esco Bar disposable e-cigarettes have been assessed. In 2023 and 2024, ELFB was selected as the most popular e-cigarette used by the youth in the U.S. by the U.S. Centres for Disease Control and Prevention (CDC) National Youth Tobacco Survey (NYTS) as compared to Esco Bars, which are ranked as the second and sixth most popular e-cigarettes among the youth in 2023 and 2024 respectively.

A: The battery: This is a source of power.
B: Activation button: causes the sensor to activate upon pushing.
C: Display screen: offers details on the settings of the device.
D: The Sensor is activated upon pushing an activation button. In devices, which do not have an activation button, sensor shall be activated as long as the user inhales.
E: The atomizer: a coil has the purpose of heating the e-liquid to aerosol.
F: The cartridge: it is where e-liquid is stored.
G: The mouthpiece: whereby a user inhales the aerosol or refillable cartridges are the second-generation. Third-generation are refillable tanks/mods and the final generations are the ones that are prefilled or refillable pod mods like the JULL devised [4].

Lung Injury

The windpipe is attached to the lungs via small branches and the alveoli via tiny capillaries in a healthy person's respiratory system, where oxygen and car bon dioxide are exchanged. Any minor changes disturbing the prefect environs mental conditions in the lungs could lead to lung injury, as in E-cig. Inappropriately, ECs have been linked to lung inflammation, leading to respiratory failure and death ultimately [5].

Cancer

Due to over seventy carcinogens in the smoke, ECs have been linked to a variability of cancers. However, it would make sense to expect cancer risk to decrease due to the absence of tobacco in ECs compared to TCs. However, there is ulcer tainty in the carcinogen of other components found in these devices, such as humectants and flavorings present in ECs. Exposure to EC vapor was shown to cause lung cancer in mice, and symptoms of early stages of bladder cancer were visible in the animals, according to findings from the National Institute of Ecological Health Science [6].

Heart Disease

Since nicotine is the key element of the e-cigarette aerosol, ECs are also associated with spiking adrenaline, elevated blood pressure, and higher heart attack risk because of hiking heart rates. Another impact of vaping is on blood supply and coronary heart disease and aggravates heart disease and stroke. Moreover, the risk of blood clots and other circulatory complications is 44 percent higher in people who use ECs [7].

Respiratory Devices

A series of mechanisms may lead to the damage of the respiratory system as a result of the exposure to the aerosol of EC that contains a number of different chemicals. To give an example, the nicotinic acetylcholine receptors regulate cystic fibrosis transmembrane conductance (CFTR) in the airways and can be influenced by inhaling nicotine. Consequently, the effect of inhaling aerosols with nicotine can affect this mechanism due to the fact that the enzyme is the one that takes in the substance into blood stream thus interfering with the CFTR functionality. It has been identified that the deterioration of CFTR action contributes to the development of asthma, hypertension, and chronic obstructive pulmonary disease (COPD).

There are two main ways of tobacco consumption: smoked (cigarettes, cigars, pipes) and smokeless (snuff, chewing tobacco) [8].

Background

[Effects of e cigarette vapour versus conventional cigarette exposure: in vivo and in vitro effects]

Numerous investigations have been conducted to assess the toxicity and safety of using e-cigarettes in both in vitro and in vivo cell cultures. Nine volunteers who used e-cigarettes, with or without nicotine, for two hours in a ventilated room were analysed in one of the earliest human investigations. Profiles of urine metabolites, exhaled nitric oxide (NO), and indoor air pollutants were examined.

Similar to platelets, neutrophils exposed to e-cigarette aerosol showed elevated expression of CD11b and CD66b, two indicators of neutrophil activation [9]. Furthermore, various human investigations on vaping have documented alterations in vascular tone, vascular endothelial damage, elevated oxidative stress, and decreased endothelial function [10].

Though not always attributable to other e-cigarette components, the majority of documented cases of lung injury were linked to the use of e-cigarettes for the intake of tetrahydrocannabinol (THC) and vitamin E additives. However, mice exposed to e-cigarette aerosols experienced significant increases in interleukin (IL)-6 but normal lung parenchyma with no evidence of apoptotic activity or elevations in IL-1β or tumour necrosis factor-α (TNFα) in a comparative study of mice exposed to lab air, e-cigarette aerosol, or cigarette smoke (CS) for three days (6 hours of exposure per day) [11]. Animals treated to CS, on the other hand, displayed increased production of inflammatory markers as TNFα, IL-1β, and IL-6 as well as lung inflammatory cell infiltration.

HISTORICAL CONTEXT & REGULATIONS

As scientific knowledge of e-cigarettes' effects on health advances, regulations pertaining to these devices are also constantly evolving. Various jurisdictions have various public health priorities, which are reflected in the regulatory measures, which range from strict regulations to more permissive frameworks.

Since 2016, the FDA in the US has categorised e-cigarettes as tobacco products. With a focus on preventing sales to minors, this regulatory framework includes supervision of product labelling, production procedures, and sales [12]. Obtaining premarket authorisation for new products is another need for producers.

Nicotine-containing e-cigarettes are controlled like medications in Australia and can only be sold with a prescription. These products are subject to strict regulations by the Therapeutic Goods Administration, which prohibits their importation and unprescriptionsale. The Tobacco and Vaping Products Act and the Vaping Products Regulations govern e-cigarettes in Canada [13]. With a focus on limiting access by minors, these regulations include particular limitations on nicotine concentration, labelling, and advertising.

METHODOLOGY

We address the relationship between common compounds in e-cigarettes and their potential for toxicity in this argumentative literature review. We searched 600 million books, e-books, and scholarly articles using the University of Nevada (UNR) library's "One Search" to find 53 references. E-journal articles, e-books, streaming video, and other subscription content are among the things that are physically

housed in the UNR libraries and research databases. E-cigarettes, nicotine, propylene glycol, flavourings, glycerine, vitamin E, heavy metals, lung damage, cancer, etc. were among the criteria, terms, or phrases we utilised in our searches. We also searched Scholar and Google for peer-reviewed research on the toxicity of e-cigarettes [14].

The literature search and data gathering were carried out by eight researchers. Within the allotted time constraints, each researcher conducted an independent evaluation of the literature, evaluating titles and abstracts according to predetermined inclusion and exclusion criteria (Toxics 2025, 13, 268 4 of 35). The researchers evaluated all of the chosen publications together.

E-CIGARETTE DEVICE

E-cigarettes are battery-operated devices that produce an aerosol by heating a liquid containing nicotine to the point of vaporisation. Both the inherent toxicity of the e-liquid that serves as the aerosol source and the toxicity of the compounds created when the e-liquid vaporises upon contact with the heating coil control the toxicity of e-cigarette aerosols. Electronic cigaretteswere Two main objectives guided its design: (a) to provide inhaled nicotine that replicated the satisfaction and use of traditional methods, and (b) to reduce the harmful health effects of smoking. In addition to not resembling traditional cigarettes, the first-generation devices, often known as "cig-a-likes," were disposable (or included disposable cartridges).

A small number of studies have examined the material of the electronic device and its possible effects, particularly the possible presence of metals like copper, nickel, or silver particles in e-liquids and aerosols originating from the filaments and wires and the atomiser [15]. The majority of studies on the effects of e-cigarette use on human health have concentrated on the components of the e-liquid and the resulting aerosols produced after heating. Silicone or silicate particles from the fibreglass wicks are other significant ingredients in the aerosols. More thorough research is needed [16].

E CIGARATTES AS A SMOKING CESSATION TOOL

There are a lot of compounds in CS-roughly 7000 distinct elements in total, ranging in size from atoms to particle matter-and many of these substances are probably what cause this habit's negative effects [17]. Manufacturers assert that e-cigarettes won't cause lung diseases like lung cancer, chronic obstructive pulmonary disease, or cardiovascular disorders that are frequently linked to traditional cigarette smoking, since e-cigarettes with different chemical compositions are largely replacing tobacco.

Moreover, both FDA and CDC are actively investigating the incidence of severe respiratory symptoms associated with the use of vaping products. In a recently published randomised trial of 886 subjects who were willing to quit smoking [18], the abstinence rate was found to be twice as high in the e-cigarette group than in the nicotine-replacement group (18.0% vs. 9.9%) after 1 year. Notably, the nicotine-replacement group's abstinence rate was lower than what is typically anticipated with this treatment.

IMPLAMENTION IN COVID 19 TIME

According to many research, people who smoke or vape are more susceptible to infections caused by the SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) or to negative consequences if they have COVID-19. However, a meta-analysis did not show that smoking cigarettes is likely linked to increased harm from COVID-19, whereas a systematic review did, and the latter had a number of problems because of its small sample sizes [19].

Regarding these claims, the available data indicates that elevated ACE2 expression is not always associated with a higher risk of contracting SARS-CoV-2 and experiencing negative consequences. In fact, ACE2 expression is lower in the elderly than in the younger population, and the SARS-CoV-2/ACE2 interaction further reduces ACE2 expression. In actuality, the majority of COVID-19-related deaths occurred in those over 60 [20].

In conclusion, it appears that smoking or vaping nicotine may have a negative effect on the outcome of COVID-19. To elucidate the impact of e-cigarette usage on pulmonary and cardiovascular problems resulting from SARS-CoV-2 infection, more follow-up research is necessary during the COVID-19 pandemic.

PERSPECTIVES

The introduction of modern techniques like mass spectrometry and gas chromatography, which enable thorough identification of the volatile and semi-volatile substances found in these products, the analysis of e-cigarettes has made great progress. Research on the long-term impacts of breathing in vapour from e-cigarettes is still lacking, though. Although e-cigarettes are thought to be less dangerous than regular cigarettes, some research has found potentially harmful substances in their liquids, which raises questions about potential health consequences. Concerns regarding nicotine addiction and its possible detrimental effects on neurological and pulmonary development are also raised by the rise in teen e-cigarette use.

The garbage produced by e-cigarettes, such as plastic cartridges and lithium batteries, poses a serious problem for the environment. Negative environmental consequences and pollution might result from improper handling of these wastes. Furthermore, the emission of specific chemical compounds during e-cigarette use may have unidentified harmful effects, underscoring the need for more research on these effects.

Recent years have seen a substantial transition in the e-cigarette industry, reflecting changes in public and governmental perceptions as well as technology

advancements. E-cigarettes were first developed as a safer substitute for regular cigarettes, and their popularity has grown on the presumption that they offer a smoking experience with less exposure to the dangerous chemicals present in traditional cigarettes.

CHALLENGES & OPPORTUNITIES

There is an urgent need to rigorously control the production, marketing, and distribution of e-cigarettes due to the teen vaping epidemic and the breakout of lung injuries and deaths caused by vaping in the United States. However, creating reasonable and practical vaping laws and, more crucially, enforcing them will probably pose particular difficulties for various nations worldwide. The difficulties might differ based on each country's unique legal,

A white paper by the Indian Council of Medical Research, which is hardly an ally of the tobacco companies, warns against the net negative impact e-cigarettes have on public health and the threat they pose to future generations.

RISK EXPOSURE

Bio- makers of Exposer

Relevant biomarkers, like as cotinine levels-byproducts of nicotine metabolism-were examined in a number of SHA exposure investigations. When exposed to SHA for one hour in a closed 60 m3 chamber, never-smokers' complete blood count (CBC) indices did not change significantly, according to Flourisetal (2012, 2013) [21]. However, their serum cotinine levels were higher right after a passive e-cigarette exposure session than those in the control group. Ballbèetal 2014), discovered that nonsmokers who lived with nicotine e-cigarette users at home had significantly higher levels of cotinine in their urine and saliva than nonsmokers from control families. Additionally, they discovered no difference in cotinine levels between nonsmokers residing in houses with traditional cigarette smokers and those with e-cigarette users [22,23].

RISK WARNINGS

Warning text

As previously mentioned, the FDA deeming mandates that the packaging must have the following language: There is nicotine in this product. This content should use at least 12-point font and fill a box that is 30% of the package's size because nicotine is an addictive substance [24]. It might be necessary for the FDA to demonstrate that this remark is more successful than others that might be suggested if they are required to defend their ban on commercial communication. For instance, in the public comments on the deeming, some asked if the warnings should make up 30% of the package or if 12-point type would be adequate.

Comparing the FDA's recommended text at 30% of the packaging with the less restrictive FDA's suggested text at 12-point font is therefore helpful [25].

Modified Risk Statement.

A useful suggestion about updated risk statements surfaced. Since our manipulation check shows that a modified risk statement can promote the perception that e-cigarettes are linked to a lower risk of tobacco-related disease than traditional cigarettes, the application for including a modified risk statement on an e-cigarette product is likely to be made on the basis that the statement can help smokers move away from traditional, more toxic cigarettes. According to this research, altered risk statements might promote quitting smoking [26-30].

CONCLUSION

Since their introduction to the market just over a decade ago, evidence regarding the health effects of e-cigarettes has continued to emerge. Importantly, controlled studies involving humans, animals, and cell models have provided biological evidence supporting the epidemiological association between vaping and cardiopulmonary diseases. This broad investigative approach is necessary because of the numerous factors that influence e-cigarette toxicity. An important unanswered question remains whether e-cigarettes are truly a safer alternative to conventional cigarettes. The composition of e-liquids requires stricter regulation, as these products can be easily purchased online and several cases of mislabeling have been reported, which may seriously affect consumers' health. In addition to their unknown long-term effects on human health, the wide variety of attractive flavors available appears to attract new "never-smokers," particularly among young individuals. Furthermore, there is still insufficient evidence supporting the effectiveness of e-cigarettes as a smoking cessation method. Although nicotine-containing e-cigarettes may reduce the craving for smoking, they do not completely address the habitual behavior associated with conventional cigarette use. With regard to the COVID-19 pandemic, current literature suggests that nicotine vaping may lead to adverse health outcomes. Therefore, further follow-up studies are necessary to clarify the impact of e-cigarette consumption on human health during SARS-CoV-2 infection.

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AUTHOR CONTRIBUTIONS

All authors contributed equally to the preparation and completion of this manuscript.

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The authors declare that there are no conflicts of interest regarding the publication of this paper.

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