



## Electronic Cigarettes: Ongoing Research

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### Abstract

Electronic cigarettes have been steadily increasing in popularity over the last few years. The sudden inflation in the use of e-cigarettes has raised interest regarding the safety and composition of these devices. With a large portion of users being adolescents, the concern has prompted investigators to research what the devices contain and try to qualitatively define the chemicals present as well as assess the associated health complications that may arise. Despite the potential health implications associated, e-cigarettes have found a place as an alternative to traditional nicotine replacement therapy as an option for smoking cessation in users who are trying to quit. Recent evidence has indicated a potentially promising place for electronic cigarettes in this facet of the market, however more research is necessary to determine the safety and the future role for these devices.



### Introduction

**E**lectronic cigarettes are battery operated devices that are utilized to deliver aerosolized liquid which often contain nicotine, flavorings and other chemicals. They resemble traditional tobacco cigarettes, pens, or memory sticks and can be recognized by the common names of e-cigs, JUULs, or vapes. Today there are more than 460 e-cigarette brands on market.<sup>1</sup> The e-cigs consist of four different components including; a cartridge or reservoir that holds the liquid solution, a heating element, a power source, and a mouthpiece. Most electronic cigarettes are activated by puffing which powers the heating device and vaporizes the liquid in the cartridge. The aerosol or vapor can then be inhaled by the user.<sup>2</sup>

The liquid solution is typically known by the names “e-liquid” or “e-juice” and contains nicotine, flavorings and other chemicals such as propylene glycol and glycerin.<sup>2</sup>

A Juul is a small form of an electronic cigarette and has shown an increase in popularity. A Juul starter kit costs \$50 which contains the Juul device, a charger and four Juul liquid cartridges called pods. A pack of four flavored pods alone costs \$16 and each pod has the nicotine content equivalent to that of 1 pack of cigarettes.<sup>3</sup> Juul pods have been shown to contain varying concentrations of nicotine ranging from 25-50 mg/mL.<sup>4</sup> Other vaping devices can range anywhere from \$20-\$100.<sup>5</sup> E-liquid varies from \$7-30 depending on the bottle size and

concentration of nicotine.<sup>6</sup> Bottle sizes range from 10-100 mls and typical juice concentrations are 3, 6, 12 mg/mL.<sup>5</sup>

### E-cigarette use on the rise

There has been a rapid evolution in the development of e-cigarettes in the past decade and a dramatic rise in their popularity. From 2008 to 2012, the use of e-cigarettes has doubled in North America.<sup>2</sup>

With e-cigarettes on the rise there is concern with the increase in use among adolescents. The U.S. Surgeon General and Commissioner of the Food and Drug Administration have both declared the rapid rise in rates of youth and e-cigarette use an “epidemic”. Deferred enforcement by federal regulation of electronic nicotine delivery system (ENDS) has prompted the industry to boom.<sup>7</sup> Center for Disease Control (CDC) data has showed that while tobacco use has remained steady from 2011-2016, the use of e-cigarettes has increased rapidly.<sup>7</sup> Tobacco use is established among adolescents. Each day about 2,000 individuals, under 18 years of age, smoke their first cigarette and more than 300 individuals become daily cigarette smokers.<sup>8</sup> Flavorings make the tobacco products more appealing to youth as well. In 2014, 73% of high school students who used tobacco products in the past 30 days reported using a flavored tobacco product.<sup>8</sup> Recent increase in e-cigarette usage is driving tobacco usage among adolescents. In 2017, an estimated 2.1 million middle school and high schoolers used e-cigarettes which rose to 3.6 million in 2018.<sup>8</sup> The increased





prevalence in e-cigarette usage has prompted recent studies to be conducted regarding the safety and efficacy of these devices. Some studies have addressed the side effects and health implications that users of e-cigarettes may be at risk for.

The findings of this research could lead healthcare providers, as well as the public to better informed conclusions regarding the use of these devices.

### **Nicotine Component**

Nicotine is the addictive component that is extracted from tobacco and found in regular cigarettes as well as the e-cigarettes.<sup>9</sup> In the article, “Electronic cigarettes and nicotine clinical pharmacology”, a literature search was performed to help gain an understanding on the physical impact of nicotine contained in e-cigs regarding dependence and public health.<sup>10</sup> The authors concluded that nicotine yields from the e-cigarettes deliver less nicotine than traditional cigarettes and deliver only modest nicotine concentrations to the inexperienced e-cigarette user. Those that currently smoke are able to achieve concentrations similar to traditional concentrations illustrating the importance of nicotine exposure as a potential smoking cessation aid. The article also touches on potential physical impacts of nicotine in which they mention that nicotine affects the central and peripheral systems and has been shown to be associated with increasing heart rate, blood pressure.<sup>10</sup> While this article shows that there may be a role for e-cigarettes in smoking cessation, it also

illustrates that there are health implications associated with the drug as well.<sup>10</sup>

In the article by Schroeder M *et al*, a literature search was done comparing the nicotine yield in varying amounts of inhalations compared to the nicotine yield from a traditional cigarette. The average nicotine yield, based on the International Organisation for Standardization (ISO) smoking conditions, from a single traditional cigarette ranges from 0.5 to 1.5 mg/cigarette.<sup>10</sup> In regards to e-cigarettes, nicotine yields measured from a 100 mL puff ranged from 0.35 mcg/100 mL puff to 31.5 mcg/100 mL puff while another study measured nicotine yields ranging from 0 to 43.2 mcg/100 mL puff.<sup>10</sup> These studies indicate that e-cigarettes deliver less nicotine than traditional cigarettes and also show that there are varying amounts of nicotine that can be obtained from these devices.<sup>10</sup>

Electronic cigarettes have been shown to have varying amounts of nicotine levels contained in them ranging anywhere from 0 to 36 mg/ml, depending on the manufacturer.<sup>9</sup> One study, conducted by Hahn et al. in 2014, sampled 54 different e-cigarette liquid samples. Among those samples, 63% contained nicotine above the detection limit and 5 samples that were allegedly “nicotine free” contained 0.11 mg/ml to 6.9 mg/ml of nicotine.<sup>11</sup>

While nicotine is the primary addictive component in tobacco, non-nicotine tobacco constituents have also been identified in these devices. In the article by Schroeder *et al*, a study was mentioned by





Etter *et al* in which the investigators measured the presence of nicotine-related alkaloids including normicotine and anabasine in the e-liquid from 20 different e-cigarette models. The two alkaloids were found to range from 0.04% to 0.45% and 0.02% to 0.1%, respectively.<sup>10</sup> The extent to which these constituents may contribute to dependence is unknown.<sup>10</sup>

Not only can the concentrations of nicotine vary among samples, but some samples have been shown to contain inaccuracies in their nicotine content claims.<sup>9-11</sup> In addition, it has been shown that e-cigarettes may also contain other tobacco constituents, with the role in dependence being unknown.<sup>10</sup> This reinforces the importance of informing individuals about the contents in these devices as there may be deviations from the labelling in some of these products.

### **Additional components**

The main components of the liquid solution are propylene glycol, which creates the artificial smoke of the e-cigarette as well as glycerol, which contains the flavoring agents.<sup>3</sup> The ratio of these ingredients varies from 0:100 (propylene glycol to vegetable glycerin) to 100:0.<sup>9</sup> In the study mentioned previously, conducted by Hahn *et al*, the authors sampled 54 different e-cigarette liquid samples. Glycerol, propylene glycol and lower levels of ethylene glycol were detected in all samples. Glycerol was not labelled on 5 of the products, propylene glycol on 2 of the products and the presence

of ethylene glycol was not labeled on any of the samples.<sup>11</sup> Another study conducted by Tierney *et al*. looked at two brands of electronic cigarette fluids and the different ingredients contained within 30 different e-cigarette fluids. They took a qualitative approach to the analysis of the fluids and overall, they found that a significant amount of flavoring chemicals were aldehydes (six out of the twenty four different compounds found) which are compounds recognized to be primary irritants of the mucosa of the respiratory tract.<sup>12</sup> Alcohols, esters and ketones were among some of the other components in the liquids.<sup>12</sup> The study found that product labels rarely provided ingredient information beyond the level of nicotine, and the inclusion of propylene glycol and/or glycerol and it concluded that certain concentrations of some flavoring chemicals in e-cigarette fluids are high for inhalation exposure by vaping and can be considered concerning in terms of toxicology.<sup>12</sup> Investigators suggested that regulatory limits should be considered for levels of some of the chemicals as well as for total flavour chemical levels, and the investigators also believe that ingredient labeling should be required.<sup>1</sup> Other investigations conducted by Bahl *et al*. and Behar *et al*. looked into the cytotoxicity in comparison to levels of cinnamaldehyde, 4-methoxycinnamaldehyde and vanillin for 10 different cinnamon flavored fluids. For the three compounds, the highest concentrations were ~40, 3 and 8 mg/mL, respectively (~4%, 0.3% and 0.8% by weight or volume).<sup>13,14</sup> In a separate study





conducted by the same investigators cytotoxicity was evident in the form of human pulmonary fibroblasts, human embryonic stem cells and mouse neural stem cells in liquids that were considered to be cinnamon-flavoured.<sup>13</sup>

### **Role in Smoking Cessation**

Electronic cigarettes have been increasing in use and recent evidence has suggested their use as a potential smoking cessation tool. As mentioned before, in the nicotine component section, there has been recent evidence which suggests that they may be effective as a smoking cessation aid. More research has recently been conducted indicating that they may be more effective than traditional nicotine replacement therapy at achieving long term abstinence. A randomized control trial performed in 2019 conducted by Hajek et al. randomized 886 participants into groups that utilized nicotine replacement therapy and e-cigarettes as smoking cessation.<sup>15</sup> Both treatment groups were supported for at least 4 weeks with behavioral support, and the measured primary outcome was sustained abstinence for 1 year. The results found 18% abstinence among the e-cigarette group as compared with 9.9% in the nicotine replacement group. The study concluded that electronic cigarettes were more effective for smoking cessation than other forms of nicotine replacement therapy when both products were accompanied by behavioral support.<sup>15</sup> This recent study shows that there may be a potential role in using these devices as a

quitting aid but more research needs to be conducted before the devices can be classified as nicotine replacement therapy.

### **Conclusion**

In conclusion, electronic cigarette use has been increasing steadily over the past decade and has recently rose in the past couple years. There is concern for the users of these devices regarding effects on long term health, especially due to the rapid prevalence in use among adolescents. Research has been conducted to dive into the constituents of the devices and potential health complications from some of these components have been identified. Despite potential implications, electronic cigarettes have recently found their place as a potential smoking cessation tool. With the varying amounts of chemicals and components that have been identified in the devices and the increase in use, it is important that research continues to be done to understand what these devices are made of and what long-term health consequences can be associated. The recent role as a smoking cessation aid is something that has promise but needs to be explored more.





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