Real-Time Intervention Framework for Nicotine Poisoning via Identification of Alternate Compound and a Smart E-Cigarette Device

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This research was not conducted in affiliation with MIT.

There has been a 200-fold increase in nicotine poisoning-related hospitalizations over the past decade which can be attributed to the rising popularity of electronic cigarette use or "vaping." E-cigarettes are battery-powered devices designed to vaporize a liquid that consists of lung-damaging additives, flavorings, and nicotine. Due to the potency and palatability of this vapor, users can easily ingest a dangerous level of nicotine and experience symptoms such as difficulty breathing, dizziness, and seizures. This paper proposes a smart e-cigarette device capable of tracking nicotine release with respect to time, stopping traditional vape liquid release when a threshold is reached, and switching to a safer compound. To find this alternate compound, two potential candidates – vanillin and menthol – were evaluated for their potential to cause lung damage and extent of thermal degradation. Through creation of a synthetic lung tissue-mimicking material and analysis of permeation, this study concludes that vanillin causes a significantly lower amount of lung damage in comparison to vape liquid. Additionally, it displayed low thermal degradation as evaluated through GC-MS analysis, establishing that vanillin is a viable alternate compound. Vanillin was therefore integrated into VapeSafe, a smart tandem e-cigarette device that detects dangerous nicotine use and intervenes in real-time by switching compound release.

1. Introduction

Over the past three years, the percentage of high school and college students who report vaping regularly has tripled, with 14% of U.S. college students reporting daily use of e-cigarettes (National Institute on Drug Abuse, 2019). Rates of e-cigarette use among high schoolers has risen from 1.5 percent to 16 percent between 2011 and 2015, and rates among middle schoolers have increased by 9 times (U.S. Food and Drug Administration, 2020). One major problem associated with the use of vape products is that nicotine is highly addictive, and users can easily become "nic-sick," which refers to symptoms experienced when nicotine beyond an individual's tolerance level is consumed (American Lung Association, 2019). America's top e-cigarette companies claim that one pod contains "as much nicotine as a whole pack of cigarettes," making it very easy to approach dangerous nicotine levels (American Lung Association, 2019). There were over 200 nicotine abuse-related hospitalizations per month in 2020, compared to only one nicotine-related hospitalization per month in 2010 (National Poison Data System, 2021). An approach by which nicotine abuse can be stopped in an automated fashion is essential to reduce the number of vape-related hospitalizations.

This study proposes a tandem smart e-cigarette device that contains regular e-cigarette liquid on one side and an alternative compound on the other. When a threshold volume of nicotine has been released within a given time span (individualized to the user based on tolerance), the device switches from releasing e-cigarette liquid to an alternative vapor, preventing nicotine poisoning in an automated fashion. This study seeks to identify a suitable non-addictive alternate compound that tackles the central problems presented by traditional vape liquid: degradation into toxic compounds and irreversible lung damage.

Traditional e-cigarettes contain over 7000 chemicals including diacetyl, formaldehyde, acrolein, and propylene glycol (National Academies of Sciences, 2018). Diacetyl is used to deepen e-cigarette flavors and has been shown to damage small passageways in the lungs. Formaldehyde has repeatedly been linked to lung/heart disease, and acrolein, a key component of weed killer, also damages the lungs. Prior literature attempts to identify alternatives to these compounds, but most proposed substances are VOCs that would still cause lung damage (Duell, 2019). In addition to parent compounds that cause physiological damage, most of these compounds degrade into other toxic substances when vaporized

within the e-cigarette device (Duell, 2019). For example, citric acid has been proposed as an alternate compound and although it is inherently safe, it degrades into toxic citraconic anhydride after thermal exposure (Kaur, 2019). This study investigates the viability of vanillin and menthol as alternatives that display low thermal degradation and cause minimal lung damage. These compounds were selected for evaluation because they are similar in flavor to traditional e-cigarette liquids, so the user would not be able to detect a difference when the device switches compounds.

To evaluate the thermal degradation potential of the two experimental compounds, this study asks, what is the effect of thermal exposure on vanillin and menthol in terms of degradation? The experimental compounds' degradation was compared to a positive control (traditional vape liquid) and negative control (water), and the hypothesis was that both vanillin and menthol will display a significantly lower amount of degradation that the positive control. Additionally, to evaluate potential lung damage caused by the experimental compounds, this study specifically investigates: what is the effect of vanillin and menthol vapor on synthetic model lung tissue in terms of tissue permeation compared to traditional vape liquid? Both vanillin and menthol were hypothesized to display a significantly lower amount of model tissue permeation than traditional vape liquid.

2. Methods

Gas chromatography-mass spectrometry (GC/MS) is an analytical method used to identify different substances within a test sample. GC/MS was applied using CFM-ID to analyze the substances that the experimental compounds (vanillin and menthol) degrade into when heated. Five trials were run for each experimental compound and controls, the settings used are shown in Table 1. The number of peaks, relative intensity of peaks, and toxicity of components with highest intensity were analyzed.

Spectrum Type	Electrospray Ionization
Ion Mode	Positive
Adduct Type	[M+H]+

Table 1: Electrospray ionization spectrum type, positive ion mode, and [M+H]+ adduct type were applied for GC/MS analysis.

For the lung damage assessment, lung tissue was synthetically modelled by creating a lattice of air beads (alveoli) in aqueous solution. A density-driven approach was employed to develop a hydrogel-based lung tissue model. The standard density of the lung's posterior plane is 0.3 g/cm^3, and to mimic this density, a hydrogel with density 1.060 g/cm^3 was created and Styrofoam beads (0.003 g/cm^3) were suspended. The material's combined density was 0.28 g/cm^3. To prepare the gel, 714 ml of water and 80g of gelatin were heated to 50 degrees Celsius. Once the gelatin dissolved, 2g hydroquinone + 48 ml diH2O, 0.02g copper (II) sulfate pentahydrate + 30 mL diH_2O, and 0.353g of ascorbic acid + 50 mL diH_2O were added. Finally, 90g of methacrylic acid were added to the solution. The gel solution was poured over Styrofoam beads in small clear acrylic boxes, and the boxes rested overnight. To prepare each compound for evaluation, one drop of food coloring was added to 30 mL of dilute menthol, dilute vanillin, vape liquid, and water for visualization. All four solutions were vaporized and dispensed onto the hydrogel (4 trials for each). The lid of the acrylic box was then closed, and pictures were taken after twenty-minutes to assess which compound adhered most to the synthetic lung tissue. Image processing in Python (scikit-image) was applied for precise surface area analysis. Based on results from both the lung damage assessment and thermal degradation assessment, one experimental compound was integrated into the right side of the VapeSafe device.

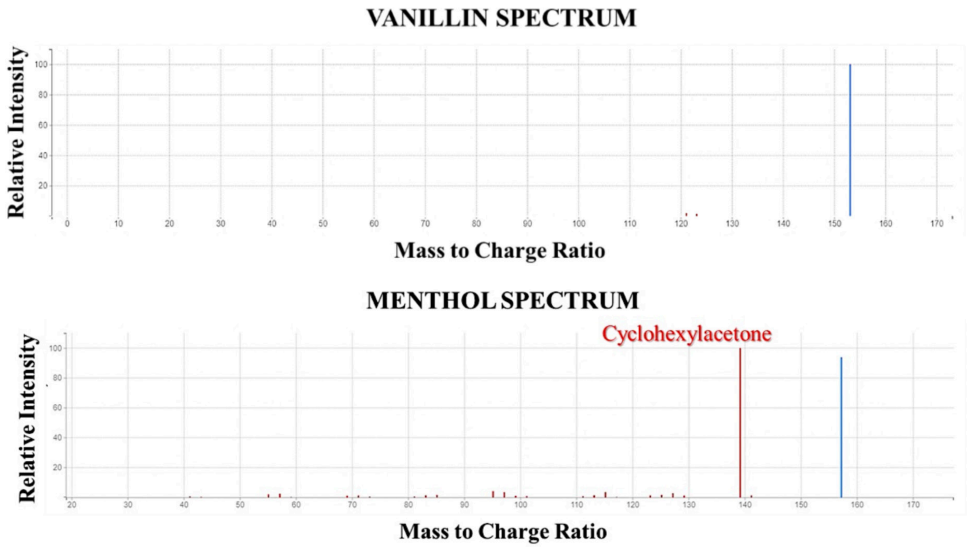

Figure 1 (top): Vanillin does not degrade into any new compounds with high relative intensity. The highest peak shown in blue represents the parent compound. **Figure 2** (bottom): Menthol degrades into one compound with high relative intensity, and this compound causes respiratory irritation.

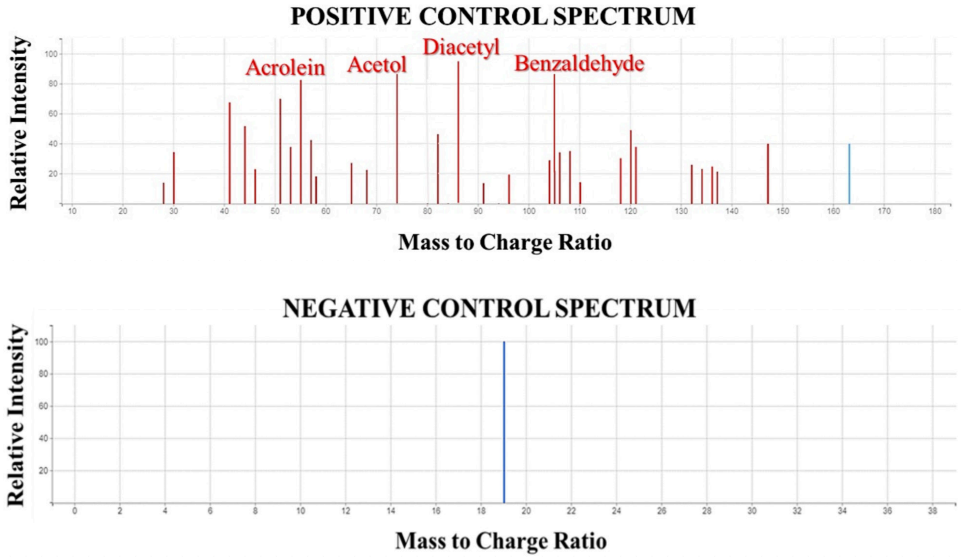

Figure 3 (top): Traditional vape liquid degraded into several compounds that have been linked to lung disease. The parent compound has a relative intensity of only 40%, meaning it degraded considerably. **Figure 4** (bottom): Water did not degrade into any new compounds as expected, making it an effective negative control.

3. Results

Figure 1 shows the GC/MS spectrum for vanillin, and the two small red peaks with a mass to charge ratio of approximately 120 indicate that vanillin degrades into two new compounds when heated. However, neither of the two new compounds have a high relative intensity. In comparison, Figure 2 shows that menthol degrades into 25 compounds when heated, but only one has high relative intensity. The compound with the highest relative intensity is $C_9H_{16}O$ (cyclohexylacetone) which causes respiratory tract irritation.

Figure 3 shows the GC/MS spectrum for traditional vape liquid (positive control), and this substance degraded into 31 new compounds with 4 of them having a relative intensity of greater than 80%. These compounds were C_3H_4O (acrolein), $C_3H_6O_2$ (acetol), $C_4H_6O_2$ (diacetyl), and C_7H_6O (benzaldehyde). The negative control's spectrum (water) displays no thermal degradation as shown in Figure 4.

Table 2 shows the means/SD of total peak counts and high intensity peak counts for the experimental compounds and controls. These values were used to run independent samples t-tests. As shown in Table 3, at a significance level of 0.01 and with 4 degrees of freedom, there is a significant difference in total number of peaks and high intensity peaks between vanillin and the positive control. There is a significant difference in high intensity peak count between menthol and the positive control but no significant difference for total peak count.

Sample	Sample Count (N)	Mean Peak Count (Rounded)	Standard Deviation of Peak Count	Mean High Intensity (>80%) Peak Count (Rounded)	Standard Deviation of High Intensity Peak Count
Vanillin	5	3	1.2	1	0
Menthol	5	26	1.8	2	0.3
Trad. Liquid	5	32	2.3	4	0.6
Water	5	1	0	1	0

Table 2: Across 5 trials for each compound, the mean peak count was greatest for traditional e-cigarette liquid and lowest for water. Menthol had a higher mean peak count (26) than vanillin (3). Similarly, for mean high intensity peak count, menthol had a higher mean (4) than menthol (2).

Sample	t-value for peak count	t-value for high intensity peak count
Vanillin w/ respect to positive control	**25.00**	**11.18**
Menthol w/ respect to positive control	4.59	**6.67**

Table 3: Bolded t-statistics values are significant at a significance level of 0.01 and with 4 degrees of freedom.

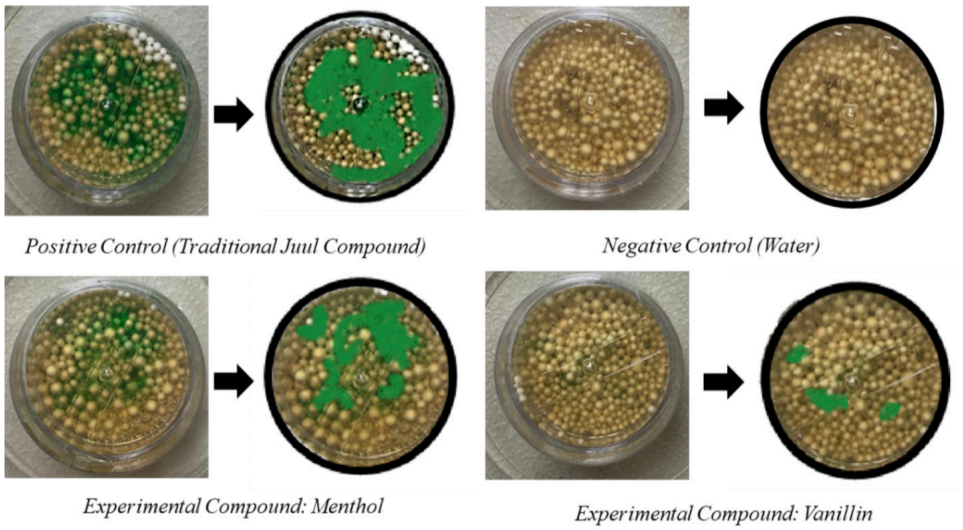

Figure 5: The surface area of synthetic lung tissue permeated by the compounds' vapor was highlighted computationally in Python. The positive control has the greatest highlighted area while the negative control has no highlighted area. The experimental compounds fall within these bounds.

Sample	Trad. Liquid	Menthol	Vanillin	Water
Affected Surface Area in Percentage Points (across 4 trials)	Mean: 73.9 SD: 5.6	Mean: 26.3 SD: 2.4	Mean: 7.4 SD: 1.3	Mean: 0.0 SD: 0.0

Sample	t-value
Menthol w/ respect to positive control	**15.6**
Vanillin w/ respect to positive control	**23.1**

Table 4 (left)**:** As computed in scikit-image, the traditional vape liquid had the highest affected surface area percentage. Menthol had the second-highest mean percentage (26.3%), and vanillin had a mean percentage of 7.4%. **Table 5** (right)**:** Bolded t-statistics values are significant at a significance level of 0.01 and with 3 degrees of freedom.

4. Discussion

In terms of thermal degradation potential, the t-test results provide preliminary confirmation that vanillin could be a safe alternative for traditional vape liquid. Given that there is a significant difference in high intensity peak count between menthol and the positive control but not for regular peak count, no definite conclusion can be drawn about the safety of menthol in terms of thermal degradation. Both compounds evaluated in this study display comparatively lower thermal degradation potential than previously investigated compounds. Previous studies rarely differentiate between high intensity peak count and total peak count. This added level of analysis provides some evidence of menthol's safety because there is a significant difference in high intensity peak count between menthol and traditional e-cigarette liquid.

Both vanillin and menthol display a significantly lower amount of lung tissue permeation than the positive control. When a t-test is run at a 0.1% significance level with 3 degrees of freedom to compare vanillin and menthol, the t-value exceeds the critical value. This indicates that vanillin displays a significantly lower amount of tissue permeation than menthol, so vanillin is the safest in terms of lung damage. The density-driven approach to model lung tissue has not been used to evaluate the effects of e-cigarette vapor before, though these results align with previous work showing that e-cigarettes cause lung damage.

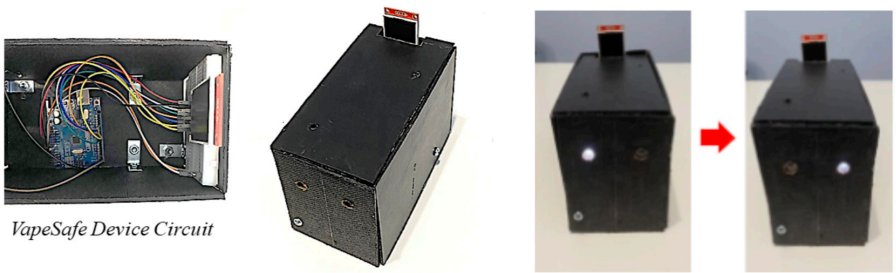

Figure 6: The VapeSafe prototype device hosts the traditional vape compound on the left and vanillin on the right.

5. Conclusions

This study provides preliminary confirmation that vanillin is a viable alternate compound for integration into a smart e-cigarette device in terms of both thermal degradation and potential for lung damage. Therefore, vanillin was integrated in the right compartment of VapeSafe, a smart e-cigarette proof-of-concept device that begins releasing the vaporized alternate compound when a threshold level of nicotine has been dispensed in a timespan to prevent nicotine poisoning. The prototype was built using an Arduino Uno and WiFi module as shown in Figure 6.

In the future, the lung damage assessment could be conducted on lung epithelial cells for more accurate results. A wider range of compounds could be tested as safer alternatives for traditional vape liquid including other diacetyl-free substances.

References

[1] National Institute on Drug Abuse. (2020, July 14). *Monitoring the future 2019 survey results: Vaping*. National Institute on Drug Abuse. Retrieved November 20, 2021, from https://www.drugabuse.gov/drug-topics/trends-statistics/infographics/monitoring-future-2019-urvey-results-vaping.

[2] Products, C. for T. (2020, September 17). *Vaporizers, e-cigarettes, and other ends*. U.S. Food and Drug Administration. Retrieved November 20, 2021, from http://www.fda.gov/tobacco-products/products-ingredients-components/vaporizers-e-cigarettes-and-other-electronic-nicotine-delivery-systems-ends#stats.

[3] Editorial Staff | October 2, 2019 T. H. & W. L. H. and D. (2019, October 2). *What it means to be Nic-sick*. EACH Breath Blog | American Lung Association. Retrieved November 20, 2021, from https://www.lung.org/blog/nic-sick.

[4] *American Association of Poison Control Centers*. American Association of Poison Control Centers - E-Cigarettes and Liquid Nicotine. (n.d.). Retrieved November 20, 2021, from https://aapcc.org/track/ecigarettes-liquid-nicotine.

[5] Sciences, N. A. of, Engineering, & Medicine, and. (2018, January 23). *Toxicology of e-cigarette constituents*. Public Health Consequences of E-Cigarettes. Retrieved November 20, 2021, from http://www.ncbi.nlm.nih.gov/books/NBK507184/.

[6] Duell, A. (2019, December 4). *Analysis of e-cigarette liquids and aerosols by NMR*. Retrieved November 20, 2021, from https://pdxscholar.library.pdx.edu/cgi/viewcontent.cgi?article=6423&context=open_access_etds.

[7] Kaur, G., Muthumalage, T., & Rahman, I. (2018, February 23). *Mechanisms of toxicity and biomarkers of flavoring and flavor enhancing chemicals in emerging tobacco and non-tobacco products*. Toxicology letters. Retrieved November 20, 2021, from https://pubmed.ncbi.nlm.nih.gov/29481849/.