Did JUUL alter the content of menthol pods in response to US FDA flavour enforcement policy?

Amira Yassine [1] Rachel El Hage,[1,2] Ahmad El-Hellani [2,3] Rola Salman,[2,4] Soha Talih [2,4] Thomas Eissenberg [2,5] Alan Shihadeh [2,4] Najat Saliba [1,2]

[1]Department of Chemistry, American University of Beirut, Beirut, Lebanon
[2]Department of Psychology, Virginia Commonwealth University Center for the Study of Tobacco Products, Richmond, Virginia, USA
[3]Division of Environmental Health Sciences, The Ohio State University College of Public Health, Columbus, Ohio, USA
[4]Department of Mechanical Engineering, American University of Beirut, Beirut, Lebanon
[5]Psychology and Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Richmond, Virginia, USA

Correspondence to
Professor Najat Saliba, Department of Chemistry, American University of Beirut, Beirut 1107 2020, Lebanon; ns30@aub.edu.lb

Received 2 May 2022
Accepted 24 June 2022

ABSTRACT

Background The JUUL electronic cigarette (e-cigarette) remains popular in the USA and has a big prevalence among youth. In response to the popularity of JUUL and similar devices among youth, the US Food and Drug Administration issued in February 2020 an enforcement policy to remove all flavoured cartridge/pod-based e-cigarettes from the market except for tobacco and menthol. Subsequent studies showed that some users of the now-removed flavoured JUUL pods (especially cool mint) switched to menthol-flavoured JUUL pods with similar satisfaction.
Methods We quantified menthol, nicotine, propylene glycol (PG) and vegetable glycerol (VG) in JUUL pod samples (Menthol, Classic Menthol and Cool Mint) that were purchased in 2017, 2018 and 2020 (only Menthol) to evaluate composition differences before and after the enforcement policy. We also analysed the samples to detect other cooling agents using a screening gas chromatography-mass spectrometry headspace method that we developed for this purpose.
Results Menthol concentration was significantly higher in 2020 products than in products from prior years. Moreover, other cooling agents varied across pods. The PG/VG volume ratio was 27/63 in all pods examined.
Conclusion This study highlights how regulations intended to reduce e-cigarette prevalence among youth may influence changes in tobacco product characteristics in ways that regulators may not have foreseen.

INTRODUCTION

In 2015, JUUL introduced a pod-based electronic cigarette (e-cigarette) system that succeed to delivered nicotine efficiently. The liquid in the pod contained nicotine in the salt form, which allowed JUUL to use unprecedentedly high nicotine concentration without making the aerosol too harsh to inhale.[1] Soon after its release, JUUL sales rose to predominate the electronic cigarette market in the USA,[2] with high prevalence among youth.[3 4]

In response to what it described as an epidemic of youth e-cigarette use, the US Food and Drug Administration (FDA) issued in February 2020 an enforcement policy to remove all flavoured cartridge or/pod-based e-cigarettes except tobacco and menthol-flavoured pods from the market.[5] One report indicated that users of the now banned flavoured JUUL pods (especially mint) switched to menthol, and experienced similar satisfaction.[6] Other studies found that by May 2020, JUUL pod sales were dominated by menthol accounting for >60% of sales.[7 8]

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ In February 2020, an enforcement policy was imposed to remove all flavoured cartridge or/pod-based e-cigarettes except tobacco and menthol pods from the market.
⇒ Reports showed that some users of the removed flavoured JUUL pods (especially mint) switched to menthol JUUL pods with similar satisfaction.
⇒ This study sought to examine whether JUUL's liquid formulations changed in the years surrounding the flavour restriction.

WHAT THIS STUDY ADDS

⇒ Following the enforcement policy, tested samples of JUUL menthol pods had significantly greater menthol content than the prerestriction products.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Menthol and other coolants in e-cigarettes should be considered as a target for regulation.

In this study, we sought to examine whether JUUL's liquid formulations changed in the years surrounding the flavour enforcement policy. We analysed the liquid composition, including nicotine content, propylene glycol (PG)/vegetable glycerol (VG) ratio and menthol concentration of Menthol, Classic Menthol and Cool Mint pods purchased in various years. In addition, we developed a gas chromatography-mass spectrometry (GC-MS) headspace method to detect other cooling agents in the tested pods.

METHODS

Tested items

Cool Mint (2017, 2018), Classic Menthol (2017, 2018) and Menthol (2018) pods were purchased in 2017 and 2018 and Menthol (2020) pods were purchased in May 2020. All products were purchased at convenience markets in the USA. Three different pods from each purchase year and flavour were analysed. Liquids were removed from the previously unopened pods using a Pasteur pipette then transferred to a vial which was stored in a darkened refrigerator at 4°C.

Determination of nicotine and PG/VG ratio

Nicotine concentration and PG/VG ratio were determined using previously described methods.[9 10]

To cite: Yassine A, El Hage R, El-Hellani A, *et al*. *Tob Control* 2022;**31**:s234–s237.

Table 1 Liquid composition of JUUL pods before and after the Food and Drug Administration flavour enforcement policy

	Cool Mint 2017	Classic Menthol 2017	Cool Mint 2018	Classic Menthol 2018	Menthol 2018	Menthol 2020
JUUL liquid composition						
Nicotine concentration (mg/mL)	58.13* (0.96)	58.14* (0.38)	57.69* (0.65)	60.14 (0.96)	60.14 (1.34)	64.09 (2.00)
Free base nicotine (%)	2.26 (0.26)	2.05 (0.31)	3.60 (0.41)	2.33 (0.20)	3.18 (0.29)	2.88 (0.06)
PG/VG (%v/v)	27/63	27/63	27/63	27/63	27/63	26/64
Menthol concentration (mg/mL)	7.44† (0.28)	7.54† (0.12)	8.05† (0.23)	7.39* (0.34)	9.71† (0.20)	11.96 (0.19)
% other compounds (semi-quantitative)						
3-Octanol	0.23 (0.02)	ND	0.41 (0.02)	ND	ND	ND
p-Mentha-1.4 (8) diene	0.03 (0.01)	ND	0.02 (0.01)	ND	ND	ND
Eucalyptol	0.40 (0.03)	ND	0.47 (0.01)	ND	ND	ND
β-Terpineole	0.03 (0.01)	ND	0.06	ND	ND	ND
β-Linalool	0.12	ND	0.15 (0.01)	ND	ND	ND
Neomenthol‡	0.51 (0.02)	ND	0.46 (0.02)	ND	ND	ND
Neoisomenthol‡	0.17 (0.01)	ND	0.16 (0.02)	ND	ND	ND
Pulegone	0.19 (0.01)	ND	0.21 (0.01)	ND	ND	ND
Carvone	0.05 (0.01)	ND	0.05	ND	ND	ND
Piperitone	0.06	ND	0.08	ND	ND	ND
Menthyl acetate	0.56 (0.04)	ND	0.54 (0.04)	ND	ND	ND
p-Menth-3-one	5.90 (0.44)	0.11 (0.02)	5.76 (0.01)	0.08 (0.01)	0.10 (0.01)	0.06 (0.01)
Isomenthol‡	20.31 (1.03)	0.9 (0.03)	21.51 (0.32)	0.78 (0.24)	0.90 (0.08)	0.70 (0.08)
Menthol‡	71.44 (0.70)	98.98 (0.01)	70.12 (0.35)	99.13 (0.25)	99.00 (0.07)	99.24 (0.09)

Results are shown as mean (SD) for n=3 samples.
Mean (SD).
*p<0.05 relative to Menthol 2020.
†p<0.01 relative to Menthol 2020.
‡Cooling agent.
ND, not detected.

Quantification of menthol

Menthol concentration was determined by injecting the diluted liquid solution onto a GC-MS. In brief, 5 µL of JUUL liquid was dissolved in 1 mL of methanol, 5 µL of an internal standard: Carvacrol (1000 µg/mL in methanol), was added and the mixture was shaken for 5 min. The prepared samples were then injected on GC-MS and quantified versus a direct calibration curve (0–50 µg/mL) prepared from standard menthol solutions. The limit of detection and the limit of quantification were determined at 0.210 and 0.637 *µ*g/mL, respectively. The tested validation parameters were found to be within acceptable limits (%RSD: 5.38–8.97). Each sample was analysed in triplicate.

For GC-MS analysis, a Trace GC Ultra system coupled with a DSQ II Quadrupole spectrometer was used, equipped with a Triplus autosampler and X-Calibur software. Compounds were separated using a DB-5MS with helium as a carrier gas in a constant flow rate of 1 mL/min. The temperature programme was set at 60°C (hold for 2 min), ramp to 150°C with 5°C/min then another ramp to 250°C with 15°C/min (hold for 2 min). The total run time was 28.67 min. The injection volume was 1 µL. The injector temperature and the transfer line temperature were set at 230°C and 280°C, respectively. The MS operated in positive electron impact mode. The ion source temperature was set at 250°C.

Screening for other cooling agents

A new method was developed to screen for other cooling agents in the tested pods. In brief, 30 µL of the e-liquid was added to 3 mL of water and shaken for 3 min in a well-sealed head-space vial. Then the samples were allowed to equilibrate in a heated compartment at 80°C for 5 min. Samples were analysed in triplicate.

Detection of cooling agents was performed in full scan mode covering 40–400 m/z. It was based on the mass fragmentation of the detected compounds. The temperature programme on the GC was set at 50°C for 3 min, then ramped at 10°C/min to 220°C (hold for 3 min) for a total run time of 23 min. All the other details of the GC-MS system are like the menthol analysis described in the previous paragraph.

A semi-quantitative analysis of the detected flavour agents was done using a previously described method.[11] In brief, areas of all the detected compounds were summed, and the percentage of each compound in the sample was computed as $\frac{Area\ compound}{Sum\ of\ all\ the\ areas} \times 100$.

Statistical methods

A two-tailed distribution and heteroscedastic t-test were used to investigate any significant difference in nicotine and menthol concentrations between the pods purchased before the enforcement policy (2017, 2018) vs those purchased after the enforcement policy (2020).

RESULTS

We found that the tested JUUL pods contained approximately the same PG/VG ratio (table 1). The nicotine content, which was predominantly in the protonated form, ranged between 57.7 and 64.1 mg/mL. The nicotine concentration was found to be significantly higher in Menthol (2020) pods than in Classic Menthol (2017): $p<0.05$, Cool Mint (2017): $p<0.05$ and Cool Mint (2018): $p<0.05$. Menthol concentration was found to be the highest in Menthol (2020) pods compared with Menthol (2018): $p<0.001$, Classic Menthol (2018): $p<0.05$, Cool Mint (2018): $p<0.001$, Classic Menthol (2017): $p<0.0001$ and Cool Mint (2017): $p<0.0001$. No significant difference was found in menthol concentration between the different batches of Menthol (2020): $p=0.5948$. The non-targeted analysis using GC-MS headspace showed various levels of isomenthol and p-menth-3-one in all the tested pods. Two additional cooling agents and many other non-cooling compounds were identified in Cool Mint (2017, 2018). All identified compounds were present at levels lower than menthol.

Discussion

Menthol has been widely used as a cooling agent in tobacco products.[12] It induces a perception of a cool sensation by activating the transient receptor potential cation channel subfamily M member 8 found in the oral cavity.[13] Studies have found that menthol in cigarettes such as Newport (menthol range: 4.21–5.30 mg/cigarette)[14] contributed to the appeal, initiation and addiction potential among youth.[15 16] Recent evidence extended this observation to e-cigarettes.[17 18] Furthermore, menthol reduces the bitterness and increases the smoothness of inhaled nicotine, impacting e-cigarette appeal.[19]

In this work, we quantified menthol and nicotine levels in JUUL pods purchased in the years surrounding the FDA flavour enforcement policy of February 2020. Our data show that Menthol pods, procured in May 2020, exhibited higher menthol concentrations than all the tested products purchased before the enforcement policy. Also, nicotine concentration for the 2020 products was greater than that of the 2017 products and the Cool Mint 2018 products. These findings therefore suggest that JUUL's menthol content increased following the FDA flavour enforcement policy, and that nicotine content may vary by product even when the label indicates the same 5% concentration. That the Cool Mint pods contained as much menthol as the Menthol pods highlights that manufacturer market flavours under different labels and may explain why previous users of Cool Mint found Menthol pods similarly satisfying.[6]

One limitation of this study is that we did not have information on the production dates of the products; what we procured from store shelves in May 2020 might have been from stocks shipped before the enforcement policy. Nonetheless, the difference in menthol content across products is clear, and manufacturers may adjust liquid composition in anticipation of enforcement policies. Another limitation is that a limited pool of products was available for sampling, and that observed differences across years may reflect chance variations by batch rather than by year due to poor quality control. This possibility can be ruled out by a more extensive independent study if samples are available.

Importantly, Krishnan-Sarin *et al*[17] evaluated the independent and interactive effects of menthol and nicotine and found that higher concentrations of menthol may increase the reward of high nicotine concentration.[17] In addition, other natural and synthetic cooling agents can be added to tobacco products to impart or enhance cooling sensation.[20–23] For example, WS-3 is a synthetic cooling agent that has replaced menthol in JUUL Mint pods sold in the European Union but not in the USA.[24] Our non-targeted analysis showed that Menthol (2018, 2020) and Classic Menthol (2017, 2018) pods have similar profiles and levels of cooling agents such as isomenthol. In contrast, Cool Mint (2017, 2018) exhibited higher levels of isomenthol and trace levels of two other cooling agents. The array of compounds that impart a cooling sensation found in JUUL pods suggests that industry may readily circumvent regulations if the later focus narrowly on menthol.

In conclusion, our findings suggest the possibility that the menthol content of JUUL pods changed in a manner that may have increased the appeal of these products when other flavoured pod-based products were no longer available. This work highlights the need to consider menthol and other natural and synthetic coolants in e-cigarettes as a possible target for regulation, as well as the need for regular independent testing to assure that products remain compliant with regulation.

Twitter Najat Saliba @aal_najat

Contributors AY, REH, AEH, AS, TE and NS: conception and design of research. AY, REH, RS: performed experiments. AY and AEH: drafted the manuscript. All the authors edited, revised and approved the final version of the manuscript.

Funding This research is supported by grant number U54DA036105 from the National Institute on Drug Abuse of the National Institutes of Health and the Center for Tobacco Products of the US Food and Drug Administration.

Competing interests TE and AS are paid consultants in litigation against the tobacco and e-cigarette industry and are named on one patent for a device that measures the puffing behaviour of e-cigarette users and another patent application for a smoking cessation intervention. TE is also named on a patent application for a smartphone app that determines e-cigarette device and liquid characteristics.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The data supporting the findings are available within the article.

ORCID iDs
Amira Yassine http://orcid.org/0000-0002-8692-6183
Ahmad El-Hellani http://orcid.org/0000-0002-1047-0597
Soha Talih http://orcid.org/0000-0002-3520-675X
Thomas Eissenberg http://orcid.org/0000-0002-8277-5437
Alan Shihadeh http://orcid.org/0000-0001-6387-8564
Najat Saliba http://orcid.org/0000-0002-4276-1524

REFERENCES

1 Leventhal AM, Madden DR, Peraza N, *et al*. Effect of exposure to e-cigarettes with salt vs free-base nicotine on the appeal and sensory experience of vaping: a randomized clinical trial. *JAMA Netw Open* 2021;4:e2032757.
2 Zaleski O. E-Cigarette Maker Juul Labs Is Raising $1.2 Billion 2018. Available: https://www.bnnbloomberg.ca/e-cigarette-maker-juul-labs-is-raising-1-2-billion-1.1101386
3 Kavuluru R, Han S, Hahn EJ. On the popularity of the USB flash drive-shaped electronic cigarette Juul. *Tob Control* 2019;28:110–2.
4 Huang J, Duan Z, Kwok J, *et al*. Vaping versus JUULing: how the extraordinary growth and marketing of JUUL transformed the US retail e-cigarette market. *Tob Control* 2019;28:146–51.
5 FDA. FDA finalizes enforcement policy on unauthorized flavored cartridge-based e-cigarettes that appeal to children, including fruit and mint, 2020. Available: https://www.fda.gov/news-events/press-announcements/fda-finalizes-enforcement-policy-unauthorized-flavored-cartridge-based-e-cigarettes-appeal-children
6 Yingst JM, Bordner CR, Hobkirk AL, *et al*. Response to flavored cartridge/pod-based product ban among adult JUUL users: "you get nicotine however you can get it". *Int J Environ Res Public Health* 2020;18:207.
7 Diaz MC, Donovan EM, Schillo BA, *et al*. Menthol e-cigarette sales rise following 2020 FDA guidance. *Tob Control* 2021;30:700–3.
8 Ali FRM, Diaz MC, Vallone D, *et al*. E-cigarette unit sales, by product and flavor type - united states, 2014-2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1313–8.
9 El-Hellani A, El-Hage R, Baalbaki R, *et al*. Free-base and protonated nicotine in electronic cigarette liquids and aerosols. *Chem Res Toxicol* 2015;28:1532–7.
10 El-Hellani A, Salman R, El-Hage R, *et al*. Nicotine and carbonyl emissions from popular electronic cigarette products: correlation to liquid composition and design characteristics. *Nicotine Tob Res* 2018;20:215–23.
11 Ruiz-Hernández V, Roca MJ, Egea-Cortines M, *et al*. A comparison of semi-quantitative methods suitable for establishing volatile profiles. *Plant Methods* 2018;14:67.
12 WHO. Menthol in tobacco products.
13 Diomede L. The soothing effect of menthol, eucalyptol and high-intensity cooling agents. *Nutrafoods* 2017;16:79.
14 Ai J, Taylor KM, Lisko JG. Menthol content in US marketed cigarettes. *N&TR* 2016;18:1575–80.
15 Hersey JC, Nonnemaker JM, Homsi G. Menthol cigarettes contribute to the appeal and addiction potential of smoking for youth. *Nicotine Tob Res* 2010;12 Suppl 2:S136–46.
16 SoberRecovery SW. Newport Cigarettes - The Top Growing Cigarette in the U.S 2014. Available: https://www.soberrecovery.com/addiction/newport-cigarettes-the-top-growing-cigarette-in-the-u-s/
17 Krishnan-Sarin S, Green BG, Kong G, *et al*. Studying the interactive effects of menthol and nicotine among youth: an examination using e-cigarettes. *Drug Alcohol Depend* 2017;180:193–9.
18 Cullen KA, Gentzke AS, Sawdey MD, *et al*. E-Cigarette use among youth in the United States, 2019. *JAMA* 2019;322:2095–103.
19 Leventhal A, Cho J, Barrington-Trimis J, *et al*. Sensory attributes of e-cigarette flavours and nicotine as mediators of interproduct differences in appeal among young adults. *Tob Control* 2020;29:679–86.
20 Jabba SV, Erythropel HC, Torres DG, *et al*. Synthetic cooling agents in US-marketed e-cigarette refill liquids and popular disposable e-cigarettes: chemical analysis and risk assessment. *Nicotine Tob Res* 2022;24:1037–46.
21 Omaiye EE, McWhirter KJ, Luo W, *et al*. High-Nicotine electronic cigarette products: toxicity of JUUL fluids and aerosols correlates strongly with nicotine and some flavor chemical concentrations. *Chem Res Toxicol* 2019;32:1058–69.
22 Pankow JF, Luo W, McWhirter KJ, *et al*. 'Menthol-Plus': a major category of cigarette found among 'concept' descriptor cigarettes from Mexico. *Tob Control* 2022;31:e18–24.
23 Erythropel HC, Anastas PT, Krishnan-Sarin S, *et al*. Differences in flavourant levels and synthetic coolant use between USA, EU and canadian Juul products. *Tob Control* 2020;30:453–5.
24 Jabba SV, Jordt S-E. Turbocharged Juul device challenges European tobacco regulators. *Eur Respir J* 2020;56:2002430.