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Emissions from heated terpenoids present in vaporizable cannabis concentrates

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Abstract

Vaporizable cannabis concentrates (VCCs) consumed as a liquid (vaping) or a waxy solid (dabbing) are becoming increasingly popular. However, their associated emissions and impacts have not been fully described. Mixtures containing different proportions of twelve VCC terpenoids and high-MW compounds were heated at 100 – 500 °C inside a room-sized chamber, to simulate emissions. Terpenoids, thermal degradation byproducts, and ultrafine particles (UFPs) were quantified in chamber air. Air samples contained over 50% of emitted monoterpenes, and less than 40% of released sesquiterpenes and terpene alcohols. Eleven degradation byproducts were quantified, including acrolein ($1.3 - 3.9 \mu\text{g m}^{-3}$) and methacrolein ($2.0 \mu\text{g m}^{-3}$). A large amount of UFPs were released upon heating, and remained airborne for at least three hours. The mode diameter increased from 80 nm at 100 °C to 140 nm at 500 °C, and particles smaller than 250 nm contributed to 90% of $\text{PM}_{1.0}$. The presence of 0.5% of lignin, flavonoid and triterpene additives in the heated mixtures resulted in a threefold increase in particle formation rate and $\text{PM}_{1.0}$ concentration, suggesting that these high MW compounds enhanced aerosol inception and growth. Predicted UFP emission rates in typical consumption scenarios ($6 \times 10^{11} - 2 \times 10^{13} \text{ \# min}^{-1}$) were higher than, or comparable with, other common indoor sources such as smoking and cooking.

Introduction

Legalization of medical and recreational uses of marijuana (cannabis) in several States of the USA, and in other countries, has led to the rapid development and visibility of new cannabis products. Manufacturing and retail was legalized in California in January 2018, becoming the largest lawful marijuana market with ~\$3B annual sales.¹ A 2017 analysis of cannabis sales in Washington State revealed that, while combustible products still accounted for most transactions, the share of vaporizable cannabis concentrates (VCCs, also referred to as *extracts* or *hash oils*) increased by 146% between 2014 and 2016, comprising 21% of sales. The average content of Δ^9 -tetrahydrocannabinol (THC) in extracts (69%) was more than three times that of flower-based products (21%).² Liquid VCCs can be consumed by vaping,³ while waxy concentrates can be aerosolized by direct application onto a heated surface to produce high impact, THC-rich puffs (“dabbing”).⁴ On a survey of more than 6,000 current marijuana users in 12 States, a significant fraction reported consuming VCCs through vaping (19.4%) and dabbing (14.5%), in most cases in conjunction with other modes of marijuana use.⁵ With legalization, innovative delivering devices became available for use with VCCs, appealing to a growing and diverse group of consumers.^{3,6} Due to their higher potency, VCCs are associated with more negative consequences than flower-based products, such as psychosis episodes and panic attacks.⁷ Vaping also facilitates access to cannabis by young users, and prompts an earlier age of onset, increasing the risks of addictive behavior.^{8,9} Yet, vaping is often perceived as healthier than smoking, because it avoids inhalation of toxic smoke constituents.^{7,10} For that reason, cannabis consumers in states that enacted medical marijuana laws are more likely to vape.¹¹

Most studies of vaping emissions have focused primarily on e-liquids containing propylene glycol (PG) and vegetable glycerin (VG), which are used as solvents and vapor-forming agents in nicotine-delivering formulations. These compounds are not typically used as the primary solvents in e-liquids containing THC and other cannabinoids, which are prepared instead by mixing VCCs with terpenes and other solvents (different from PG and VG) to decrease its viscosity.^{3,12} Major constituents consumed from the oily or waxy VCCs include the active cannabinoids and a large amount of volatile, semi-volatile and polymeric materials extracted from buds, trichomes, flowers and leaves. Particularly relevant are terpenes, terpenoids, lignans and flavonoids,¹³⁻¹⁶ which may form harmful byproducts when heated. Monoterpenes, sesquiterpenes, sesquiterpenoid alcohols and triterpenes are of particular concern because they are present in large amounts,¹⁷ and their decomposition is likely to generate ultrafine particles and low molecular weight oxidized byproducts that irritate the respiratory system.

Thermal degradation of terpenoids results in byproducts from dehydrogenation, epoxidation, double bond cleavage, allylic oxidations and rearrangements.¹⁸ Some of these byproducts become condensation nuclei for the formation of ultrafine secondary organic aerosol particles.^{19, 20} THC is present in the plant as tetrahydrocannabinolic acid (THCA), an inactive carboxylate, which is activated by decarboxylation upon heating. High temperatures up to 340 – 482 °C are needed to vaporize VCCs, and are significantly higher than those commonly used with PG/VG formulations.²¹ The aerobic decomposition of PG occurs at 127 °C, and that of glycerin at 200 – 290 °C.²² Their thermal decomposition byproducts include acrolein, formaldehyde and acetaldehyde, which are emitted at higher rates as the applied power of vaping devices increases.^{23, 24} A study evaluating the formation of formaldehyde and acetaldehyde in the vapor from heated e-liquids containing carboxylated and decarboxylated cannabinoids found that the latter emitted higher aldehyde levels, possibly due to the higher temperatures required for THC activation.²⁵ Thermal decomposition of cannabis terpenoids was found to produce isoprene, methacrolein, benzene, 1,3-butadiene and other compounds upon heating.^{12, 21}

Emissions associated with cannabis vaping and dabbing can lead to acute and chronic health effects in users and bystanders. On rare occasions, such emissions have led to severely toxic effects. A deadly outbreak of vaping product-associated lung injury (EVALI) took place in the United States between June 2019 and February 2020. It resulted in at least 68 deaths and more than 2800 hospitalizations.²⁶ THC-containing products were shown to be linked to most EVALI cases.²⁷ Vitamin E acetate (α -tocopheryl acetate, $C_{31}H_{52}O_3$, MW 473 g mol⁻¹), an illicit additive in THC vaping liquids, was found in many of the consumed products and in bronchoalveolar lavage fluid extracted from EVALI patients, and is considered to be a key factor associated with the disease.²⁸ Since the volatility of vitamin E acetate is very low, this compound was likely transported to the lung by particles produced in the inception of the THC-containing aerosol. Mice exposure experiments showed that ultrafine aerosol particles generated by vaping were able to deliver vitamin E acetate to the lung.²⁹ Other low-volatility species such as methamphetamine (MW 149 g/mol) and methadone (MW 309 g/mol), when vaped in PG/VG formulations, were also shown to be transported in particles smaller than 0.3 μ m that can reach the alveolar regions of the lungs.³⁰

Despite the growing amount of research on chemical emissions from cannabis use, little is known about the impact of thermal degradation byproducts and ultrafine particles (UFPs) generated from heating non-cannabinoid VCC constituents. As VCCs become more widely used, their impacts on consumers and the indoor environment need to be better understood. The goals of this study are to identify potentially harmful thermal decomposition byproducts, and to determine the concentration, particle size distribution,

and chemical transformations of aerosols produced from heated mixtures simulating non-cannabinoid VCC fractions. This study illustrates the role of UFPs as carriers of low-molecular weight species, a process that could deliver these chemicals deep into the user's respiratory system, and could expose non-users by dispersing otherwise non-volatile and semi-volatile species in the indoor environment.

Experimental Methods

Preparation of test mixtures

Despite legalization at the State level, cannabis products, THC and other cannabinoids continue to be listed by the US Drug Enforcement Administration (DEA) as a Schedule 1 controlled substance. For this reason, our experiments did not use cannabis products nor included cannabinoids. Instead, we focused on concomitant substances present in VCCs, including monoterpenes (β -myrcene, d-limonene, α -pinene, β -pinene), terpene alcohols (linalool), sesquiterpenes (β -caryophyllene, α -humulene), sesquiterpenoid alcohols (cedrol, α -bisabolol), triterpenes (friedelin), lignans (secoisolariciresinol), and flavonoids (quercetin). The reported composition of extracts and hash oils varies depending on the cannabis strain, process of extraction and storage conditions.^{13, 14, 16}

To evaluate the impact of these substances on indoor air quality after heating and decomposition, we studied a "full terpenoid" mixture comprising nine compounds commonly found in VCCs, and two separate mixtures containing the corresponding light and heavy terpenoid fractions. In addition, a "complex" mixture was prepared by adding a small amount (~0.5%) of high MW compounds (triterpenes, lignans and flavonoids) to the full terpenoid mixture. Mixture compositions are shown in Table 1, with molecular structures shown in Figure S1 in the Supporting Information (SI). Mixing ratios were based on those reported in the literature.^{14, 16} All mixtures were prepared separately, by combining research-grade pure compounds (>95% purity, Sigma Aldrich), most of which were in the liquid form.

Aerosol emission tests

Experiments were carried out by heating small volumes of the different mixtures listed in Table 1, consistent with typical amounts of terpenoids released during product use. In each test, 20 μ L of a liquid mixture were applied with a syringe onto a glass Petri dish that had been pre-heated to temperatures between 25 and 500 °C, using a heat plate inside a 20-m³ stainless-steel environmental chamber. The Petri dishes used in these experiments had been pre-baked at 450 °C for 4 h in a muffle furnace, to eliminate all organic vestiges from their surface. Temperature was measured directly at the Petri dish surface with a

type K thermocouple connected to a data logger thermometer (Omega, Model HH309A). Due to the size of the chamber and the fact that it was housed inside an air-conditioned room, the chamber air temperature remained at room level (between 19 and 25 °C), and temperature variation due to the presence of the heating element was negligible. The chamber air exchange rate was 0.2 h⁻¹, as determined by injection of CO₂ followed by monitoring its concentration change using a EGM-4 CO₂ monitor (PP Systems). Two mixing fans were positioned inside the chamber at different heights, pointing at different angles, to ensure quick and complete mixing.

Experiments were conducted by releasing into the chamber the emissions resulting from rapid heating of the different mixtures under controlled conditions (i.e., surface temperature, mixture composition and amount delivered). These emissions can be considered representative of those produced during vaping or dabbing. The method was not developed to reproduce the design and operation characteristics of vaping or dabbing devices, but rather to facilitate accurate measurement of the above-mentioned experimental parameters. Volatile/semivolatile organic compound (VOC/SVOC) indoor air concentrations during the first hour, and particle size distribution and concentration was recorded for several hours. The effect of changing the heating temperature was studied only with the full terpenoid mixture, which was allowed to evaporate without heating (surface temperature 25 °C), and by heating the surface at 100, 250, 400, and 500 °C. The effect of mixture composition was evaluated by heating the light, heavy fraction, and complex mixture at the highest temperature, 500 °C.

Table 1. Composition of mixtures used in this study, expressed as mass proportion.

Compound	MW	Formula	log P _{vap} [*]	Light terpenoid mixture (%)	Heavy terpenoid mixture (%)	Full terpenoid mixture (%)	Complex mixture (%)
<i>Light terpenoids</i>							
α-Pinene	136	C ₁₀ H ₁₆	0.68	11.3	–	5.2	5.2
β-Pinene	136	C ₁₀ H ₁₆	0.47	14.2	–	6.6	6.5
β-Myrcene	136	C ₁₀ H ₁₆	0.30	40.0	–	18.3	18.3
d-Limonene	136	C ₁₀ H ₁₆	0.19	28.2	–	12.8	12.8
Linalool	154	C ₁₀ H ₁₈ O	-0.80	6.3	–	2.9	2.9
<i>Heavy terpenoids</i>							
β-Caryophyllene	204	C ₁₅ H ₂₄	-1.9	–	16.1	8.7	8.7
α-Humulene	204	C ₁₅ H ₂₄	-2.1	–	14.2	7.7	7.6
Cedrol	222	C ₁₅ H ₂₆ O	-4.1	–	35.1	19.1	18.9
α-Bisabolol	222	C ₁₅ H ₂₆ O	-3.8	–	34.6	18.7	18.6

<i>High molecular weight compounds</i>							
Friedelin (triterpene)	427	C ₃₀ H ₅₀ O	N.V.	-	-	-	0.2
Secoisolariciresinol (lignan)	362	C ₂₀ H ₂₆ O ₆	N.V.	-	-	-	0.1
Quercetin (flavonoid)	302	C ₁₅ H ₁₀ O ₇	-13.6	-	-	-	0.2

*Pvap: vapor pressure expressed in mmHg

N.V.: non-volatile species

Gas phase chemical characterization

In each test, gas phase terpenoids and their degradation byproducts were analyzed in three pairs of duplicate chamber air samples collected during the first 10 min (sample A), 10–30 min (sample B), and 30–60 min (sample C) after the mixture was applied onto the heated surface. VOCs/SVOCs were collected onto Carbopack sorbent tubes (Supelco). Quantification of terpenoids and their degradation byproducts was carried out by thermal desorption gas chromatography mass spectrometry (TD-GC/MS) using bromofluorobenzene as an internal standard, following an established EPA method.³¹ An Agilent GC/MS system (model 6890/5973) was operated in electron impact mode, and was interfaced with a thermal desorption inlet with an autosampler (Gerstel). Calibration curves were created for VOCs/SVOCs for which authentic standards were available. Standards for 2,5-dihydrotoluene and 6-MHO were not available, and were tentatively identified through a NIST database and quantified via a surrogate compound (toluene) by interpolating the corresponding response factor in the calibration curve of the surrogate. Since the toluene response factor could differ from those of other compounds, this method should be considered a preliminary quantification for those two compounds. Blank chamber measurements were also performed prior to heating the mixtures, to subtract background levels when applicable.

Volatile carbonyls were collected onto duplicate dinitrophenylhydrazine (DNPH)-impregnated cartridges (Waters Corp., PN WAT037500) collected simultaneously with the VOC/SVOC samples. The collected DNPH cartridges were extracted with 2 mL of carbonyl-free acetonitrile (Honeywell) and analyzed by high performance liquid chromatography (HPLC) with UV detection (Agilent 1200), following the EPA TO-11 method.³² A certified mixture of DNPH derivatives was obtained from Sigma-Aldrich as standards for analysis of formaldehyde, acetaldehyde, acrolein, acetone, propanal, crotonaldehyde, methacrolein, butanal, 2-butanone, benzaldehyde, m-tolualdehyde, and hexaldehyde. Calibration curves were generated

for quantification of each analyte using those standards. Chamber blank measurements were subtracted from the values obtained for the samples.

Both for TD-GC/MS and HPLC analysis, the reported values are the average of two duplicate determinations. Experimental uncertainties were estimated as the absolute difference of those duplicates.

A photometric monitor (2B Tech, Model 202) was reading continuously ozone concentration inside the chamber, with a time resolution of one measurement every 10 s.

Aerosol measurements

Aerosols formed in the chamber during the heating process were measured using a Fast Mobility Particle Sizer (FMPS) spectrometer (Model 3091, TSI Inc., MA), an Aerodynamic Particle Sizer spectrometer (APS, Model 3321, TSI Inc., MA), and an Optical Particle Sizer (OPS, Model 3330, TSI Inc., MA). The FMPS measured concentration and size distribution of particles between 5 and 500 nm at a sampling rate of 1 Hz, operating at a flow rate of 10 L/min to minimize particle loss of ultrafine and nanoparticles via diffusion. A dedicated PM_{1.0} cyclone was used to remove particles larger than 1 μm prior to measurement. The APS measured the concentration and size distribution of particles between 500 nm and 20 μm at a sampling rate of 1 Hz. The OPS measured the concentration and size distribution of particles between 300 nm and 10 μm , also at 1 Hz. The three instruments are calibrated by the manufacturer on an annual basis. Prior to each experiment, the FMPS electrometers were zeroed with ultra-zero air. The APS and OPS were checked with ultra-zero air to confirm that the measurement was zero. Digital outputs from the three instruments were integrated into a single file to capture the whole mass range 5 nm – 20 μm . Mass distribution of particles was calculated by assuming particle density as 1 g cm⁻³, and a sub-set of results was re-calculated using a lower density of 0.9 g cm⁻³, to evaluate the effect of particle density on particle number and mass concentrations. Figure S2 (SI) demonstrates good agreement among aerosol instruments using the collected data, when measuring aerosols from the terpenoid mixtures in the above described conditions.

Results and Discussion

Mixture constituents in chamber air

Chemical analysis of samples collected after heating the full terpenoid mixture at different temperatures confirmed the presence of the nine terpenoids in chamber air. Individual analyte chamber air concentrations after evaporation were in the range 16-122 $\mu\text{g m}^{-3}$ in sample A (0-10 min), 9.1-103 $\mu\text{g m}^{-3}$

in sample B (10-30 min), and $9.7\text{--}83\ \mu\text{g m}^{-3}$ in sample C (30-60 min). The measured analyte concentrations in the three samples are reported in Table S1 (SI). The fraction of each compound quantified in sample A during each experiment is illustrated in Figure 1. Upon evaporation at ambient temperature without heating the surface, the amount of light terpenoids found in the air was 42%-96% of the respective mass released in the 20 μL aliquot. On the other hand, the heavier compounds (β -caryophyllene, α -humulene, cedrol, and α -bisabolol) showed very low concentrations in chamber air (less than 5%). Because a small fraction of liquid remained on the Petri dish, we assume that the heavier compounds did not fully evaporate at room temperature.

Heating at different temperatures, in the range 100 – 500 $^{\circ}\text{C}$, evaporated all of the liquid. Upon heating, the airborne fraction of the light terpene fraction was consistently above 50% during the initial 10 minutes (sample A), while that of heavy terpenoids remained below 40% of the hypothetical total mass concentration derived from complete evaporation of the delivered mixture. Such relatively low concentration of airborne terpenoids (comprising both gas phase and particle-bound species) is primarily due to compound adsorption to chamber walls, and loss due to chemical degradation in the heating process. Removal by ventilation during the short duration of sample A was in the order of 3%, considering that the air exchange rate was $0.2\ \text{h}^{-1}$.

Emissions from the different mixtures were compared in experiments where the surface was held at 500 $^{\circ}\text{C}$, in order to compare UFP and byproduct formation under extreme but realistic conditions. Measured terpene concentrations are reported in Table S2 (SI). Heating the complex mixture, which included a small amount of three high MW compounds added to the full terpene mixture, resulted in similar concentrations of most compounds in chamber air with respect to the full terpene mixture, as shown in Figure 1(B). Most constituents of the light terpene and heavy terpene mixtures also maintained their composition when heated individually. Only linalool (a terpene alcohol) showed an increasing trend in the following order: light terpene mixture (34%) < full terpene mixture (53%) < complex mixture (76%). This could be attributed to differential partitioning between aerosol particles, gas phase and indoor surfaces, influenced by stronger interactions (e.g., hydrogen bonding) of linalool with heavier terpene alcohols and high MW compounds, compared with those from monoterpenes. Due to these differences, the relevant partitioning parameters (Henry's law constant and octanol-water coefficient) for linalool are several orders of magnitude different than those of monoterpenes.³³ Similarly, the higher airborne concentrations of β -caryophyllene and α -humulene in the complex mixture may also be due to enhanced partition from indoor surfaces to aerosol particles, and are consistent with the higher PM concentration when the complex mixture was heated, as described in the next section.

An analysis of the precision achieved in the VOC/SVOC concentration determinations is presented in Figures S3 and S4 (SI). Duplicate measurements of the light terpene concentrations were consistently very similar, with relative deviation below 20% in most cases, with the exception of β -pinene. By contrast, the analytical precision for the determination of heavier terpenoids was poorer, with higher relative deviations (notably in the case of β -caryophyllene and α -humulene). For these reasons, trends observed for α -pinene, β -myrcene and limonene (e.g., as a function of temperature or mixture composition) can be described in more quantitative terms than those for β -pinene and the heavier compounds. Compared with the magnitude of their relative experimental error, Figure 1 shows small or negligible changes in the concentrations of many terpenoids as a function of heating temperature, and when different mixtures were tested. In a few samples, the relative deviation exceeded 100% due to the presence of outliers, which were not considered. Outliers were determined by comparing with results from three duplicate measurements (samples A, B and C) in each experiment.

Thermal degradation byproducts

Heating the mixtures at different temperatures led to evaporation, and to the formation of degradation byproducts. Figure 2 presents the chamber air concentration of several byproducts measured in sample A for several experiments where the full terpene mixture was heated at different temperatures, and for the complex, light and heavy terpene mixtures heated at 500 °C. These concentrations are also reported in Table S3 (SI). The most abundant heating byproducts included isoprene, 2,5-dihydrotoluene, 6-methyl-5-hepten-2-one (6-MHO), benzene, acrolein, formaldehyde, acetaldehyde, acetone, methacrolein, valeraldehyde, hexaldehyde, and 2-butanone. Among these compounds, levels of isoprene, 2,5-dihydrotoluene and acetone increased with temperature significantly –compared with the corresponding experimental uncertainties–, suggesting that these compounds were produced upon heating. Similarly, compounds such as methacrolein and hexaldehyde were only observed at high temperatures, for the same reason. Many of the byproducts described here are consistent with those reported after heating individual terpenoids at comparable temperatures by Meehan-Atrash et al.²¹ Those authors postulated a mechanism in which the degradation of β -myrcene, d-limonene and linalool led to isoprene, as an intermediate to the formation of several other oxygenated and aromatic hydrocarbons. In the case of methacrolein, the same authors reported formation at temperatures exceeding 400 °C, in coincidence with our observations. Our measured indoor air concentrations of methacrolein during the initial 10 minutes after heating (sample A) was $2.0 \mu\text{g m}^{-3}$, which is very close to the existing reference exposure levels (RELs) for this compound; the Texas long-term noncancer REL for methacrolein is $2.4 \mu\text{g m}^{-3}$.³⁴ We also report chamber concentrations for acrolein ($1.1\text{--}3.7 \mu\text{g m}^{-3}$), benzene ($0.2\text{--}2.3 \mu\text{g m}^{-3}$) and formaldehyde ($2.5\text{--}4.7 \mu\text{g m}^{-3}$).

272 From those, acrolein exceeded the 8-hour REL established by the California Office of Environmental
273 Health Hazard Assessment (OEHHA), of $0.7 \mu\text{g m}^{-3}$. Benzene and formaldehyde concentration were in
274 the same order of magnitude as the corresponding OEHHA 8-h RELs (3 and $9 \mu\text{g m}^{-3}$, respectively).³⁵
275 These comparisons of short-term chamber concentration spikes with 8-h RELs are made solely to identify
276 byproducts with the potential to approach or exceed health-based guidance levels. The comparison of
277 RELs with predicted 8-h indoor air concentrations under different scenarios is discussed in the
278 Implications section, below.

A

B

281 **Figure 1.** Relative fraction of gas-phase terpenes measured by GC/MS in chamber air with respect to their theoretical mass concentration assuming 100%
282 evaporation (A) from the full terpenoid mixture measured at room (~25 °C) and elevated temperatures (100-500 °C), and (B) from full mixture, complex mixture,
283 light fraction and heavy fraction mixture at 500 °C. Error bars represent the difference of two duplicate measurements.

A

284

B

285

286 **Figure 2.** Concentrations of degradation byproducts ($\mu\text{g m}^{-3}$) in sample A, produced (A) upon heating the full terpenoid mixture at different temperatures, and (B)
287 after heating the complex mix, full mix, light fraction and heavy fraction at 500 °C. Error bars represent the difference of two duplicate measurements.

Particle formation and size distribution

A large burst of UFPs was observed immediately after evaporation of the mixtures, which remained largely within the ultrafine range over a 2 to 3-hour period. About 90% of the total $PM_{1.0}$ (total mass of particulate matter with a diameter less than $1.0\ \mu m$) produced from heating the full terpenoid mixture was composed of particles with diameters less than 250 nm. As shown in Figure S5 (SI), very few particles were larger than $1.0\ \mu m$, as the curves corresponding to $PM_{1.0}$ and $PM_{2.5}$ almost overlap. Hence, the reported aerosol results correspond primarily to the FMPS measurements.

The effect of heating temperature on UFP formation was evaluated by comparing the aerosol particle mass concentration in each experiment carried out with the full terpenoid mixture. When the heating plate temperature was increased from $100\ ^\circ C$ to $250\ ^\circ C$, the particle number (PN) and $PM_{1.0}$ mass concentration increased. Further heating the plate to $400\ ^\circ C$, and eventually $500\ ^\circ C$, resulted in lower PN and $PM_{1.0}$ concentrations than those measured at $250\ ^\circ C$ (Figure 3-A). Aerosol formed by heating at the four different temperatures were all primarily within the ultrafine range ($<100\ nm$), and the smaller particles decayed faster than the larger ones. The highest number of particles in the nucleation mode was formed upon heating at $250\ ^\circ C$. As illustrated in Figure S6 (SI), the mode diameters of particle mass distributions were larger than those of particle number concentrations in each experiment. The mode diameter increased with the increasing temperature, from 80 nm at $100\ ^\circ C$ to $\sim 140\ nm$ at $500\ ^\circ C$.

Figure 3-B shows that heating the same amount of the heavy terpenoid fraction produced a higher $PM_{1.0}$ mass concentration than the full terpenoid mixture. By contrast, the same amount of the light terpenoid mixture produced about half of the mass concentration, suggesting a smaller contribution to aerosol formation. When heating the complex mixture, it was observed that the addition of a small amount ($<0.5\%$ in mass) of high MW compounds lead to a more than 3-fold increase in aerosol mass with respect to emissions from the full terpenoid mixture. These results suggest that these additives contribute significantly to particle formation. Figure 4 shows that formed particles were still mostly within the UFP size range, with the mode diameter of mass distribution between 100 and 120 nm.

Ozone chamber concentrations were deliberately kept very low, at just a few ppb, by removing ozone from incoming air using an activated carbon bed. Upon rapid increase of terpenoid concentration after heating each mixture, ozone levels dropped to zero, as illustrated in Figure S7 (SI). The formation of a large number of ultrafine particles upon heating cannot be explained by reaction of terpenoids with a small ($< 5\ ppb$) residual amount of ozone. Similarly, small variations of a few degree in chamber

308 temperature recorded in different tests –in all cases within typical room values–, are not expected to affect
309 UFP yields significantly.

310

311 **Figure 3.** Time series of PN (left) and PM_{1.0} mass (right) concentration for aerosols formed from (A) heating the full terpenoid mixture at four different
 312 temperatures: 100, 250, 400, and 500 °C, and (B) heating at 500 °C four different mixtures: light fraction, heavy fraction, full mixture, and complex mixture. The
 313 background PM_{1.0} mass before the delivery of terpenoid mixture in each test was subtracted from the data shown in the plot.

B**Particle number** cm^{-3} **Particle mass** m^{-3}

330 **Figure 4.** Evolution of particle number concentration (left) and mass concentration (right) of aerosols within 8-200 nm diameter range, formed from (A) heating
331 the full terpenoid mixture at 500 °C, and (B) heating the complex mixture at 500 °C.

The effect of changing particle density on the calculation of $PM_{1.0}$ concentrations was explored by re-calculating results corresponding to the full terpenoid mixture heated at 500 °C, using a density of 0.9 g cm^{-3} instead of 1 g cm^{-3} . This heating temperature was chosen for this analysis because it was the same used in results plotted in Figure 3(B). The results are shown in Figures S8 and S9 (SI). A lower particle density could be attributed to the density of the pure liquids, which is approximately 0.85 g cm^{-3} for monoterpenes, 0.90 g cm^{-3} for sesquiterpenes and 0.95 g cm^{-3} for sesquiterpene alcohols. Using a reduced particle density in the $PM_{1.0}$ calculation led to a linear decrease in concentrations, which is a relatively small effect compared with those associated with changes in heating temperature and mixture composition.

Implications for users' intake and indoor environmental quality

Heating terpenoid mixtures during vaping or dabbing may be a source of potentially harmful byproducts and secondary organic aerosol, primarily in the ultrafine size range. Most of the aerosol is inhaled by the user, and only a fraction is released to indoor air. The inhaled chemicals are effectively absorbed in the respiratory system, with a smaller fraction present in exhaled breath. Furthermore, part of the aerosol produced in each puff is directly discharged from the mouth prior to inhalation. In this study, we followed an approach used in our previous work to estimate the retained fraction R (unitless) remaining in the user's mouth and respiratory tract during vaping.²⁴ In studies using conventional tobacco cigarettes, it was established that between 20% and 40% of the smoke was released to indoor air.³⁶ Here, we adopted the same values to represent a broad range of vaping scenarios, resulting in retention fractions of $0.6 < R < 0.8$. It should be noted that cannabis vaping patterns can be very different from tobacco smoking and, for that reason, this approach is only a first approximation, in the absence of more specific information. In the case of dabbing, predicting the fraction of emissions retained by the user is even more uncertain, due to lack of measurements and to the diversity of devices and VCCs used. One of the few studies addressing dabbing emission rates described retention of approximately 2/3 of the THC available for absorption in a laboratory-simulated test, by accounting for the fraction collected in simulated lung traps, transfer lines and the aerosol source.⁴ In the absence of more specific information on retention factors, we used for dabbing the same values used in vaping ($R = 0.6$ to 0.8) as a first order approximation.

The emission rates of thermal degradation byproducts generated from cannabis vaping and dabbing were calculated for acrolein and methacrolein, the two compounds that exceeded or were close to reference exposure levels in chamber air. Concentrations of other byproducts (including carcinogens such as benzene), measured with the TD/GC/MS and HPLC/DNPH methods, were too low to significantly contribute to poor indoor air quality. Levels of precursor terpenoids were much higher than typical indoor

levels of those compounds, but they are not particularly harmful even at such high concentrations, in the absence of ozone. Similarly, the contribution of secondary organic aerosol PN and PM_{1.0} to impacts on users and bystanders were estimated. Table 2 summarizes predicted acrolein, methacrolein, PN and PM_{1.0} emission rates (*E*) for cannabis vaping and dabbing, the estimated daily intake (*DI*) by users, and the increment in indoor air concentration (ΔC) expected to occur due to use of the products in two common scenarios. The scenarios considered were: (a) an individual vaping or dabbing at home, and (b) multiple simultaneous vaping or dabbing events taking place at a public venue (e.g., a bar or a dispensary). In both cases, the predicted ΔC correspond to an 8-h average that takes into consideration the corresponding air exchange rates. Details on the calculation of *E*, *DI* and ΔC are provided in the Supporting Information.

The estimated acrolein and methacrolein emission rates reported in Table 2 can be compared with those determined in our previous study using nicotine/PG/VG e-liquids in conventional e-cigarettes.²³ Acrolein *E* values measured from vaping nicotine/PG/VG formulations using different e-liquids, heating power and type of vaporizer were in the range of 0.3 to 71 $\mu\text{g puff}^{-1}$, which comprises the values reported in Table 2 for that compound. By contrast, methacrolein emission rates are roughly one order of magnitude higher than those measured in nicotine vaping (0.05 to 4 $\mu\text{g puff}^{-1}$). The predicted acrolein daily intake reported in Table 2 was compared with values derived from the maximum acrolein limit recommended by the National Institute for Occupational Exposure and Health (NIOSH) for an 8- or 10-h time-weighted average (TWA) exposure and/or a ceiling is 250 $\mu\text{g m}^{-3}$.³⁷ Considering an average breathing rate of 15 $\text{m}^3 \text{day}^{-1}$,³⁸ the amount of acrolein inhaled during 8 hours at the NIOSH-determined limit is 1.3 mg. This value is comparable (albeit higher) than the maximum predicted daily intake rates from vaping, and is several orders of magnitude higher than intake predicted for dabbing. No occupational guidelines exist for methacrolein. Considering their contribution to poor indoor air quality, the predicted ΔC from vaping exceeded in some cases the above mentioned 8-h RELs levels for both acrolein (0.7 $\mu\text{g m}^{-3}$) and methacrolein (2.4 $\mu\text{g m}^{-3}$) in both scenarios. By contrast, contributions from dabbing were significantly lower, and did not exceed RELs.

The emission of secondary organic aerosol PN and PM_{1.0} can be compared with those reported from other common indoor sources, to assess the relative impact on indoor air quality. Figure 5 illustrates PN emission rates as a function of particle size for tobacco smoking,³⁹⁻⁴¹ heated tobacco products,⁴⁰⁻⁴² vaping (nicotine formulations),^{40, 41} cooking,⁴³⁻⁴⁶ incense use,⁴⁷ wax scented candles,⁴³ laser printers,^{48, 49} ironing,⁴³ and operation of unvented cookstoves.⁵⁰ The values used to map emission rates in Figure 5 are presented in Table S4 (SI). Predicted emissions from heating cannabis terpenoids during vaping and dabbing were relatively higher than most other sources, largely exceeding the threshold of 10¹⁰ particles per minute for a

period of at least 10 minutes suggested by Banghar *et al* for sources to be clearly discernible in homes.⁵¹ Particle emitted from heated terpenoids were primarily in the ultrafine range, of comparable or relatively smaller size than those reported from several other sources. The highest emission rates corresponded to particles of size below 50 nm in experiments carried out at different heating temperatures and with different mixtures, as illustrated in Figure S10 (SI).

Two significant features can be highlighted from concentration time profiles presented in Figure 3 and PN emission rate time profiles in Figure S10:

- a) For the full terpenoid mixture, heating at 250 °C resulted in a larger ultrafine particle burst than those recorded at lower and higher temperatures, suggesting that particle inception and growth is optimized at intermediate heating temperatures. For particles in the range 5-50 nm, PN emission rates at 250 °C were approximately 4 time higher than those at 400 and 500 °C, and even higher than those at 100 °C. However, these enhanced emissions at 250 °C were not observed for particles larger than 50 nm. As a result, PM_{1.0} concentrations were ~20% higher at 250 °C during the first hour post-heating, the period during which the smallest particles predominated.
- b) Heating the complex mixture at 500 °C resulted in higher PN emission rates (E_{PN}) than the other mixtures across the whole particle size range. However, the largest differences were for particles larger than 50 nm. On the 50-100 nm size range, E_{PN} of the complex mixture was ~3 times higher than that for the full terpenoid mixture. That gap increased to >6 times for particles in the 100-250 nm range. These higher emission rates resulted in a PM_{1.0} concentration of the complex mixture that was ~3 times higher than that generated from heating the full terpenoid mixture.

The latter effect highlights the critical role played by high MW compounds in the inception and growth of condensational secondary organic aerosols. The presence of a small amount of lignin, flavonoids and triterpenes, amounting to just 0.5% of the liquid mass, resulted in significantly higher PN formation rates and PM_{1.0} concentrations. The fact that the growth rate was highest for relatively larger particles (>50 nm) suggests that enhanced aerosol nucleation proceeded by condensing a large number of terpenoids and other compounds associated with high-MW compounds. This phenomenon is likely to be induced also by the presence of THC, other cannabinoids, and additives such as vitamin E acetate.

Table 2: Predicted emission rates, daily users' intake, and impact on indoor air quality of acrolein, methacrolein, particle number (PN) and particle mass concentration (PM_{1.0}) for the full terpenoid mixture heated at 500 °C.

	Acrolein		Methacrolein		PN		PM _{1.0}	
	Vaping	Dabbing	Vaping	Dabbing	Vaping	Dabbing	Vaping	Dabbing
Emission rate (<i>E</i>)	1 – 7 µg puff ⁻¹	1.2 µg puff ⁻¹	4 – 35 µg puff ⁻¹	6 µg puff ⁻¹	2×10 ¹² – 2×10 ¹³ part puff ⁻¹	3×10 ¹² part puff ⁻¹	88 – 823 µg puff ⁻¹	141 µg puff ⁻¹
Daily intake (<i>DI</i>)	9 – 336 µg day ⁻¹	1.4 – 5.8 µg day ⁻¹	45 – 1680 µg day ⁻¹	7 – 29 µg day ⁻¹	2×10 ¹³ – 8×10 ¹⁴ part day ⁻¹	4×10 ¹² – 1×10 ¹³ part day ⁻¹	1 – 39 mg day ⁻¹	0.16 – 0.67 mg day ⁻¹
ΔC in a home	0.03 – 1.5 µg m ⁻³	0.005 – 0.03 µg m ⁻³	0.14 – 7.6 µg m ⁻³	0.02 – 0.13 µg m ⁻³	7×10 ⁴ – 4×10 ⁶ part cm ⁻³	1×10 ⁴ – 6×10 ⁴ part cm ⁻³	3 – 178 µg m ⁻³	0.5 – 3.1 µg m ⁻³
ΔC in a public venue	0.11 – 2.0 µg m ⁻³	0.03 – 0.07 µg m ⁻³	0.53 – 9.8 µg m ⁻³	0.17 – 0.34 µg m ⁻³	3×10 ⁵ – 6×10 ⁶ part cm ⁻³	9×10 ⁴ – 2×10 ⁵ part cm ⁻³	14 – 253 µg m ⁻³	4.3 – 8.7 µg m ⁻³

Figure 5. Particle emission rate (E_{PN}) during the first 30 min for three different size bins: 5-50 nm, 50-100nm and 100-250 nm after heating (A) the full terpenoid mixture at different temperatures, and (B) different mixtures at 500 °C.

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Supporting Information

Molecular structures of studied compounds; Integration of results for, three different aerosol instruments; Concentrations of mixture constituents and degradation byproducts measured in chamber experiments; Analysis of relative deviation in concentration measurements; Comparison of $PM_{2.5}$, $PM_{1.0}$ and $PM_{0.25}$ results; Contour plots showing PN and PM concentration as a function of time and particle size; Ozone chamber concentration; Comparison of aerosol results assuming a particle density of 1 g/cm³ and 0.9 g/cm³, respectively; Calculation of emission rates, daily users' intake and increment in indoor pollutant concentrations; PN emission rates reported in the literature; and PN emission rates for different size bins.

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