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Emissions from heated terpenoids present in vaporizable cannabis concentrates

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24 **Abstract**

25

26 Vaporizable cannabis concentrates (VCCs) consumed as a liquid (vaping) or a waxy solid (dabbing) are
27 becoming increasingly popular. However, their associated emissions and impacts have not been fully
28 described. Mixtures containing different proportions of twelve VCC terpenoids and high-MW compounds
29 were heated at 100 – 500 °C inside a room-sized chamber, to simulate emissions. Terpenoids, thermal
30 degradation byproducts, and ultrafine particles (UFPs) were quantified in chamber air. Air samples
31 contained over 50% of emitted monoterpenes, and less than 40% of released sesquiterpenes and terpene
32 alcohols. Eleven degradation byproducts were quantified, including acrolein ($1.3 - 3.9 \mu\text{g m}^{-3}$) and
33 methacrolein ($2.0 \mu\text{g m}^{-3}$). A large amount of UFPs were released upon heating, and remained airborne for
34 at least three hours. The mode diameter increased from 80 nm at 100 °C to 140 nm at 500 °C, and
35 particles smaller than 250 nm contributed to 90% of $\text{PM}_{1.0}$. The presence of 0.5% of lignin, flavonoid and
36 triterpene additives in the heated mixtures resulted in a threefold increase in particle formation rate and
37 $\text{PM}_{1.0}$ concentration, suggesting that these high MW compounds enhanced aerosol inception and growth.
38 Predicted UFP emission rates in typical consumption scenarios ($6 \times 10^{11} - 2 \times 10^{13} \text{ \# min}^{-1}$) were higher
39 than, or comparable with, other common indoor sources such as smoking and cooking.

40 **Introduction**

41 Legalization of medical and recreational uses of marijuana (cannabis) in several States of the USA, and in
42 other countries, has led to the rapid development and visibility of new cannabis products. Manufacturing
43 and retail was legalized in California in January 2018, becoming the largest lawful marijuana market with
44 ~\$3B annual sales.¹ A 2017 analysis of cannabis sales in Washington State revealed that, while
45 combustible products still accounted for most transactions, the share of vaporizable cannabis concentrates
46 (VCCs, also referred to as *extracts* or *hash oils*) increased by 146% between 2014 and 2016, comprising
47 21% of sales. The average content of Δ^9 -tetrahydrocannabinol (THC) in extracts (69%) was more than
48 three times that of flower-based products (21%).² Liquid VCCs can be consumed by vaping,³ while waxy
49 concentrates can be aerosolized by direct application onto a heated surface to produce high impact, THC-
50 rich puffs (“dabbing”).⁴ On a survey of more than 6,000 current marijuana users in 12 States, a significant
51 fraction reported consuming VCCs through vaping (19.4%) and dabbing (14.5%), in most cases in
52 conjunction with other modes of marijuana use.⁵ With legalization, innovative delivering devices became
53 available for use with VCCs, appealing to a growing and diverse group of consumers.^{3,6} Due to their
54 higher potency, VCCs are associated with more negative consequences than flower-based products, such
55 as psychosis episodes and panic attacks.⁷ Vaping also facilitates access to cannabis by young users, and
56 prompts an earlier age of onset, increasing the risks of addictive behavior.^{8,9} Yet, vaping is often
57 perceived as healthier than smoking, because it avoids inhalation of toxic smoke constituents.^{7,10} For that
58 reason, cannabis consumers in states that enacted medical marijuana laws are more likely to vape.¹¹

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

70 Thermal degradation of terpenoids results in byproducts from dehydrogenation, epoxidation, double bond
71 cleavage, allylic oxidations and rearrangements.¹⁸ Some of these byproducts become condensation nuclei
72 for the formation of ultrafine secondary organic aerosol particles.^{19, 20} THC is present in the plant as
73 tetrahydrocannabinolic acid (THCA), an inactive carboxylate, which is activated by decarboxylation upon
74 heating. High temperatures up to 340 – 482 °C are needed to vaporize VCCs, and are significantly higher
75 than those commonly used with PG/VG formulations.²¹ The aerobic decomposition of PG occurs at 127
76 °C, and that of glycerin at 200 – 290 °C.²² Their thermal decomposition byproducts include acrolein,
77 formaldehyde and acetaldehyde, which are emitted at higher rates as the applied power of vaping devices
78 increases.^{23, 24} A study evaluating the formation of formaldehyde and acetaldehyde in the vapor from
79 heated e-liquids containing carboxylated and decarboxylated cannabinoids found that the latter emitted
80 higher aldehyde levels, possibly due to the higher temperatures required for THC activation.²⁵ Thermal
81 decomposition of cannabis terpenoids was found to produce isoprene, methacrolein, benzene, 1,3-
82 butadiene and other compounds upon heating.^{12, 21}

83 Emissions associated with cannabis vaping and dabbing can lead to acute and chronic health effects in
84 users and bystanders. On rare occasions, such emissions have led to severely toxic effects. A deadly
85 outbreak of vaping product-associated lung injury (EVALI) took place in the United States between June
86 2019 and February 2020. It resulted in at least 68 deaths and more than 2800 hospitalizations.²⁶ THC-
87 containing products were shown to be linked to most EVALI cases.²⁷ Vitamin E acetate (α -tocopheryl
88 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
89 consumed products and in bronchoalveolar lavage fluid extracted from EVALI patients, and is considered
90 to be a key factor associated with the disease.²⁸ Since the volatility of vitamin E acetate is very low, this
91 compound was likely transported to the lung by particles produced in the inception of the THC-containing
92 aerosol. Mice exposure experiments showed that ultrafine aerosol particles generated by vaping were able
93 to deliver vitamin E acetate to the lung.²⁹ Other low-volatility species such as methamphetamine (MW
94 149 g/mol) and methadone (MW 309 g/mol), when vaped in PG/VG formulations, were also shown to be
95 transported in particles smaller than 0.3 μ m that can reach the alveolar regions of the lungs.³⁰

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

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

105 **Experimental Methods**

106 *Preparation of test mixtures*

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

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

123

124 *Aerosol emission tests*

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

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

138 Experiments were conducted by releasing into the chamber the emissions resulting from rapid heating
 139 of the different mixtures under controlled conditions (i.e., surface temperature, mixture composition
 140 and amount delivered). These emissions can be considered representative of those produced during
 141 vaping or dabbing. The method was not developed to reproduce the design and operation
 142 characteristics of vaping or dabbing devices, but rather to facilitate accurate measurement of the
 143 above-mentioned experimental parameters. Volatile/semivolatile organic compound (VOC/SVOC)
 144 indoor air concentrations during the first hour, and particle size distribution and concentration was
 145 recorded for several hours. The effect of changing the heating temperature was studied only with the
 146 full terpenoid mixture, which was allowed to evaporate without heating (surface temperature 25 °C),
 147 and by heating the surface at 100, 250, 400, and 500 °C. The effect of mixture composition was
 148 evaluated by heating the light, heavy fraction, and complex mixture at the highest temperature, 500
 149 °C.

150

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

Compound	MW	Formula	log Pvap *	Light terpeno id mixture (%)	Heavy terpeno id mixture (%)	Full terpeno id mixture (%)	Comple x mixtur e (%)
<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

152

153 *Pvap: vapor pressure expressed in mmHg

154 N.V.: non-volatile species

155 ***Gas phase chemical characterization***

156 In each test, gas phase terpenoids and their degradation byproducts were analyzed in three pairs of
 157 duplicate chamber air samples collected during the first 10 min (sample A), 10–30 min (sample B), and
 158 30–60 min (sample C) after the mixture was applied onto the heated surface. VOCs/SVOCs were
 159 collected onto Carboxpack sorbent tubes (Supelco). Quantification of terpenoids and their degradation
 160 byproducts was carried out by thermal desorption gas chromatography mass spectrometry (TD-GC/MS)
 161 using bromofluorobenzene as an internal standard, following an established EPA method.³¹ An Agilent
 162 GC/MS system (model 6890/5973) was operated in electron impact mode, and was interfaced with a
 163 thermal desorption inlet with an autosampler (Gerstel). Calibration curves were created for VOCs/SVOCs
 164 for which authentic standards were available. Standards for 2,5-dihydrotoluene and 6-MHO were not
 165 available, and were tentatively identified through a NIST database and quantified via a surrogate
 166 compound (toluene) by interpolating the corresponding response factor in the calibration curve of the
 167 surrogate. Since the toluene response factor could differ from those of other compounds, this method
 168 should be considered a preliminary quantification for those two compounds. Blank chamber
 169 measurements were also performed prior to heating the mixtures, to subtract background levels when
 170 applicable.

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

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

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

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

184 *Aerosol measurements*

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

202

203 **Results and Discussion**

204 *Mixture constituents in chamber air*

205 Chemical analysis of samples collected after heating the full terpenoid mixture at different temperatures
206 confirmed the presence of the nine terpenoids in chamber air. Individual analyte chamber air
207 concentrations after evaporation were in the range 16-122 µg m⁻³ in sample A (0-10 min), 9.1-103 µg m⁻³

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

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

224 Emissions from the different mixtures were compared in experiments where the surface was held at 500
225 $^{\circ}\text{C}$, in order to compare UFP and byproduct formation under extreme but realistic conditions. Measured
226 terpenoid concentrations are reported in Table S2 (SI). Heating the complex mixture, which included a
227 small amount of three high MW compounds added to the full terpenoid mixture, resulted in similar
228 concentrations of most compounds in chamber air with respect to the full terpenoid mixture, as shown in
229 Figure 1(B). Most constituents of the light terpenoid and heavy terpenoid mixtures also maintained their
230 composition when heated individually. Only linalool (a terpene alcohol) showed an increasing trend in the
231 following order: light terpenoid mixture (34%) < full terpenoid mixture (53%) < complex mixture (76%).
232 This could be attributed to differential partitioning between aerosol particles, gas phase and indoor
233 surfaces, influenced by stronger interactions (e.g., hydrogen bonding) of linalool with heavier terpene
234 alcohols and high MW compounds, compared with those from monoterpenes. Due to these differences,
235 the relevant partitioning parameters (Henry's law constant and octanol-water coefficient) for linalool are
236 several orders of magnitude different than those of monoterpenes.³³ Similarly, the higher airborne
237 concentrations of β -caryophyllene and α -humulene in the complex mixture may also be due to enhanced
238 partition from indoor surfaces to aerosol particles, and are consistent with the higher PM concentration
239 when the complex mixture was heated, as described in the next section.

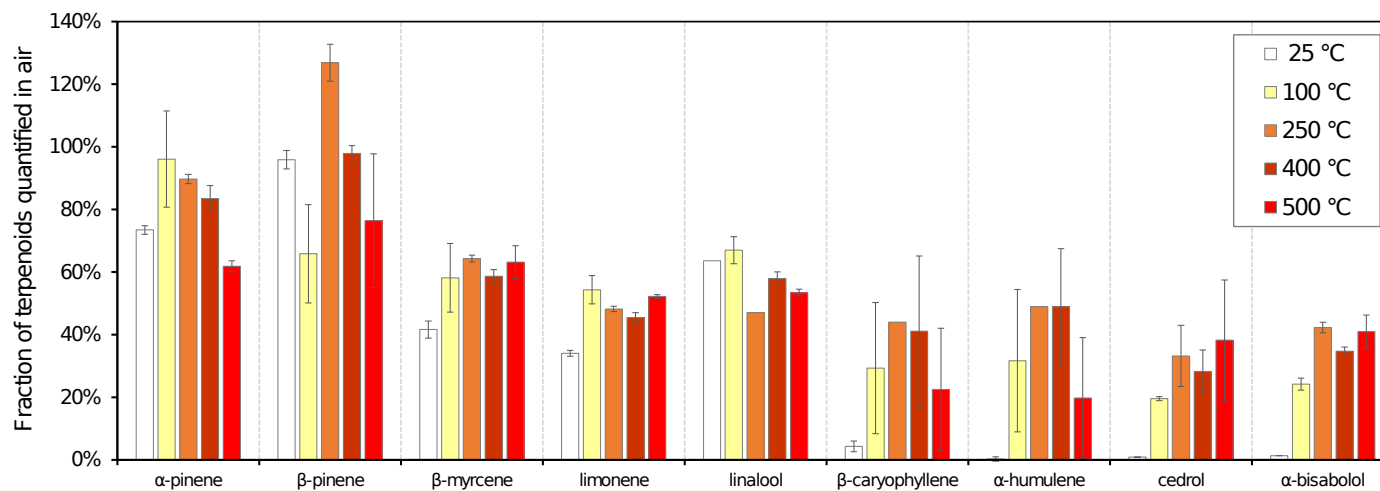
240 An analysis of the precision achieved in the VOC/SVOC concentration determinations is presented in
241 Figures S3 and S4 (SI). Duplicate measurements of the light terpenoid concentrations were consistently
242 very similar, with relative deviation below 20% in most cases, with the exception of β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

252 ***Thermal degradation byproducts***

253 Heating the mixtures at different temperatures led to evaporation, and to the formation of degradation
254 byproducts. Figure 2 presents the chamber air concentration of several byproducts measured in sample A
255 for several experiments where the full terpenoid mixture was heated at different temperatures, and for the
256 complex, light and heavy terpenoid mixtures heated at 500 °C. These concentrations are also reported in
257 Table S3 (SI). The most abundant heating byproducts included isoprene, 2,5-dihydrotoluene, 6-methyl-5-
258 hepten-2-one (6-MHO), benzene, acrolein, formaldehyde, acetaldehyde, acetone, methacrolein,
259 valeraldehyde, hexaldehyde, and 2-butanone. Among these compounds, levels of isoprene, 2,5-
260 dihydrotoluene and acetone increased with temperature significantly –compared with the corresponding
261 experimental uncertainties–, suggesting that these compounds were produced upon heating. Similarly,
262 compounds such as methacrolein and hexaldehyde were only observed at high temperatures, for the same
263 reason. Many of the byproducts described here are consistent with those reported after heating individual
264 terpenoids at comparable temperatures by Meehan-Atrash et al.²¹ Those authors postulated a mechanism
265 in which the degradation of β -myrcene, d-limonene and linalool led to isoprene, as an intermediate to the
266 formation of several other oxygenated and aromatic hydrocarbons. In the case of methacrolein, the same
267 authors reported formation at temperatures exceeding 400 °C, in coincidence with our observations. Our
268 measured indoor air concentrations of methacrolein during the initial 10 minutes after heating (sample A)
269 was $2.0 \mu\text{g m}^{-3}$, which is very close to the existing reference exposure levels (RELs) for this compound;
270 the Texas long-term noncancer REL for methacrolein is $2.4 \mu\text{g m}^{-3}$.³⁴ We also report chamber
271 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 ($2.5\text{-}4.7 \mu\text{g m}^{-3}$).

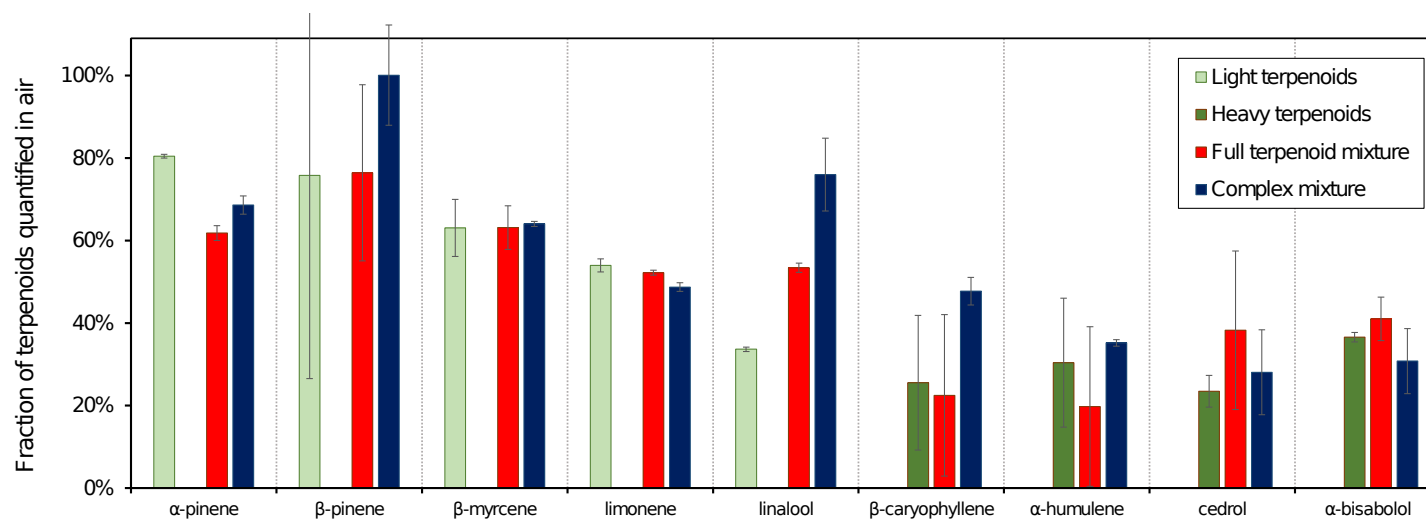
272 From those, acrolein exceeded the 8-hour REL established by the California Office of Environmental
273 Health Hazard Assessment (OEHHA), of $0.7 \mu\text{g m}^{-3}$. Benzene and formaldehyde concentration were in
274 the same order of magnitude as the corresponding OEHHA 8-h RELs (3 and $9 \mu\text{g m}^{-3}$, 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



279

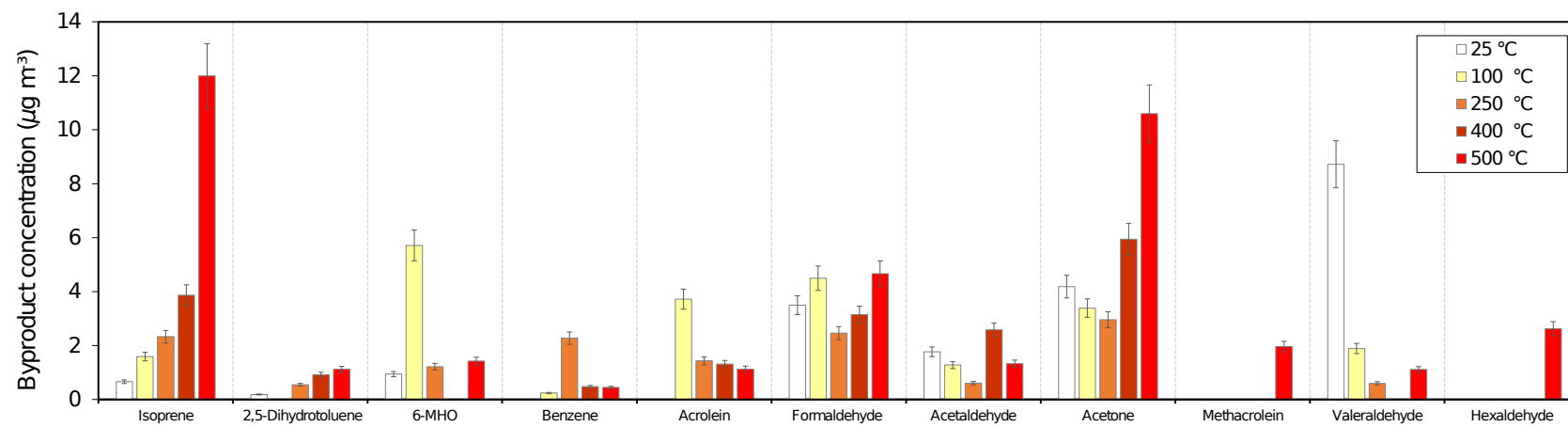
B



280

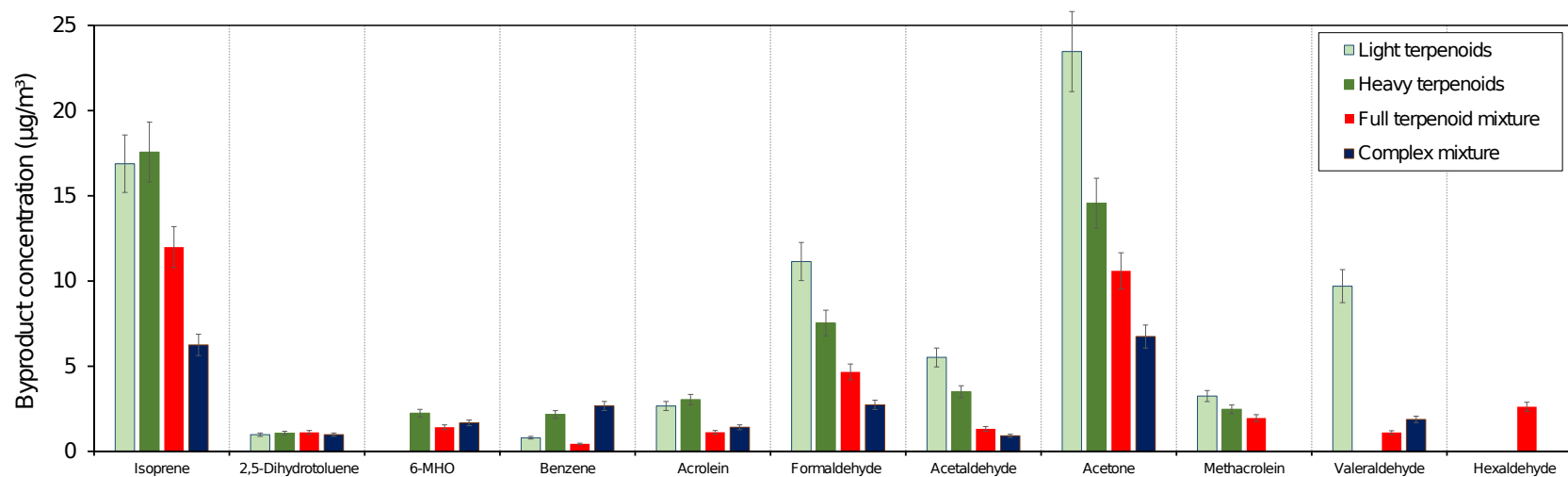
281 **Figure 1.** Relative fraction of gas-phase terpenes measured by GC/MS in chamber air with respect to their theoretical mass concentration assuming 100%
282 evaporation (A) from the full terpenoid mixture measured at room (~25 °C) and elevated temperatures (100-500 °C), and (B) from full mixture,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

278 Particle formation and size distribution

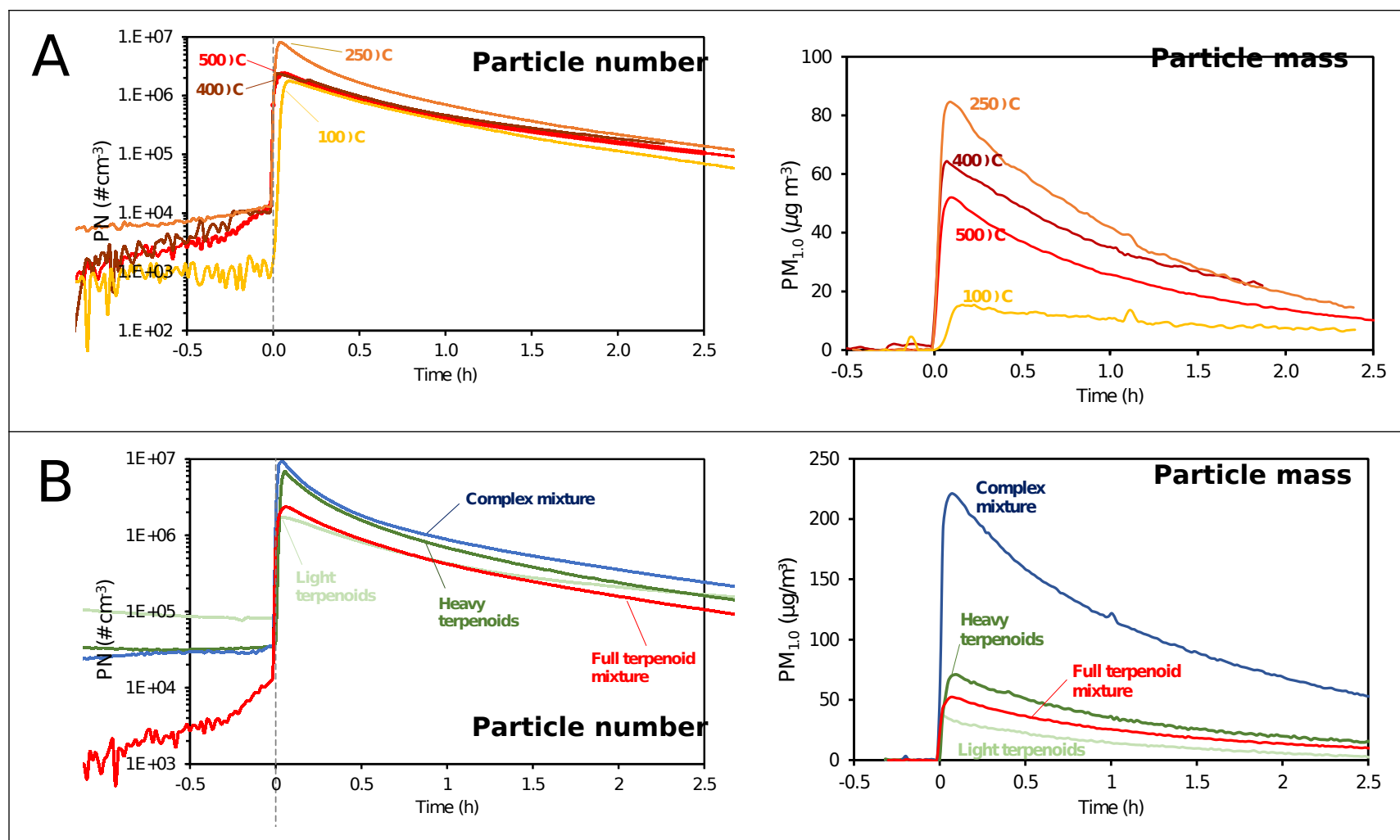
279 A large burst of UFPs was observed immediately after evaporation of the mixtures, which remained
280 largely within the ultrafine range over a 2 to 3-hour period. About 90% of the total PM_{1.0} (total mass of
281 particulate matter with a diameter less than 1.0 μm) produced from heating the full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

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

295 Figure 3-B shows that heating the same amount of the heavy terpenoid fraction produced a higher PM_{1.0}
296 mass concentration than the full terpenoid mixture. By contrast, the same amount of the light terpenoid
297 mixture produced about half of the mass concentration, suggesting a smaller contribution to aerosol
298 formation. When heating the complex mixture, it was observed that the addition of a small amount
299 (<0.5% in mass) of high MW compounds lead to a more than 3-fold increase in aerosol mass with respect
300 to emissions from the full terpenoid mixture. These results suggest that these additives contribute
301 significantly to particle formation. Figure 4 shows that formed particles were still mostly within the UFP
302 size range, with the mode diameter of mass distribution between 100 and 120 nm.

303 Ozone chamber concentrations were deliberately kept very low, at just a few ppb, by removing ozone
304 from incoming air using an activated carbon bed. Upon rapid increase of terpenoid concentration after
305 heating each mixture, ozone levels dropped to zero, as illustrated in Figure S7 (SI). The formation of a
306 large number of ultrafine particles upon heating cannot be explained by reaction of terpenoids with a
307 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.

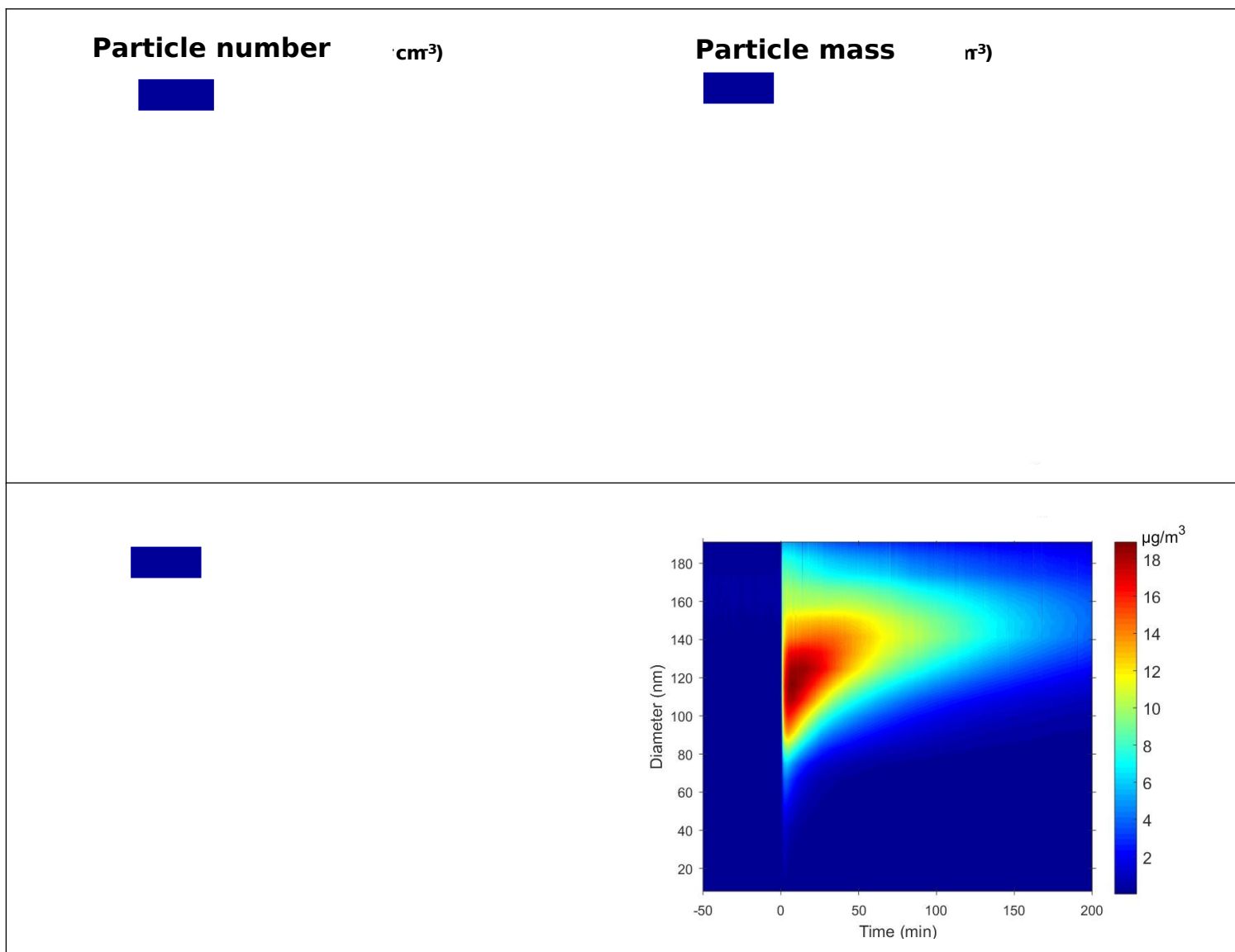


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311 **Figure 3.** Time series of PN (left) and PM₁ mass (right) concentration for aerosols formed from (A) heating the full terpenoid mixture at four different
312 temperatures: 100, 250, 400, and 500 °C, and (B) heating at 500 °C four different mixtures: 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.

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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.

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

341 ***Implications for users' intake and indoor environmental quality***

342 Heating terpenoid mixtures during vaping or dabbing may be a source of potentially harmful byproducts
343 and secondary organic aerosol, primarily in the ultrafine size range. Most of the aerosol is inhaled by the
344 user, and only a fraction is released to indoor air. The inhaled chemicals are effectively absorbed in the
345 respiratory system, with a smaller fraction present in exhaled breath. Furthermore, part of the aerosol
346 produced in each puff is directly discharged from the mouth prior to inhalation. In this study, we followed
347 an approach used in our previous work to estimate the retained fraction R (unitless) remaining in the
348 user's mouth and respiratory tract during vaping.²⁴ In studies using conventional tobacco cigarettes, it was
349 established that between 20% and 40% of the smoke was released to indoor air.³⁶ Here, we adopted the
350 same values to represent a broad range of vaping scenarios, resulting in retention fractions of $0.6 < R <$
351 0.8 . It should be noted that cannabis vaping patterns can be very different from tobacco smoking and, for
352 that reason, this approach is only a first approximation, in the absence of more specific information. In the
353 case of dabbing, predicting the fraction of emissions retained by the user is even more uncertain, due to
354 lack of measurements and to the diversity of devices and VCCs used. One of the few studies addressing
355 dabbing emission rates described retention of approximately 2/3 of the THC available for absorption in a
356 laboratory-simulated test, by accounting for the fraction collected in simulated lung traps, transfer lines
357 and the aerosol source.⁴ In the absence of more specific information on retention factors, we used for
358 dabbing the same values used in vaping ($R = 0.6$ to 0.8) as a first order approximation.

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

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

373 The estimated acrolein and methacrolein emission rates reported in Table 2 can be compared with those
374 determined in our previous study using nicotine/PD/VG e-liquids in conventional e-cigarettes.²³ Acrolein
375 *E* values measured from vaping nicotine/PD/VG formulations using different e-liquids, heating power and
376 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
377 for that compound. By contrast, methacrolein emission rates are roughly one order of magnitude higher
378 than those measured in nicotine vaping (0.05 to 4 $\mu\text{g puff}^{-1}$). The predicted acrolein daily intake reported
379 in Table 2 was compared with values derived from the maximum acrolein limit recommended by the
380 National Institute for Occupational Exposure and Health (NIOSH) for an 8- or 10-h time-weighted
381 average (TWA) exposure and/or a ceiling is 250 $\mu\text{g m}^{-3}$.³⁷ Considering an average breathing rate of 15 m³
382 day⁻¹,³⁸ the amount of acrolein inhaled during 8 hours at the NIOSH-determined limit is 1.3 mg. This
383 value is comparable (albeit higher) than the maximum predicted daily intake rates from vaping, and is
384 several orders of magnitude higher than intake predicted for dabbing. No occupational guidelines exist for
385 methacrolein. Considering their contribution to poor indoor air quality, the predicted ΔC from vaping
386 exceeded in some cases the above mentioned 8-h RELs levels for both acrolein (0.7 $\mu\text{g m}^{-3}$) and
387 methacrolein (2.4 $\mu\text{g m}^{-3}$) in both scenarios. By contrast, contributions from dabbing were significantly
388 lower, and did not exceed RELs.

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

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

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

403 a) For the full terpenoid mixture, heating at 250 °C resulted in a larger ultrafine particle burst than
404 those recorded at lower and higher temperatures, suggesting that particle inception and growth is
405 optimized at intermediate heating temperatures. For particles in the range 5-50 nm, PN emission
406 rates at 250 °C were approximately 4 time higher than those at 400 and 500 °C, and even higher
407 than those at 100 °C. However, these enhanced emissions at 250 °C were not observed for
408 particles larger than 50 nm. As a result, PM_{1.0} concentrations were ~20% higher at 250 °C during
409 the first hour post-heating, the period during which the smallest particles predominated.

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411 b) Heating the complex mixture at 500 °C resulted in higher PN emission rates (E_{PN}) than the other
412 mixtures across the whole particle size range. However, the largest differences were for particles
413 larger than 50 nm. On the 50-100 nm size range, E_{PN} of the complex mixture was ~3 times higher
414 than that for the full terpenoid mixture. That gap increased to >6 times for particles in the 100-
415 250 nm range. These higher emission rates resulted in a PM_{1.0} concentration of the complex
416 mixture that was ~3 times higher than that generated from heating the full terpenoid mixture.

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

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

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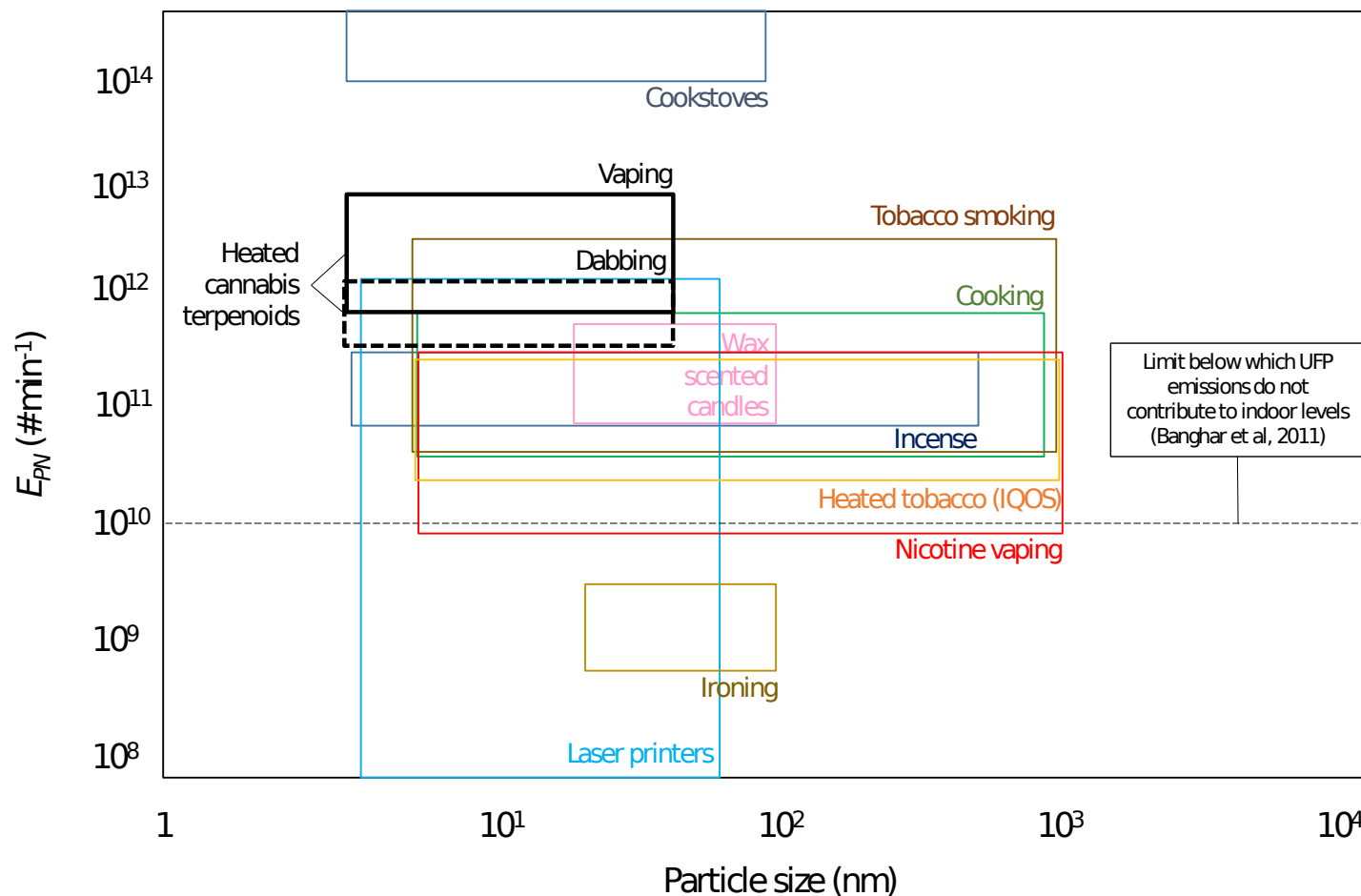
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	Acrolein		Methacrolein		PN		$PM_{1.0}$	
	Vaping	Dabbing	Vaping	Dabbing	Vaping	Dabbing	Vaping	Dabbing
Emission rate (E)	1 – 7 $\mu\text{g puff}^{-1}$	1.2 $\mu\text{g puff}^{-1}$	4 – 35 $\mu\text{g puff}^{-1}$	6 $\mu\text{g puff}^{-1}$	$2 \times 10^{12}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

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435 **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
 436 mixture at different temperatures, and (B) different mixtures at 500 °C.

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408

409 **Supporting Information**

410 Molecular structures of studied compounds; Integration of results for, three different aerosol instruments;
411 Concentrations of mixture constituents and degradation byproducts measured in chamber experiments;
412 Analysis of relative deviation in concentration measurements; Comparison of $PM_{2.5}$, $PM_{1.0}$ and $PM_{0.25}$
413 results; Contour plots showing PN and PM concentration as a function of time and particle size; Ozone
414 chamber concentration; Comparison of aerosol results assuming a particle density of 1 g/cm^3 and 0.9
415 g/cm^3 , respectively; Calculation of emission rates, daily users' intake and increment in indoor pollutant
416 concentrations; PN emission rates reported in the literature; and PN emission rates for different size bins.

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419

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