Real-Time Measurements of Botanical Disinfectant Emissions, Transformations, and Multiphase Inhalation Exposures in Buildings

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ABSTRACT: Thymol-based botanical disinfectants have emerged as natural alternatives to traditional chemical disinfectants given their effectiveness as antimicrobial pesticides and ability to inactivate SARS-CoV-2. This study investigates the impact of botanical disinfectants on indoor air chemistry and human exposure. Controlled surface disinfection experiments were conducted in a mechanically ventilated zero-energy tiny house laboratory. Volatile organic compounds (VOCs) and aerosol size distributions were measured in real-time (1 Hz) with a proton transfer reaction time-of-flight mass spectrometer and a high-resolution electrical low-pressure impactor, respectively. Botanical disinfectant spray and wipe products drove sudden changes in the chemical composition of indoor air. Mixing ratios of monoterpenes (C10H16) and monoterpenoids (C10H14O, C10H16O, C10H18O, and C10H20O) increased suddenly during the disinfection events (10^{-1} to 10^2 ppb) and exhibited volatility-dependent temporal emission profiles. VOC emission factors ranged from 100 to 10^4 μgg^{-1}, and thymol intake fractions ranged from 6 to 7 × 10^3 ppm. Rapid new particle formation events were observed due to ozonolysis of monoterpenes and monoterpenoids, increasing sub-100 nm particle number concentrations by 10^4 to 10^5 cm^{-3}. Botanical disinfectant sprays initiated multiphase inhalation exposure to VOCs, secondary organic aerosol, and sub-10 μm droplets, with large deposited doses in each respiratory tract region associated with the latter two.

INTRODUCTION

The COVID-19 pandemic has led to increased levels of chemical disinfection of high-touch indoor surfaces in buildings to minimize fomite transmission.1–3 Antimicrobial pesticides proven to be effective in inactivating SARS-CoV-2 are summarized in the U.S. Environmental Protection Agency List N: Disinfectants for Coronavirus.4 The most widely used active ingredients among disinfectant products included in List N can be classified as (1) quaternary ammonium salts, e.g., benzalkonium chlorides; (2) oxidizers, e.g., sodium hypochlorite and hydrogen peroxide; and (3) alcohols, e.g., ethanol and isopropyl alcohol.4,5 The ubiquitous use of these compounds in buildings has raised concern given their adverse impact on indoor environments and human health.5–12 Botanical or essential oil-based disinfectants have emerged as natural and green alternatives to traditional chemical disinfectants. Many of these products incorporate thymol (C10H14O) as the active ingredient. Thymol has been shown to be effective as an antioxidant13,14 and antimicrobial.15–18 Thymol has been used in wound dressings,19,20 in-feed antibiotics,21 and antibacterial products22–28 as it can disrupt bacterial cell membrane integrity and initiate cell death.29 Thymol-based oral rinses have shown >99.9% efficacy in inactivating SARS-CoV-2 surrogates.30,31 Thymol-based disinfectants are included in List N.4 Routine use of thymol-based botanical disinfectants in buildings has important implications for indoor chemistry as products containing essential oils are expected to emit a variety of monoterpenes and monoterpenoids32–34 that can be oxidized by ozone (O3) to form secondary organic aerosol (SOA).35–37 However, little is known regarding how botanical disinfectants alter the chemical composition of indoor air. The objective of this study is to characterize botanical disinfectant emissions, transformations, and exposures through real-time (1 Hz) measurements of volatile organic compounds (VOCs) with a proton transfer reaction time-of-flight mass spectrometer (PTR-TOF-MS) and aerosols with a high-resolution electrical low-pressure impactor (HR-ELPI+).
MATERIALS AND METHODS

The measurement campaign was conducted in a residential architectural engineering laboratory, the Purdue zero Energy Design Guidance for Engineers (zEDGE) Tiny House (volume of 60.35 m³) (Figures S1 and S2). The zEDGE Tiny House is configured with a powered ventilator with a MERV 16 filter that maintained an outdoor air exchange rate (AER) of 3 h⁻¹. Mixing ratios of VOCs were measured with a PTR-TOF-MS.

Figure 1. Time series for botanical disinfection experiment B2 using spray product B (thymol, 0.05 wt %). (A) Mixing ratio of C₁₀H₁₆ (orange line, left y-axis), C₁₀H₁₄O (dark green line, right y-axis), C₁₀H₁₆O (yellow line, right y-axis), C₁₀H₁₆O (light green line, right y-axis), and C₁₀H₂₀O (dark red line, right y-axis). (B) Mixing ratio of water vapor (orange line, left y-axis) and indoor relative humidity (dark green line, right y-axis). (C) Mixing ratio of ozone (orange line). (D) Aerosol number size distribution at Dₙ values from 10 to 300 nm. (E) Aerosol mass size distribution at Dₙ values from 300 to 10000 nm. (F) Size-integrated aerosol number concentration at Dₙ values from 10 to 10000 nm (orange line, left y-axis) and size-integrated mass concentration at Dₙ values from 10 to 2500 nm (PM₂.₅, dark green line, right y-axis) and from 10 to 10000 nm (PM₁₀, yellow line, right y-axis). (G) Thymol mass concentration in the gas phase (orange line, left y-axis) and sub-10 μm droplets (dark green line, right y-axis). Gray shading represents the period of disinfectant application, and light yellow shading represents the period of dry wiping the disinfectant residue off the glass slides. The dry wiping process likely enhances mass transfer from the liquid disinfectant on the glass panels and dry wipes, which can explain the slight increase in VOC mixing ratios during this period.
Vaporization, Δ£ nearly 4 min after application of the botanical disinfectant. The gradually increased over time, reaching a peak (7.56 ppb) the monoterpenes (Figure 1A). The thymol mixing ratio detected at episodic sources of monoterpenes during routine building. This suggests that botanical disinfectants can be important pinene, or γ-pinene, or γ-terpinene) increased rapidly. A peak mixing ratio of 76.11 ppb was reached within seconds of application, 40-fold greater than background levels in the 2EDGE Tiny House. This suggests that botanical disinfectants can be important episodic sources of monoterpenes during routine building disinfection.

The emission profile of the disinfectant itself, thymol (C$_{10}$H$_{14}$O, m/z 151), was distinctly different from that of the monoterpenes (Figure 1A). The thymol mixing ratio gradually increased over time, reaching a peak (7.56 ppb) nearly 4 min after application of the botanical disinfectant. The observed variations in the emission profiles between thymol and monoterpenes are likely due to their different enthalpies of vaporization, Δ$_{vap}$H°. A higher Δ$_{vap}$H° indicates a lower volatility, expressed as the saturation concentration, C° (Table S3). With a higher Δ$_{vap}$H° and a lower C°, thymol evaporates more slowly than various monoterpenes. The thymol emission profiles for the wet wipe (G) were similar to those for the sprays (A–E); however, thymol mixing ratios were the lowest among the thymol-containing products tested.

The PTR-TOF-MS measurements revealed the presence of several additional monoterpenoids in the botanical disinfectant emissions, including C$_{10}$H$_{16}$O (m/z 153, possibly camphor or citral), C$_{10}$H$_{18}$O (m/z 155, possibly linalool, α-pineneol, eucalyptol, citronellol, or terpinene-4-ol), and C$_{10}$H$_{20}$O (m/z 157, possibly decanal, citronellol, or menthol). Such compounds are found in various essential oils, and some of which were listed on the product label (Table S1). Peak mixing ratios typically remained below 10 ppb. As illustrated in Figure S13, the temporal emission profiles for C$_{10}$H$_{14}$O and C$_{10}$H$_{16}$O are more like that of the monoterpenes, likely due to their similar C° values. Among the six thymol-based botanical disinfectants evaluated in this study (A–E and G), none were found without the coexistence of monoterpenes and other monoterpenoids due to their inclusion in essential oils. For five of the six products, monoterpenes were associated with the highest peak mixing ratios, often >50 ppb, among the identified VOCs. However, for product E, thymol mixing ratios exceeded those of monoterpenes, likely due to the inclusion of thymol at 0.23 wt %.

Mixing ratios of monoterpenes, thymol, and other monoterpenoids remained elevated during the 10 min contact time of the botanical disinfectant on the surface (Figure 1A). Of the products tested, a majority specify a 10 min contact time for surface disinfection with thymol. This extends the effective volatilization period for VOCs included in the liquid disinfectant solution, thereby maintaining elevated indoor concentrations of volatile species. The removal of the liquid surface film of disinfectant with a dry wipe initiates the nearly exponential decay in mixing ratios due to VOC loss via ventilation and surface sorption.

**Temporal Variations in VOC Concentrations during Indoor Botanical Disinfection Events.** Real-time aerosol measurements with a HR-ELPI+ during the botanical disinfection experiments revealed two distinct aerosol generation events: (1) new particle formation (NPF) due to the ozonolysis of selected VOCs released by the disinfectants and (2) disinfectant droplet formation during the spray process (for products A–F). The pulse release of monoterpenes and monoterpenoids was associated with a decrease in O$_3$ mixing ratios from 25 to 20 ppb (Figure 1C). Depletion of O$_3$ was observed across most of the disinfection events. Various monoterpenes and monoterpenoids can be oxidized by O$_3$ to more oxygenated and less volatile products that can initiate the formation of indoor SOA. Indoor NPF events were observed during six of the 21 botanical surface disinfection experiments (Table S5); an example is shown in panels D and F of Figure 1. VOC, O$_3$, and SOA concentrations for each NPF event are listed in Table S6.

For products B and D, particle number (PN) concentrations began to steadily increase approximately 5 min after application of the thymol-based botanical disinfectant (B2 in Figure 1F, B3 in Figure S10F, and D1 in Figure S14F). Peak PN concentrations were reached several minutes after dry wiping the disinfectant film from the glass panels. Product F, a non-thymol-based disinfectant, exhibited a different temporal profile in PN concentrations, with levels rising sharply 2–3 min after disinfectant application and peaking several minutes before the dry wipe (Figures S20F–S22F). Higher sub-100 nm PN concentrations were obtained during the indoor NPF events with the non-thymol-based disinfectant [e.g., F2 peak, 4.45 × 10$^5$ cm$^{-3}$ (Figure S21F)] as compared to the two thymol-based botanical disinfectants [e.g., B2 peak, 1.96 × 10$^4$ cm$^{-3}$ (Figure 1F)], likely due to greater emissions of C$_{10}$H$_{16}$O and C$_{10}$H$_{18}$O from the former (Table S5). Production of sub-100 nm particles on the order of 10$^4$–10$^5$ cm$^{-3}$ demonstrates the strong SOA-forming potential of botanical disinfectants used in the presence of O$_3$ in mechanically ventilated buildings undergoing routine surface disinfection. Among the observed NPF events, the newly formed particles grew quickly, at D$_a$ values from <10 to >40 nm in several minutes (e.g., Figure 1D and Figure S21D).

The concurrent release of a variety of VOCs that have high reactivities with O$_3$ (Table S3) suggests that the indoor NPF events were initiated by the ozonolysis of both the emitted monoterpenes (C$_{10}$H$_{16}$O) and monoterpenoids (C$_{10}$H$_{14}$O, C$_{10}$H$_{16}$O, C$_{10}$H$_{18}$O, and C$_{10}$H$_{20}$O). The former likely played a leading role in the production of highly oxygenated organic molecules (HOMs) given the high mixing ratios observed (Table S5). While SOA production due to monoterpane ozonolysis has been well studied, comparatively less is known with regard to monoterpenoid ozonolysis. A few studies have observed SOA production due to the ozonolysis of C$_{10}$H$_{14}$O and C$_{10}$H$_{16}$O isomers, while C$_{10}$H$_{16}$O and C$_{10}$H$_{18}$O isomers have not yet been evaluated. In addition to...
HOMs produced by the ozonolysis of monoterpenes and monoterpenoids, it is likely that human-emitted ammonia (NH₃)₆³,₆⁴ (via the researcher applying the disinfectant) and outdoor-to-indoor transported sulfuric acid (H₂SO₄)₆⁵−₆⁸ (via the powered ventilator) participated in the initial steps of particle nucleation and growth. Given a per-person NH₃ emission factor₆³ of 0.6 mg h⁻¹ person⁻¹, a researcher in the zEDGE Tiny House for 10 min can increase indoor NH₃ mixing ratios by ∼1.9 ppb. Outdoor H₂SO₄ measurements in Indiana have reported concentrations in the range of 10⁶−10⁷ molecules cm⁻³.₆⁹ Prior observations₆⁵,₇₀ of atmospheric NPF events at similar or lower H₂SO₄ and NH₃ concentrations would suggest that both species contributed to the observed indoor NPF events.

The HR-ELPI+ measurements revealed the formation of coarse mode liquid droplets during the application of the botanical disinfectant sprays. As illustrated in panels E and F of Figure 1, particle mass concentrations at D₅₀ values from 1 to 10 μm sharply increased at the inception of the spray event. Peak PM₁₀ and PM₂.₅ mass concentrations were on the order of 10²−10³ and 10¹−10² μg m⁻³, respectively, across the disinfection events (Table S5). Thus, botanical disinfectant sprays are important episodic indoor sources of coarse mode particles. The observed formation of sub-10 μm droplets during botanical disinfection events can be attributed to three physical processes: (1) direct emissions of sub- and super-10 μm droplets from the spray jet,₇¹,₇² (2) impaction of super-10 μm droplets onto the glass panels, followed by droplet rebound or initiation of splashes that can release smaller droplets into the air;₇¹,₇₃ and (3) shrinkage of super-10 μm droplets due to evaporation.₇¹,₇₃,₇₄ The rapid decrease in PM₁₀ concentrations after the spray event is due to droplet evaporation, gravitational settling, and ventilation. The former can explain the concurrent increase in water vapor mixing ratios (Figure 1B).

There exist two pathways by which monoterpenes and monoterpenoids included in the liquid disinfectant solutions...
can be released into the air: (1) evaporation from the liquid film on the surface to be disinfected and (2) evaporation from the sub- and super-10 μm droplets (for products A–F). The disinfectant itself, thymol, can therefore exist in two phases concurrently. Figure 1G illustrates the measured mass concentration of thymol in the gas phase and that contained in the sub-10 μm droplets, estimated on the basis of the measured PM10 mass concentrations and initial thymol weight percentage. The distribution of thymol between the two phases was temporally variant, with a spike in the droplet phase occurring ~4 min before the peak in the gas phase.

Botanical Disinfectant Emission Factors for VOCs and Sub-10 μm Droplets. Real-time measurements of the botanical disinfectant emissions via the PTR-TOF-MS and HR-ELPI+ enabled determination of emission factors (EFs) for VOCs (Figure 2a) and sub-10 μm droplets (Figure S27). EFs are a generalizable metric for quantifying the total amount of species emitted per unit of a product applied.33,75 VOC EFs are reported as micrograms per gram, micrograms per milliliter, and micrograms per spray for products A–F and micrograms per wipe for product G (Table S7). Speciated EFs in micrograms per gram for sprays A–F are presented in Figure 2a. Thymol EFs for the nonpressurized sprays containing thymol at 0.05 wt % (A, B, and D) were similar, ranging from 106 to 134 μg g⁻¹. Thymol EFs scaled with the amount of thymol included in the disinfectant. The mean thymol EF for product E (0.23 wt %) was 489 μg g⁻¹, 3.6–4.6-fold greater than EFs for products containing 0.05 wt % thymol (A, B, and D); all for nonpressurized sprays). This agrees with the ratio of the thymol weight percentage (0.23 wt %/0.05 wt % = 4.6).

EFs varied among the monoterpenes and monoterpenoids released from the botanical disinfectants, with the following mean EFs aggregated across all spray products (A–F): C10H16 (2701 μg g⁻¹); C10H16O (223.2 μg g⁻¹); C10H18O (106.7 μg g⁻¹); C10H18O, 136.9 μg g⁻¹; C10H20O, 11.7 μg g⁻¹ (Figure 2a, bottom right subplot). Product F, a non-thymol-based disinfectant, had the highest EFs for C10H16 and C10H18O. Among the thymol-based sprays (A–E), product C had the highest EFs for C10H16 and C10H18O. One of the thymol-based sprays (A–E), product C had the highest EFs for C10H16 and C10H18O. EFs for sub-10 μm droplets ranged from 0.5 to 4.5 mg spray⁻¹, corresponding to emission rates from 0.5 to 2.4 mg s⁻¹, respectively (Figure S27).

For the spray products, the VOC EFs depend in part on the amount of each compound added to the liquid disinfectant solution and the compound’s volatility. The former was given for only thymol. In the United States, manufacturers are required to disclose the weight percentage for only nonfunctional constituents included at >0.01 wt %, as per California’s SB-258 Cleaning Product Right to Know Act of 2017.76 Despite the inclusion of monoterpenes at ≤0.01 wt %, EFs were greater than that for thymol for all products with 0.05 wt % thymol due to the higher volatility of monoterpenes (e.g., the l-limonene C10H16O is 86-fold greater than the thymol C10H18O). Thus, policies regarding consumer products intended to be sprayed in indoor environments should consider not only the weight percentage of a particular ingredient but also the extent to which they can partition into the air. In this study, the EFs were determined for disinfectants applied to impermeable glass panels. It is expected that the VOC emission profiles and EFs would vary among different application surfaces, such as porous wood and fabric-covered furniture.

Human Exposure Implications of Botanical Disinfectant Events in Buildings. The use of botanical disinfectants in mechanically ventilated residential buildings in the presence of O3 initiates a temporally variant multiphase inhalation exposure scenario. As illustrated in Figure 1, one is first exposed to primary emissions of gas-phase monoterpenes and monoterpenoids and coarse mode liquid droplets of the disinfectant solution, followed by ozonolysis-initiated sub-100 nm SOA. Thymol inhalation intake fractions (iFs)77–79 and aerosol respiratory tract deposited doses in number (RTDDNs) and mass (RTDDMs) were determined to characterize human exposure to botanical disinfectant emissions at different breathing rates.35 One of the three periods, accounting for ~40% of the total IFs. Thus, one can inhale a significant amount of thymol after the liquid film of disinfectant is removed from a surface. The variability in the iFs among the spray, wipe, and decay periods demonstrates the utility of real-time indoor VOC exposure measurements with a PTR-TOF-MS.

Inhalation exposure to ozonolysis-initiated SOA resulted in RTDDMs on the order of 10⁴–10⁷ particles [Figure 2c(I)]. NPF due to non-thymol-based product F was associated with the largest number dose (mean RTDDN of 5.0 × 10¹⁰ particles), 10-fold larger than the dose associated with the thymol-based products (mean of B2, B3, and D1, 5.9 × 10⁹ particles). The pulmonary region received the largest fraction of the total number dose (40–46%), followed by the tracheobronchial region and head airways. The high RTDDN in the pulmonary region is due to the high deposition fractions (DFs) for particles at D values from 20 to 50 nm in this region (Figure S28), which overlaps with the prominent mode of the SOA PN size distributions (Figure 1D). The number doses received during the indoor NPF events are equivalent to what one would receive when exposed to urban outdoor aerosols in a North American city for 30–100 min.24 The SOA-forming potential of botanical disinfectants should be considered when evaluating the health risks associated with the indoor use of such products given the adverse toxicological effects associated with exposure to sub-100 nm SOA.25–27

The high PM10 mass concentrations of disinfectant droplets resulted in RTDDMs from 10 to 28 μg [Figure 2c(II)]. Much of the mass dose was received in the head airways (63–75%) due to the high DFs of coarse mode particles in this region (Figure S28). While botanical disinfectants are commonly marketed as natural, green, and nontoxic alternatives to traditional chemical disinfectants, the multiphase exposures that they induce should not be overlooked and require further toxicological evaluation.
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**Notes**

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