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12-4-2020

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Alisha Ortiz
Portland State University

Recommended Citation

Ortiz, Alisha, "Identification of Degradation Products Formed from Glycerol and Terpenes in Aromatherapy Vaporizers" (2020). *University Honors Theses.* Paper 1067.
https://doi.org/10.15760/honors.1093

Identification of Degradation Products Formed from Glycerol and Terpenes in
Aromatherapy Vaporizers

By Alisha D. Ortiz

An undergraduate honors thesis submitted in the partial fulfillment of the requirements
for the degree of

Bachelor of Science

in

University Honors

and

Chemistry

Thesis Adviser

Dr. Robert M. Strongin

Portland State University

2020

Abstract

Degradation chemistry has been widely studied to assess the safety of aerosols in many fields. The study herein investigates the degradation products formed from MONQ personal aromatherapy devices- a new non-nicotine aromatherapy vape pen device on the market. These pens are marketed to alleviate symptoms of an unrecognized medical syndrome called "terpene deficiency". These pens contain a glycerin (GL), or glycerol (VG), base and a blend of terpene-rich essential oils. Previous studies have investigated the degradation of both VG and terpenes and have shown that concerning compounds are released in the gas phase, including benzene, benzaldehyde, methacrolein and methyl vinyl ketone. [8,12] However, a study has not been done that focuses on the thermolysis reaction of terpenes combined with GL. Here, the purpose of these experiments is to bridge this gap in understanding. Adsorption-thermal desorption gas chromatography-mass spectroscopy (ATD-GCMS) is implemented to identify the compounds in both the gas phase of MONQ devices. Methacrolein, benzene, benzaldehyde, and other organic acids and compounds were successfully identified in selected blends of MONQ devices. Considering most of these compounds are respiratory irritants, and benzene is a carcinogen, MONQ devices pose questionable benefits to consumers.

Keywords: glycerol, terpenes, glycerin, vape, aromatherapy, essential oils, vaporizer, ATD-GCMS, gas phase, aerosol chemistry, degradation chemistry, vaporization chemistry.

<u>Introduction</u>

1.1 Applications of Aromatherapy

Plant based medicines have been used as a form of naturopathic medicine since as early as 5000 B.C.[14] Aromatherapy is a branch of this naturopathy, using plant essences topically or by inhalation to assuage symptoms of different ailments. Modern aromatherapy began in 19th century France when chemist René Gattefossé burned his arm badly and treated the burns with pure lavender oil. He noted the powerful healing properties of the oil and further investigated other therapies using essential oils. This inspired research into the healing potentials of plant extracts and the psychological effects of essential oils.[14,15] One such research paper highlights the possibility of plant essences having sedative or stimulating effects. Since then, aromatherapy has become a popular natural alternative for many people seeking relief from headaches, anxiety, depression, and many other symptoms.[13]

1.2 Degradation Chemistry

Degradation products from e-cigarettes and vape pens has long been an interest to both the chemical and public health communities. Nicotine vapes have long been studied along with the "e-liquid" carrier components, propylene glycol (PG), glycerol (GL), and ethylene glycol (EG). However, non-nicotine vapes are newer on the market and assessing their safety has become an area for novel research. These devices are marketed as personal aromatherapy diffusers, containing a GL carrier, essential oils and other naturally occurring components. Given previous studies investigating the

reaction of terpenes and GL upon heating, the MONQ devices in this study are of questionable benefit. GL has been shown to produce benzene upon vaporization, a known carcinogen.[11] Additionally, terpenes when vaporized alone have been shown to form several gaseous irritants and carcinogens.[8]

1.3 Terpene & Glycerol Chemistry

Terpenes are organic compounds that are made up of so-called *isoprene units*. Terpenes have applications in perfumes, flavorings, pharmaceuticals, and environmental applications.[1] The scent of conifer trees, lavender, peppermint, and many more plants, is due to terpenes. Essential oil extracts from plants are rich in a variety of terpenes and have become a popular homeopathic treatment for several ailments. Terpenes can further be classified on the number of isoprene units they contain. Monoterpenes, sesquiterpenes, and diterpenes are present in MONQ devices, each containing 2,3, and 4 isoprene units, respectively. It also follows that as the terpene increases in mass and size, so does its vapor pressure and boiling point.[12] A study has been done to assess the degradation products formed from the pure monoterpenes limonene, myrcene, and linalool, using a "dabbing" type protocol.[8] The method of "dabbing" a type of flash vaporization used for the consumption of cannabis extract. While this study investigated the degradation of certain terpenes in thermolysis, it does not take into consideration the oxidation or dehydration reactions that can occur with other degradation products, such as those formed in glycerol. This study creates an excellent baseline for the degradation of terpenes in thermolysis but does not actively study any other reactions. Several key compounds of concern were found, including

methacrolein and benzene, and many others. It is believed that similar products will be found from the MONQ devices.

Similarly, glycerol, sometimes known as *vegetable glycerin*, has become a popular base for vaporizer e-liquids as it is marketed as a safer, natural, and food-grade option to propylene glycol. Both propylene glycol and glycerol as used in the vape industry as bases for flavorings and nicotine in vape products. The safety of these components has been widely studied, but there is no mandated limit for inhalation of PG or VG.[6] A study done in 2017 focused on the mechanism behind propylene glycol (PG) and glycerol (GL) degradation in e-cigarettes.[4] This study lays out the chemical pathways for the formation of these products from PG/GL- mostly thermolysis catalyzed abstraction, dehydration, and cleavage. This study also includes clear ^{1}H-NMR spectra for enols and glycidol formed from this thermolysis reaction. The methodology within has been replicated in other similar studies[8,9,12], and will be the basis for the MONQ device study when using H-NMR assessment. This study concludes the formation of several toxic by-products from the thermolysis of PG/GL, such as formaldehyde and benzene, and shows a linear relationship between e-cigarette battery wattage and amount of product formed. Another study confirms the formation of benzene and benzene derivatives in JUUL brand vape pens.[12] The key difference in this study is that these devices contain nicotine, which could affect the formation of degradation products. Even in previous work[11], benzene is formed from vaping of products containing a GL base. Studies also conclude the formation of formaldehyde releasing agents (FRA) from PG and GL.[5] FRA is formed from formaldehyde hemiacetals that are produced when PG/GL is heated in the presence of oxygen. From these studies, it is

prevalent that benzene, formaldehyde, and formaldehyde releasing agents (FRA's), are compounds of serious interest in the MONQ study.

1.4 MONQ Devices & Study

MONQ aromatherapy devices first appeared on the market in 2014 and are the investment of Dr. Eric Fishman. These novel devices blend the use of aromatherapy with the popular and portable "pen vaporizer" technology. Fishman claims these aromatherapy devices can be used to alleviate symptoms of an unrecognized medical condition he terms "terpene deficiency syndrome."[10] He believes this syndrome could be responsible for disorders such as anxiety, depression, and general emotional distress. With MONQ devices, users can "feel the way you want" and select a blend of essential oils targeted to illicit a favorable emotional response. MONQ devices are comprised of a battery, a silica wick in a heating coil, and use an 80:20 glycerol-essential oil liquid, all housed in a metal tube. The battery heats the liquid to approximately 121°C, where the user then intakes the resulting vapor.[10] However, not many terpenes or terpenoid compounds would become vaporized into the gas phase at this temperature. MONQ states that its users do not inhale the vapors but are instructed to breathe in through the mouth and exhale through the nose to prevent the vapors from reaching the lungs.[10] Regardless if MONQ is used as directed or not, this manner still exposes the sensitive olfactory and salivary glands in the mouth and nose to the vapors, and resulting degradation products, formed from these devices.

The purpose of this study is to investigate the degradation products formed from the glycerin-terpene blend present in MONQ essential oil vape pens. It is thought that

the thermolysis products of both terpenes and GL can interact with one another during their oxidation and produce other products which have not been previously documented. It is also possible that due to the blend of these products, other known compounds such as isoprene oxidation products may be formed.

Focus was placed on these MONQ vaporizers due to their popularity and composition; certain blends contain known irritants and unique chemical mixtures. The "Love" blend contains davana, cacao, and Siam wood. Davana is common flavoring additive for cigarettes and all these compounds are often considered aphrodisiacs. "Love" also contains a benzoin additive which can cause respiratory irritation. More interesting is the "Sleepy" blend with lavender, chamomile, and kava. Lavender is rich in linalool which has been documented to create upper respiratory irritants,[4] and the main constituent of kava are a series of kavalactones which can cause liver toxicity. Finally, the "Zen" blend contains frankincense, which contains a compound called boswellic acid. Boswellic acid has not been studied for its inhalation toxicology, but other organic acids have been known to cause severe respiratory symptoms upon exposure.

Methods

1.1 Materials

MONQ Original Personal Aromatherapy Devices in "Love", "Zen" and "Sleepy" blends. The internal liquid is comprised of an 80:20, GL: essential oil, vape liquid. Each device has its own unique blend of essential oils, but the same coconut derived GL.

1.2 ATD Sample Collection

Samples from MONQ devices were collected using a CH technologies Cigarette Smoking Machine (CSM, Westwood, NJ) that ran a CORESTA puff program. This program was run for a single puff of 3 seconds to generate a volume of 55 mL of aerosol. Aerosol was generated from the device's internal lithium ion battery and nickel-chromium resistance coil that heated the liquid to ~121 °C. Samples were collected through set up containing a 47mm Cambridge filter pad (CFP, GE Healthcare) connected to an ATD cartridge. The cartridge contains 100 mg of 35/60 mesh Tenax TA and 200 mg of 60/80 mesh Carbograph 1 TD (both, Camsco Inc., Houston, TX). All connections were made using 3/8-inch outer diameter ACF0017-F Tygon S3 E-3603. Figure 1 shows the actual set up for ATD-GCMS collection.
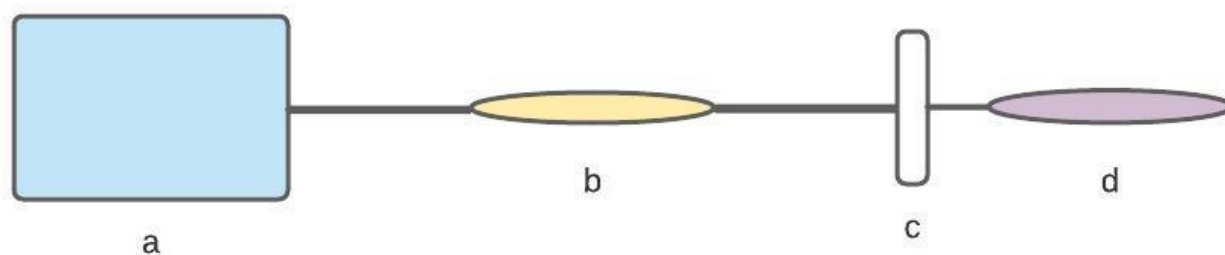

Figure 1: Experimental setup used for vapor collection for ATD-GCMS. Components depicted are: *a,* SCSM machine; *b,* ATD cartridge; *c*, CFP holder; *d*, MONQ device.

1.3 ATD-GCMS

Cartridges were thermally desorbed with a TurboMatrix 650 ATD unit (PerkinElmer, Waltham, MA). Before desorption, internal standards (IS) of 20 ng of fluorobenzene, 18.6 ng of d_8-toluene, 21.7 ng of 4-bromofluorobenzene, and 20.3 ng of d_4-1,2-dichlorobenzene were automatically added to all cartridges. The ATD unit desorbed the cartridges at 285 °C for 10 minutes with a helium desorption flow of 40 mL/min, a split flow of 10 mL/min and the stream was trapped at -10 °C on a "Tenex® trap". Desorption of the Tenex® trap was done at 295 °C at a constant pressure of helium at 35 psi, on a split flow of 12 mL/min for 4 minutes. Through a 1 m long, 0.25 mm i.d. deactivated fused silica transfer line at 235 °C, the unsplit portion of the stream was run through a 60 m long, 0.25 mm i.d., and 1.4 µm film thickness Agilent (Santa Clara, CA) DB-VRX capillary GC column mounted in an Agilent 7890A GC. The GC was interfaced to an Agilent 5975C MS with an impact ionization at 70 eV in positive ion mode. The GC oven temperature was programmed to be held at 45 °C for 10 minutes, raised to 190 °C at 12 °C/min, held at 190 °C for 2 minutes, raised to 240 °C at 6 °C/min, held at 240 °C for 5 minutes, and then lowered to 210 °C at 10 °C/min. The MS scan range was 34 to 400 amu and the electron multiplier voltage was 1725 V.

Results

Organic compounds of interest identified by ATD-GCMS across the 3 MONQ devices are highlighted in Table 1. These include several previously documented compounds such as methacrolein, benzene, benzaldehyde, and methyl vinyl ketone.

Table 1. Of these compounds, methacrolein, 3-buten-2-one (methyl vinyl ketone), and benzene are of interest. But key interest lies with compounds not previously reported, such as the weak organic acids and similar alkanes and alkenes.

Organics		
Compound	Retention (min)	Qual.
sulfur dioxide	2.803	90
2-propanol	4.499	86
acetone	4.608	80
dichloromethane	5.418	94
methacrolein	6.819	91
3-buten-2-one	7.661	83
2-methyl furan	8.445	90
2-methyl-3-buten-2-ol	8.573	81
carbonic acid	9.402	90
dichloroethane	10.752	96
benzene	12.037	95
pentanal	13.444	80
1-methyl-1,4-cyclohexadiene	16.194	95
methyl benzene	16.413	95
toluene	16.406	95
hexanal	17.145	96
dimethylhex-5-en-3-yn-2-ol	18.559	80
heptanal	19.806	81
propanoic acid	20.011	90
crotonic acid	20.898	53
benzaldehyde	21.451	96
propanoic acid	22.074	90
1,3-cyclohexadiene	22.164	95
2-butenoic acid	22.762	90
1,2-dichlorobenzene d4	22.993	93
1,4-cyclohexadiene	23.109	97
benzylacetate	25.274	98

All the compounds listed above have a match quality of 80 or higher, to ensure an accurate match against the PBM internal library. Of these compounds, the most interesting are the weak organic acids; carbonic, propanoic, crotonic and butanoic

acids. These acids are also listed as respiratory irritants on MDS. All these acids have

not been previously reported as being present in the aerosols produced by terpenes or

glycerol. It is unclear what the mechanism of their formation is, or if they are present in

the device to begin with. Similarly, compounds such as acetone, toluene, and

dichloromethane are organic solvents, also not previously reported. These solvents

could be residues from the extraction process of the essential oils or formed from the

heating of glycerol.

Likewise, a variety of terpene and terpene derived produced were also found

alongside other organic materials. Most of these compounds were found in the aromatic

region, between retention times of 20 to 33 minutes, and were the highest abundance of

any other compounds. These compounds are listed in Table 2.

Table 2. The listed variety of terpene and their complexes across MONQ

devices. These were the most diverse and largest peaks shown in the

spectrograph, corresponding to the largest percentage of products in the

gas phase.

Terpenes and Terpene Derivatives		
Compound	Retention (min)	Qual.
alpha terpinene	20.05	96
3-thujene	20.468	94
alpha pinene	20.757	96
2,4(10)-thujadiene	20.918	91
alpha fenchene	21.078	96
camphene	21.162	97
(+) Sabinene	21.528	97
beta-mycene	21.618	96
beta-pinene	21.727	97
2,3-dehydro-1,8 cineole	21.843	86

alpha-phelladrene	22.164	97
(+)-3-caren	22.273	97
(+)-4-carene	22.383	97
trans-alpha ocimene	22.427	83
alpha limonene	22.627	99
eucalyptol	22.729	98
1,8-cineol	22.73	99
gamma terpinene	23.109	97
alpha-acetophenone	23.636	90
alpha terpinolene	23.726	98
alpha, 4-dimethylstyrene	23.938	96
(+)-3-thujone	24.49	98
alpha thujone	24.67	98
2,6-dimethyl 2,3,6 octatriene	24.786	96
(2-methylprop-1-enyl)-cyclohexa-1,5-diene	24.972	93
(+)-camphor	25.493	98
(-) pinocarvone	25.795	87
dill ether	26.078	93
dihydro-carvone	26.36	98
(-) myrtenal	26.502	98
vetiverol	26.874	91
(-)-R-carvone	27.35	97
eugenol	29.58	98
copaene	30.332	99
(-) beta bourbonene	30.659	96
alpha bergamotene	31.257	98
4,11,11-trimethyl-8-methylenebicyclo undec-3-ene	31.565	99
alpha humulene	32.336	99
beta bisabolene	32.658	92
alpha muurolene	32.838	93
alpha bulnesene	33.056	94
delta cadinene	33.255	98

Given the richness of the essential oils in terpenes, it is not surprising that these compounds make up most of the gas phase sample. Even though the terpene profile varies from device to device, due to the complexity of each blend, many of these terpene products were shared across samples. This leads to some predictability of degradation products formed from terpenes across all devices studied. Much like the

weak organic acids, these terpenes can also act as irritants, as well as oxidize with atmospheric oxygen to create products like methacrolein and methyl vinyl ketone. The presence of methyl vinyl ketone and methacrolein seems to reveal some level of terpene oxidation happening within the heating of the essential oil liquid.

Conclusions

Preliminary results from the ATD-GCMS shows the presence of benzene, benzaldehyde, methacrolein, weak organic acids, and diverse terpene and terpene derived compounds. These results are in line with previous studies showing the degradation products formed from standalone terpenes and glycerol, as well as yielding new compounds that have not been previously reported. Most of the reported compounds are respiratory irritants or carcinogens and could potentially cause adverse reactions in users if used frequently.

Future work is needed to assess whether these compounds are present in the primary sample or if they are created in the heating process, and to detail a mechanism of formation. ATD-GCMS was not successful in identifying the presence of formaldehyde releasing agents (FRAs). In future studies, ^{1}H-NMR can be used to readily detect and quantify FRA compounds. Further work is also needed to quantify these compounds and apply a qualitative risk analysis (QRA) model to deduct a risk associated with exposure. This study would like to be expanded to include other manufacturers of devices of similar composition to extract more data on aromatherapy devices overall. Experiments in the time ahead will also probe into identifying kavalactones from kava containing compounds as noted previously.

Acknowledgment

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