SQUALENE AND SQUALANE AS ADULTERANTS

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What are Squalene and Squalane?

- **Squalene**: squalene is a *terpene*. It can be derived from animal sources (primarily shark livers) and plant sources (e.g. olives, amaranth, and sugarcane).
- **Squalane**: is a *hydrogenated oil*, made from squalane.
- Squalene is present in cannabis in trace amounts. Squalane is not present in cannabis.
- Both squalene and squalane are popular in the cosmetics industry due to their moisturizing properties.
- Both squalane and squalene have been found in commercially available "cuts" or "diluents" being sold for use in the cannabis industry.[1]
    - Both compounds plus "olive extract" were discovered in "Viscosity," a commercially available diluent used by some OLCC licensees to formulate vape cartridges.
- Oregon VALI ("Vaping Associated Lung Injury) investigation: in 7 products tested by CDC, *no* Vitamin E Acetate found; ***squalene*** found in all 7 products

1. Bryan Duffy, Lingyun Li, Shijun Lu, Lorie Durocher, Mark Dittmar, Emily Delaney-Baldwin, Deepika Panawennage, David Lemaster, Kristen Navarette, and David Spink, "Analysis of Cannabinoid-Containing Fluids in Illicit Vaping Cartridges Recovered from Pulmonary Injury Patients: Identification of Vitamin E Acetate as a Major Diluent," *Toxics* 8, no. 1 (2020): 15, https://doi.org/10.3390/toxics8010008.

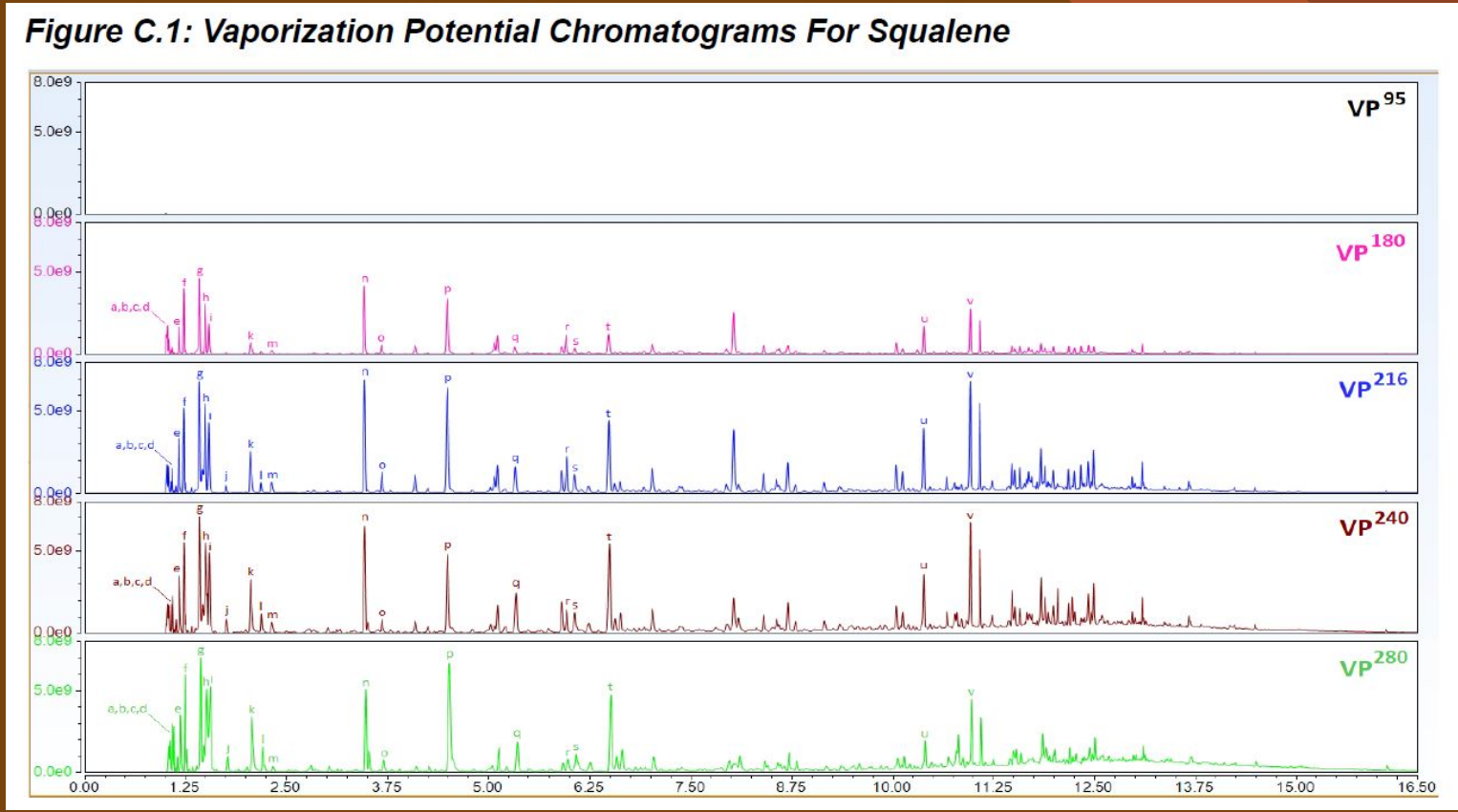
Squalene and Squalane – Adulterants in Inhalable Products

- OLCC commissioned research by Canadian firm Supra Research and Development to determine what byproducts are created when squalene, squalane, and vitamin E acetate are exposed to common cannabis vaping temperatures.
- Supra's method heats the sample in a controlled manner and collects and analyzes the byproducts.
- Based on the assessment protocol created by Supra, all three compounds failed. Supra recommends that products that fail this protocol should not be used in any product intended for inhalation.
- The data "suggests that squalane and squalene thermally degrade in a manner that **produces higher levels of chemical agents than we observed for Vitamin E acetate**."

Supra Research…

- At 240°C (or 464°F) squalene and squalane produce amounts of the following chemicals that **exceed** the United States Pharmacopeia (USP) levels for residual solvents in drugs that are meant to be **ingested***:*
  - Acetone;
  - Methanol;
  - Acetic acid; and
  - Formic acid.
- Cannabis vape batteries typically operate between 300 – 800 degrees Fahrenheit.
- Even at lower temperatures, squalane and squalene are thermally unstable as the following chromatogram illustrates.

Supra Research: Squalene



- Starting at 180°C (356°F) – squalene begins to break down into other compounds, indicating it is highly thermally unstable. Squalane is slightly more thermally stable (but not by much).
- The more thermally unstable a compound is, the greater chances are it can cause harm.

…Compared to Vitamin E Acetate

Figure C.1: Vaporization Potential Chromatograms For Squalene

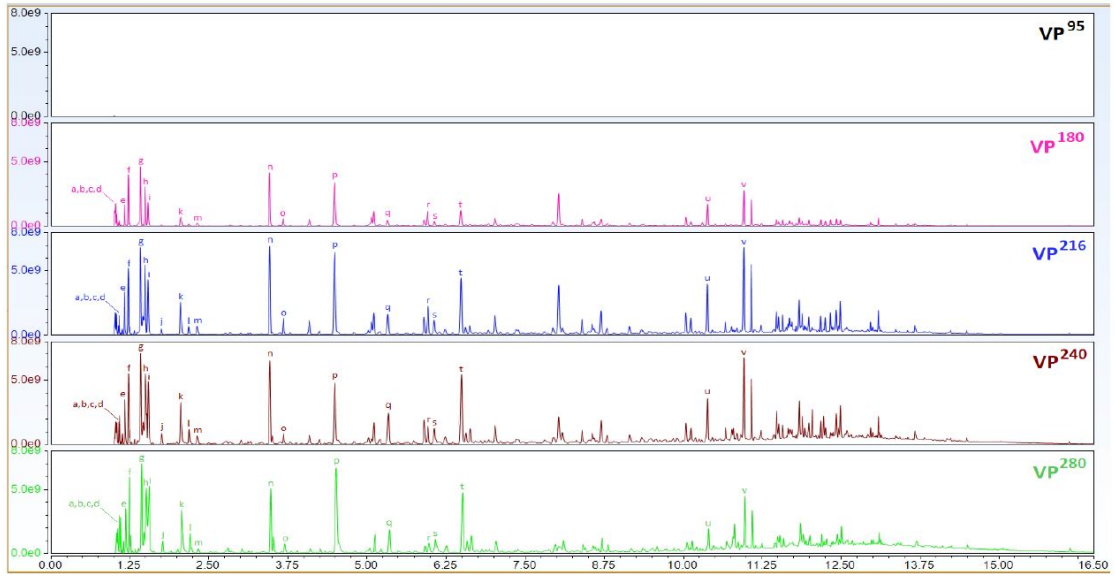
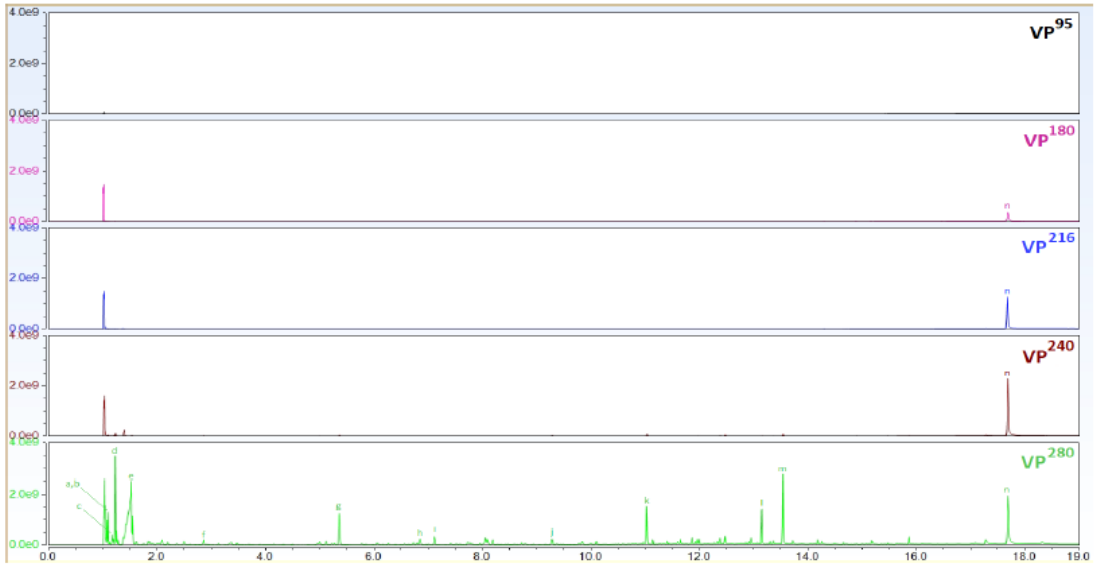


Figure A.1: Vaporization Potential Chromatograms For Vitamin E Acetate



Additional Research

- Inhalation of squalene has been associated with exogenous lipoid pneumonia (inhalation of oil into the lungs).[1]
- It is well documented that inhaling any kind of oil (e.g. squal***ane***) can cause exogenous lipoid pneumonia.[2]
- More recent research shows that under vaping conditions, squalane produces chemicals that can kill lung cells and interfere with the lung's ordinary functioning.[3]
    - These results are consistent with Supra's.

1. Lee, Jin Seong, Gyungyub Gong, and Tae Hwan Lim, "Squalene Aspiration Pneumonia: Thin-Section CT and Histopathologic Findings," *Journal of the Korean Radiological Society* 38, no. 3 (1998): 453, https://doi.org/10.3348/jkrs.1998.38.3.453.
2. *See, e.g.*, Beck, Lauren R, "Lipoid Pneumonia," StatPearls [Internet], U.S. National Library of Medicine, June 22, 2020, https://www.ncbi.nlm.nih.gov/books/NBK554577/.
3. Jiang, Huanhuan, C. M. Sabbir Ahmed, Thomas J. Martin, Alexa Canchola, Iain W. H. Oswald, Jose Andres Garcia, Jin Y Chen, et al, "Chemical and Toxicological Characterization of Vaping Emission Products from Commonly Used Vape Juice Diluents," *Chemical Research in Toxicology*, 2020, https://doi.org/10.1021/acs.chemrestox.0c00174.

Adulteration – Statutory and Rule Authority:

- **ORS 475B.232(2)** states: “[t]he Oregon Liquor Control Commission may prohibit a licensee from selling any brand of marijuana item that in the commission’s judgment is deceptively branded or labeled or contains injurious or adulterated ingredients.”
- **OAR 845-025-1015(2)** "Adulterated" means to make a marijuana item impure by adding foreign or inferior ingredients or substances.
- A marijuana item may be considered to be adulterated if it bears or contains any poisonous or deleterious substance in a quantity rendering the marijuana item injurious to health, including but not limited to tobacco or nicotine.

Adulterated Products are Prohibited:

- **OAR 845-025-1300(1)(e)** A licensee may not maintain a noisy, disorderly or insanitary establishment or supply adulterated marijuana items.
- **OAR 845-025-3220(3)** A processor may not treat or otherwise adulterate a cannabinoid product, concentrate or extract with any non-cannabinoid additive that would increase potency, toxicity or addictive potential, or that would create an unsafe combination with other psychoactive substances. Prohibited additives include but are not limited to nicotine, caffeine, polyethylene glycol, or any chemicals that increase carcinogenicity or cardiac effects.
- **OAR 845-025-8540(2)(b)** A licensee may not treat or otherwise adulterate usable marijuana with any chemical, biologically active drug, plant, substance, including nicotine, or other compound that has the effect or intent of altering the usable marijuana's color, appearance, weight or smell or that has the effect or intent of increasing potency, toxicity or addictiveness.
- **OAR 845-025-8540 (3)(a)** A licensee may not supply adulterated marijuana items.

Context: Vitamin E Acetate (VEA) as an adulterant

- VEA linked by CDC to VALI cases in other states (samples did not include Oregon)
- In November, 2019, Commission declared VEA as an adulterant; specific motion as approved:

  "To approve of staff's interpretation that, based on recent findings from the Center for Disease Control regarding a potential cause of the national outbreak of e-cigarette, or vaping, product use–associated lung injury (also known as EVALI), and vitamin E acetate's harmful effects if inhaled, that vitamin E acetate meets the definition of an "adulterant" under OAR 845-025-1015(2) as it pertains to cannabinoid vaping products, and therefore is prohibited as an ingredient in cannabinoid vaping products manufactured or sold in Oregon, effective November 20, 2019."

Motion: Squalene and Squalane as an Adulterant

- Based on available research and data, when heated and inhaled, squalene and squalane meet the definition of an “adulterant” under OAR 845-025-1015(2) as it pertains to cannabinoid products intended for inhalation, and therefore is prohibited as an ingredient in cannabinoid products intended for inhalation manufactured or sold in Oregon, effective December 17, 2020.