


Looking Ahead to Toxicology in 2020

A Presentation from the NAME Toxicology Committee


Chair: Laura Labay, PhD; Vice-Chair: Charles Catanese, MD
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 Alison Miller, MA; Frank Miller, MD; D. Kimberley Molina, MD; Abraham Philip, MD;
 Megan Quinn, MD; Robert Stoppacher, MD; Linda Sullivan, BS



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OBJECTIVES


- 1 • To discuss drugs and chemicals that are important to the practice of toxicology in 2020
- 2 • Mitragynine
• Interpretation
- 3 • Sodium Nitrate/Nitrite
• No direct test for postmortem samples
- 4 • Tianeptine
• Antidepressant with an opioid high
- 5 • Vaping
• Emerging data about adverse effects and lethal outcomes
- 6 • Delta-8 THC
• Analytical impact to Delta-9 THC



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KRATOM – Introduction

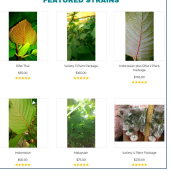
- KRATOM (*Mitragyna speciosa*) is a tropical tree found in southern Thailand and northern states of the Malay peninsula.
- In its native regions, leaves of the Kratom tree are typically consumed as a tea or chewed directly
- Purported to induce stimulant and opioid-like analgesic effects in a dose- and time-dependent manner
- Been reported to be useful in ameliorating withdrawal symptoms following cessation of opioid use




KRATOM 100% SATISFACTION
SHOP NOW

1 gram – Slight or very mild effects
 5 grams – Reasonable effects
 10 grams – This is a potent effect for the average users
 15 grams – Very Strong effect
 18+ grams – Super strong effect – only recommended for the seasoned and experienced users

FEATURED STRAINS





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KRATOM – Human Performance Impairment and PM Concentrations

HUMAN PERFORMANCE IMPAIRMENT	POSTMORTEM
Order Date: 1/2018 - 8/2019	
N = 30	N = 1030
Range: 11 – 490 ng/mL*	Range: 6 – 4500 ng/mL*
Average: 106 ng/mL ± 117	Average: 282 ng/mL ± 484
Median: 66 ng/mL	Median: 110 ng/mL

* Other drugs may be present
NMS Labs Data



KRATOM – Interpretation - Stability

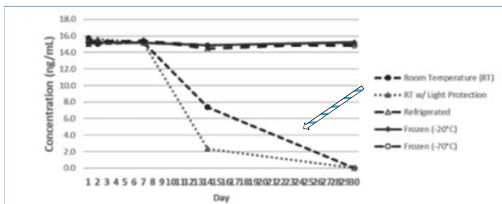


Figure 4. Stability of spiked low control (16 ng/mL) across conditions over 30 days. Data points are an average of three replicates.

Papsun DM, Chan-Hosokawa A, Friederich L, Brower J, Graf K, Logan B. The Trouble With Kratom: Analytical and Interpretative Issues Involving Mitragynine. J Anal Toxicol. 2019 Aug 19.



SODIUM NITRATE/NITRITE – Suicides

Suicide Discussion

Aug 5, 2019 < #1

Hi all, just wondering if we have any idea of how effective a stat dose is when attempting with SN. Do we know of any successful attempts using the stat dose? Thanks.

Response: "If you do a trial run of the regimen with Metoclopramide and experience adverse side effects you can use Domperidone instead."

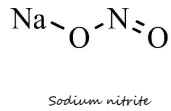
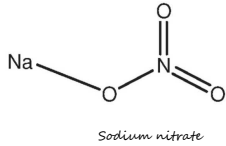
EXIT INTERNATIONAL (<https://exitinternational.net/docs/ExitActBC.pdf>)

The two salts in question are sodium nitrite and sodium azide. Both are described in the Peaceful Pill eHandbook in the chapter on 'Lethal Inorganic Salts'. P.126 of Jan 2018 edition.

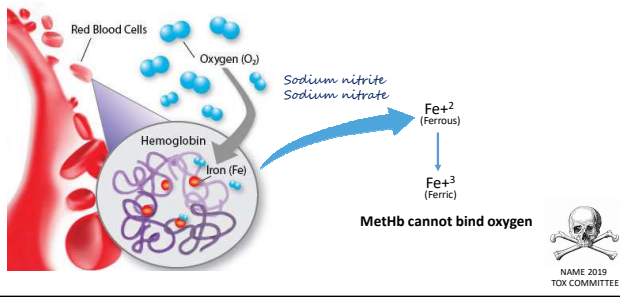
<https://www.peacefulpillhandbook.com/preview-contents/>



SODIUM NITRATE/NITRITE



SODIUM NITRATE/NITRITE – MethHb



SODIUM NITRATE/NITRITE – Levels

LEVEL	SYMPTOMS
1-2%	Normal Physiological State
10-20%	Cyanosis
20-50%	Respiratory distress, dizziness, headache, and fatigue
50-70%	Loss of consciousness and death
(>90%)	(Survival Reported)



Katabami K, Hayakawa M, Gando S. Severe Methemoglobinemia due to Sodium Nitrite Poisoning. Case Rep Emerg Med. 2016

SODIUM NITRATE/NITRITE – MetHb in PM Blood



- Met-Hb formed is rapidly reduced to Hb when blood samples are stored without freezing
- MetHb formation can also occur by auto-oxidation or by putrefaction after sampling

Sato K, Tamaki K, Okajima H, Katsumata Y. Long-term storage of blood samples as whole blood at extremely low temperatures for methemoglobin determination. *Forensic Sci Int.* 1988 Apr;37(2):99-104

Introduction

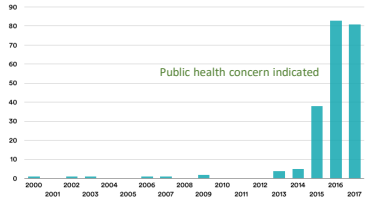
Determination of methemoglobin (Met-Hb) in blood is important for the diagnosis of poisoning by oxidants such as nitrites and nitrates. Met-Hb itself, however, is very unstable and both formation and reduction of Met-Hb can occur even after sampling. Met-Hb formed is rapidly reduced to hemoglobin (Hb) by intraerythrocytic Met-Hb reductase when blood samples are stored as whole blood without freezing [1–3]. Met-Hb formation can also occur by autoxidation or by putrefaction after sampling [2–4]. Thus, care should be taken to prevent both formation and reduction of Met-Hb during storage of blood samples. For this purpose, blood samples are immediately hemolyzed with large volumes of a chilled buffer, and Met-Hb concentrations are determined as soon as possible [2,4].



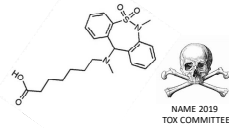
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TIANEPTINE – Introduction

Tianeptine exposure calls to U.S. poison control centers



- Atypical tricyclic drug used as an antidepressant in Europe, Asia, and Latin America
- Not approved for use by the FDA in the United States
- Animal and human studies show that tianeptine is an opioid receptor agonist

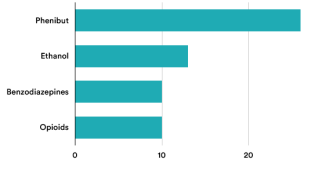


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MEGAN THIELKING/STAT
SOURCE: CHARACTERISTICS OF TIANEPTINE EXPOSURES REPORTED TO THE NATIONAL POISON DATA SYSTEM – UNITED STATES, 2000–2017, MORBIDITY AND MORTALITY WEEKLY REPORT

TIANEPTINE – Symptoms & Co-exposures

Other drugs reported in tianeptine exposure calls to poison control centers



- SYMPTOMS:
 - Neurologic,
 - Cardiovascular
 - Gastrointestinal signs and symptoms
 - Some effects mimicking opioid toxicity
 - 83 tianeptine exposures with noted co-exposures



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MEGAN THIELKING/STAT
SOURCE: CHARACTERISTICS OF TIANEPTINE EXPOSURES REPORTED TO THE NATIONAL POISON DATA SYSTEM – UNITED STATES, 2000–2017, MORBIDITY AND MORTALITY WEEKLY REPORT

VAPING – Introduction

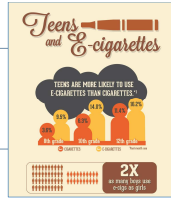
VAPING DEVICES

- E-cigarettes
- Vape pens
- Advanced personal vaporizers



CONTENTS

- Propylene glycol or vegetable glycerin-based liquid with nicotine
- Flavoring (e.g., gummy bear, tobacco, coffee, cotton candy)
- Other chemicals and metals



VAPING – Explosion Injuries



VAPING – Reports of Injury & Death

Illinois patient's death from lung disease may be first vaping-related fatality in U.S.

AUGUST 24, 2019 / 6:35 PM / CBS/AP

One man's brush with death after vaping-related lung failure

He went from hiking enthusiast to "on death's door" within days. Doctors blamed vaping.

Juul CEO Says Lung Illnesses Tied to Vaping Are 'Worrisome' but Has No Plans to Remove Product

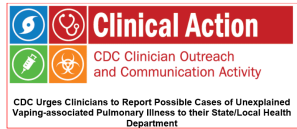
The Centers for Disease Control is currently investigating nearly 200 cases of severe respiratory illness linked to vaping.

By Julie Moxton August 28, 2019 11:33 AM



Illustration: Michael, son of Perry. This was one of the patients treated at the University of Utah hospital for serious lung injuries related to vaping. He eventually recovered. —Michael's family

VAPING – CDC Communication



CDC Urges Clinicians to Report Possible Cases of Unexplained Vaping-associated Pulmonary Illness to their State/Local Health Department

- o As of 8/14/19, 30 cases of severe pulmonary disease have been reported to the WI Department of Health Services
 - o 15 cases are confirmed (ages 16-34 years)
 - o 15 cases are still under investigation (ages 16-53 years)
- o **SYMPTOMS:**
 - o Patients presented with respiratory symptoms including cough, shortness of breath, and fatigue.
 - o Symptoms worsened over a period of days or weeks before admission to the hospital.
 - o Other symptoms reported by some patients included fever, chest pain, weight loss, nausea, and diarrhea.
 - o Chest radiographs showed bilateral opacities, and CT imaging of the chest demonstrated diffuse ground-glass opacities, often with sub-pleural sparing.



VAPING – Radiology

Check X-ray of patients with various forms of VAPIL.
 (AEP = acute eosinophilic pneumonia; OP = organizing pneumonia; LP = lipid pneumonia).

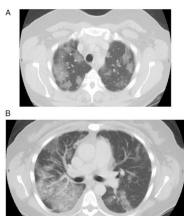
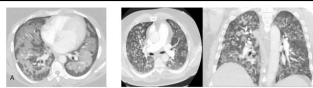
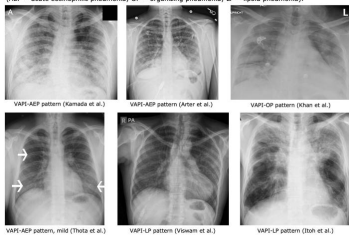
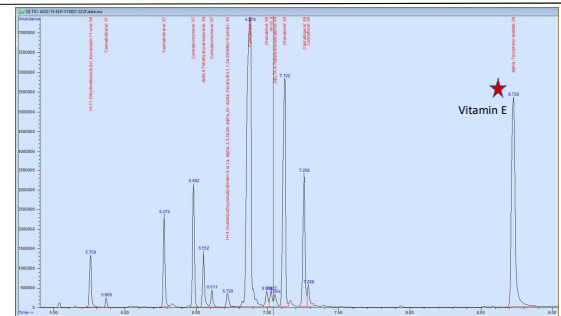


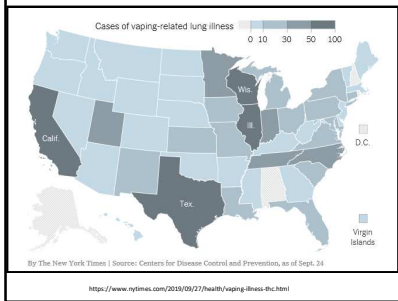
Figure 1. Representative CT images show the "crazy paving" pattern and patchy ground glass opacities in interlobular septal thickening. A, Bilateral upper lobes. B, Bilateral lower lobes.



VAPING – Vaping Pen Extract

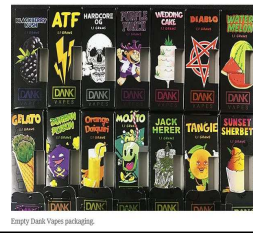


VAPING INJURIES BY LOCALE & BRAND



Dank Vapes, TKO and Other THC Vaping Brands Are Linked to Illnesses, C.D.C. Says

Health officials released the names of several products identified by patients who have been sickened in Illinois and Wisconsin.

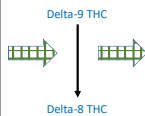


Delta-8 THC – Introduction

- A naturally occurring cannabinoid found in most cannabis plants
- Has been identified in botanicals, vape oils, and edibles
- Legal Status - Since the compound shares such a close molecular design with delta-9 THC, it currently falls under the same legal status per the Federal Analogue Act



Delta-8 THC – Manufacturing



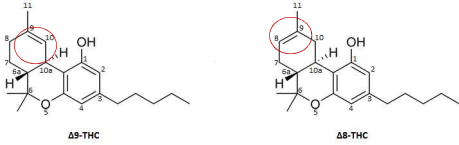
Delta-8 THC: Not present in enough quantity to prepare a distillate

The reaction
Mix in 4% acidic alumina silicate with your extracted and winterized crude cannabis oil. Distill the cannabis oil and collect the THC distillate as you normally would. The combination of the acidic alumina silicate and boiling flask heat will catalyze the rearrangement of the THC molecule from delta-9 to delta-8-THC. The conversion rate should be at least 90 – 95%.



<https://brincumb.com/blog/cannabis-distillation/how-to-convert-the-delta-9-to-the-delta-8/>

Delta-8 THC – Structure



Delta-9 THC and Delta-8 THC are isomers as are their metabolites.

In samples where Delta-8 THC and Delta-9 THC are present, the chromatography of the Delta-9 THC and the Delta-9 THCC metabolite may be adversely affected.



Delta-8 THC – Effects

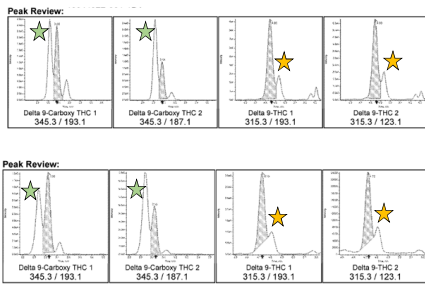
- Properties:
 - antiemetic
 - anxiolytic
 - appetite-stimulating
 - analgesic



- Binds to the cannabinoid CB1 and CB2 receptors
- Exhibits a lower psychotropic potency than Delta-9 THC



Delta-8 THC – Chromatographic Challenge



- ★ Delta-8 THC
- ★ Delta-8 THCC



Delta-8 THC – Impact

Delta-8 THC INTERFERENCE IMPACT:

- Qualitative Identification
- Quantitation

To obtain baseline separation, a longer column may be needed. This results in a longer run-time, which may affect instrument capacity.



SUMMARY

- 1 • Mitragynine
• Interpretation – Stability
- 2 • Sodium Nitrate/Nitrite
• No direct test for postmortem samples – MetHb is the clinical marker, but not a good marker for PM blood. Clinical correlation is a must!
- 3 • Tianeptine
• Antidepressant with an opioid high – Not available in U.S., but used in the U.S.
- 4 • Vaping
• Emerging data about adverse effects and lethal outcomes – Data is still emerging
- 5 • Delta-8 THC
• Analytical impact to Delta-9 THC – Identification and Quantitative Challenges