Poppy Seeds and Interpreting Opiates Drug Testing

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Today’s Discussion

• The poppy plant, opium composition and poppy seed opiates
• Poppy seeds as a dietary product
• Fundamentals of opiates drug testing
• Ingesting poppy seeds and opiates drug testing results
• Interpreting morphine test results
• Heroin drug test options
Objectives

- Understand the drug composition of poppy seeds
- How to interpret drug tests and poppy seed claims
- What tests to order to better differentiate heroin use
Poppy Plant, Opium

*Papaver somniferum*

Cultivation of opium, derived from *P. somniferum*, predates written history. Early Sumerian records (3400 BC) refer to this poppy as the ‘joy plant’.¹

As demands increased, opium trading followed the Silk Roads and spread throughout the Mediterranean, Asia, and China. Intercontinental immigration (expanding railways and the Gold Rush) brought opium to the Americas.

Today, the licit and illicit trade of opium is global.

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Pharmaceutical-licensed opium production occurs in India, Turkey, Australia with illicit operations present in Burma, Afghanistan and Colombia.

Opium refers to the milky latex fluid that oozes from cuts made into the green seed pod (~ 2-3 weeks after flower petals fall away).

The opium latex is scraped from the pod cuts, air dried and balled or bagged for sale.
Opium contains psychoactive phenanthrene alkaloids including morphine, codeine, and thebaine. Morphine is the major constituent (8-19%)\(^2\) of air-dried opium. Codeine concentration is \(~3\%\).

Thebaine (poisonous) is primarily used for synthesis of hydrocodone and oxycodone.

The yield of the alkaloids is affected by crop, rain fall and method of harvest.

Heroin is a diacetylated synthetic product of morphine.

Morphine is THE prototypical opioid. Opioids include natural and synthetic μ receptor agonists. Medical use for palliative effects includes: analgesia, antitussive, anti-diarrheal.

Undesirable opioids effects include:
• High potential for addiction & abuse
• Respiratory depression
• Constipation

Effects of drug abuse also include:
• Infectious disease (HCV, HIV)
• Abscesses
• Endocarditis
Poppy Plant, Opium, Pharmacokinetics

Opioid Metabolic Pathways

Codeine and heroin undergo transformation into multiple metabolites including morphine.

Morphine is excreted into urine as glucuronide conjugates (60% morphine-3-glucuronide, 5-10% morphine-6-glucuronide)\(^3\).

Heroin is excreted into urine as 6-monoacetylmorphine (6-MAM) and also as morphine glucuronide conjugates.

Poppy Plant, Opium, Poppy Seeds

*P. somniferum* is the same plant species for our edible poppy seeds. The seeds are kidney-shaped, less than 1 mm in length and it takes >3,000 seeds to weigh one gram\(^4\).

Poppy seeds are harvested when the seed pods have fully matured.

Poppy seed morphine and codeine is a result of the opium residue that coats the seeds. The drugs are *on* the seeds rather than in the seeds.

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Poppy Plant, Opium, Poppy Seeds

The seed flavors range from fruity (ground seeds) to nutty (whole seeds).

Many forms of poppy seeds dietary uses include:

- Whole poppy seeds used as a spice or a decoration in and/or on top of baked goods (bagels, breads, muffins, cakes, etc).
- Whole poppy seeds used to make ‘seed bars’ (candy bars).
- Poppy seeds finely ground and combined with adjuvants (butter, milk, sugar, preservatives, etc) to create pastes for use as fillings/toppings for baked goods.

*Always note: whole seeds stick in your teeth!"
Drug test immunoassays (IA) are used to differentiate “negative” from “presumptive positive” specimens. Antibody cross reactivity to the antigen (drug/metabolites) may be broad or narrow and all results that are equal to or greater than the cutoff are considered to be “presumptive”:

- Immunoassays cannot provide a definitive identification of what drug/metabolites are present, and
- False positive results cannot be distinguished from true positive results

Morphine is most common calibrant among the immunoassays and represents the analyte with the most sensitivity for detection.
Opiates Drug Testing, Definitive Assays

Definitive assays rule out “false positive” results and identify “true positive” drug/metabolite.

Contemporary methods utilize mass spectrometry coupled to chromatographic retention to identify drugs/metabolites.

Examples of mass spectrometry include:

- Liquid chromatography-tandem mass spectrometry (LC/MS/MS)
- Liquid chromatography-time of flight mass spectrometry (LC/TOF)
- Gas chromatography-mass spectrometry (GC/MS)

Definitive tests may be qualitative or quantitative.
Investigators have confirmed that positive morphine results can occur following consumption of poppy-containing foodstuffs. Factors affecting urine drug/metabolite concentrations include:

- Amount and form of poppy seeds ingested
- Time lapse between ingestion and urine collection
- Patient’s hydration state
- Patient’s genome for metabolism
- Inter-individual pathophysiologic variances

Studies also demonstrate wide variances for urine morphine ng/mL concentration following ingestion:

- Cakes – ranged up to thousands\(^5\) ng/mL
- Bagels – ranged up to hundreds\(^6\) ng/mL

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US Navy Bagel Study

A volunteer consumed 3 poppy-seed bagels. Bagel and urine morphine and codeine were measured.

Three bagels were found to contain a total of ~5 grams of poppy seeds with:
- morphine=963 ng/g
- codeine=73 ng/g.

**Conclusion** – positive urine codeine or morphine results do not necessarily indicate heroin, morphine or codeine use.

Opiates Drug Testing, Cutoffs Levels

Workplace/Employment Testing
To reduce the instances of positive drug tests following ingestion of poppy-containing foodstuffs, both the presumptive (initial) and the definitive (confirmatory) drug test cutoffs for federal workplace opiates were changed (in 1998) from 300 ng/mL to 2,000 ng/mL.

Clinical Abstinence/Compliance Testing
In clinical settings, a cutoff threshold of 2,000 ng/mL for opiates testing is impractical – too many false negative results would occur. Clinical drug testing requires cutoffs of 300 ng/mL or less to monitor the patients’ adherence to treatment plans.

It is important to recognize that assay cutoffs of 300 or 2,000 ng/mL will not eliminate a positive drug test following ingestion of poppy seeds.

Interpreting Test Results

From the SAMHSA, Medical Review Officer Manual for Federal Agency Workplace Drug Testing Programs:

- Eating a normal dietary amount of poppy seeds can cause a urine specimen to test positive for morphine and codeine.
- Following poppy seed ingestions, the concentration of morphine can be substantial, with usually very low concentrations or no detectable codeine.
- In many instances, a donor will not know that poppy seeds can cause a positive test or realize that he or she had eaten poppy seeds around the time the urine was collected.

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For interpreting quantitative urine drug test results less than 15,000 ng/mL morphine and codeine, the Substance Abuse Mental Health Services Agency (SAMHSA), *Medical Review Officer Manual for Federal Agency Workplace Drug Testing Programs* provides the following medical review officer (MRO) guidance:

- If there is clinical evidence of illegal use of any opium, opiate, or opium derivative (e.g., morphine or codeine) listed in the DEA Schedule I or II, **the MRO verifies the result as positive.**
- If there is no clinical evidence of illegal use, **the MRO verifies the result as negative.**
Provider and Patient Actions

In clinical settings where opiates drug testing is utilized for pharmacotherapeutic compliance monitoring, it may be required to:

- Educate patients as to the outcomes of poppy seed ingestion and
- Require patients to abstain from consuming poppy-containing foodstuffs such as:
  - Bagels
  - Muffins
  - Breads
  - Cakes
  - Poppy confectionary bars
Heroin Metabolite Testing

When illicit heroin use is suspect, the heroin metabolite test (6-monoacetylmorphine) is available.

Quest Diagnostics research\(^\text{10}\) indicates 6% of donors positive for heroin metabolite may show negative results for morphine.

- among 1,672 urine specimens positive for heroin metabolite and tested for morphine, 93.4% (1,562 patient specimens) also tested positive for morphine.

- Thus, 6.6% (110 patient specimens) had no morphine detected and would not have been identified of having recent heroin use if co-testing for heroin metabolite and morphine had not been conducted.

\(^{10}\) Quest Diagnostics Health Trends Report, *Prescription Drug Misuse in America, Diagnostic Insights into Managing the Drug Epidemic*, 2014
Conclusion

- Drug composition of poppy seeds
- Interpret drug tests and poppy seed claims
- Tests to order to better differentiate heroin use
Questions?