



DEPARTMENT OF THE ARMY
Office of the Judge Advocate General
Criminal Law Division
2200 Army Pentagon
Washington, D.C. 20310-2200

DAJA-CL

7 February 2023

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: Brady Notice – Poppy Seed Products and Positive Codeine Results from Forensic Toxicology Drug Testing Laboratory (FTDTL)

1. This information is being released pursuant to Brady v. Maryland 373 U.S. 83 (1963) and Rule for Courts-Martial 701. Please ensure this notice is disseminated to all judge advocates in your command as well as judge advocates in subordinate commands.
2. The Office of Drug Demand Reduction, Office of Force Resiliency, Office of the Under Secretary of Defense (Personnel and Readiness) (ODDR) has determined that the ingestion of certain legally purchased food products could, in some circumstances, result in a positive urinalysis for codeine. Attached are all available materials.
3. On 19 January 2023, ODDR temporarily suspended reporting of codeine results on all urinalyses processed at Department of Defense Forensic Toxicology Drug Testing Laboratories and suspended the destruction of urine specimens previously reported as a codeine positive. On 24 January 2023, Army Forensic Toxicology Program suspended the Medical Review Officer review process IAW AR 600-85, para 4-14, for pending codeine positives.
4. ODDR and the Services will identify affected servicemembers with a previously reported positive codeine urinalysis for any appropriate remedial actions.
5. Army Resiliency Directorate will provide notice and education on consumption of poppy seed products to all Soldiers through the Army Substance Abuse Program.

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SUBJECT: Brady Notice – Poppy Seed Products and Positive Codeine Results from Forensic Toxicology Drug Testing Laboratory (FTDTL)

6. POC for further information is LTC Tiffany Heady, Director, Army Forensic Toxicology Program, tiffany.n.heady.mil@health.mil. If you have questions particular to this legal notice, please contact Ms. Janet Mansfield at 571-256-8138 or at janet.k.mansfield.civ@army.mil. Additional information will be provided when available.



CHRISTOPHER A. KENNEBECK
Colonel, JA
Chief, Criminal Law Division

5 Encls

1. Letter from Corin Stone, Principal Deputy General Counsel
2. Codeine and Morphine Concentrations in Brand Name Poppy Seeds
3. Poppy Seed Consumption May be Associated with Codeine-Only Urine Drug Test Results
4. Interpreting Urine drug Test Results in the Context of Chronic Opioid Analgesic Therapy and Poppy Seed Consumption
5. Letter from Jamie L. Lewis, M.D.

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SUBJECT: Brady Notice – Poppy Seed Products and Positive Codeine Results from Forensic Toxicology Drug Testing Laboratory (FTDTL)

Staff Judge Advocate, U.S. Army Africa/Southern European Task Force
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DEPARTMENT OF DEFENSE
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1600 DEFENSE PENTAGON
WASHINGTON, DC 20301-1600

FEB 03

MEMORANDUM FOR THE JUDGE ADVOCATES GENERAL OF THE MILITARY
DEPARTMENTS
STAFF JUDGE ADVOCATE TO THE COMMANDANT OF THE
MARINE CORPS

SUBJECT: Notification Pursuant to Rule for Courts-Martial 701(a)(6) and *Brady v. Maryland*,
373 U.S. 83 (1963)

The DoD Office of Drug Demand Reduction has determined that the ingestion of certain legally purchased food products could, in some circumstances, result in a positive urinalysis for codeine. Attached are four documents concerning the potential ingestion of codeine from a non-drug product.

1. Codeine and Morphine Concentrations in Brand Name Poppy Seeds (TAB A)
2. Poppy Seed Consumption May Be Associated with Codeine-Only Urine Drug Test Results (TAB B)
3. Interpreting Urine Drug Test Results in the Context of Chronic Opioid Analgesic Therapy and Poppy Seed Consumption (TAB C)
4. Letter from Jamie L. Lewis, M.D. (TAB D)

I request that you ensure disclosure of these documents pursuant to Rule for Courts-Martial 701(a)(6) and any applicable implementing regulations.

A handwritten signature in cursive script, appearing to read "Corin Stone".

Corin Stone
Principal Deputy General Counsel

Attachments:
As stated

cc:
Judge Advocate General of the Coast Guard



Chesapeake Toxicology Resource

Shawn P Vorce / Research Section / 12.13.2022

The background of the slide is a photograph of a laboratory setting. A glass pipette with a blue cap is positioned diagonally, dispensing a small amount of yellow liquid into a clear glass petri dish. The petri dish is placed on a blue surface. The background is slightly blurred, showing other laboratory equipment and a bright light source.

Codeine and Morphine Concentrations in Brand Name Poppy Seeds

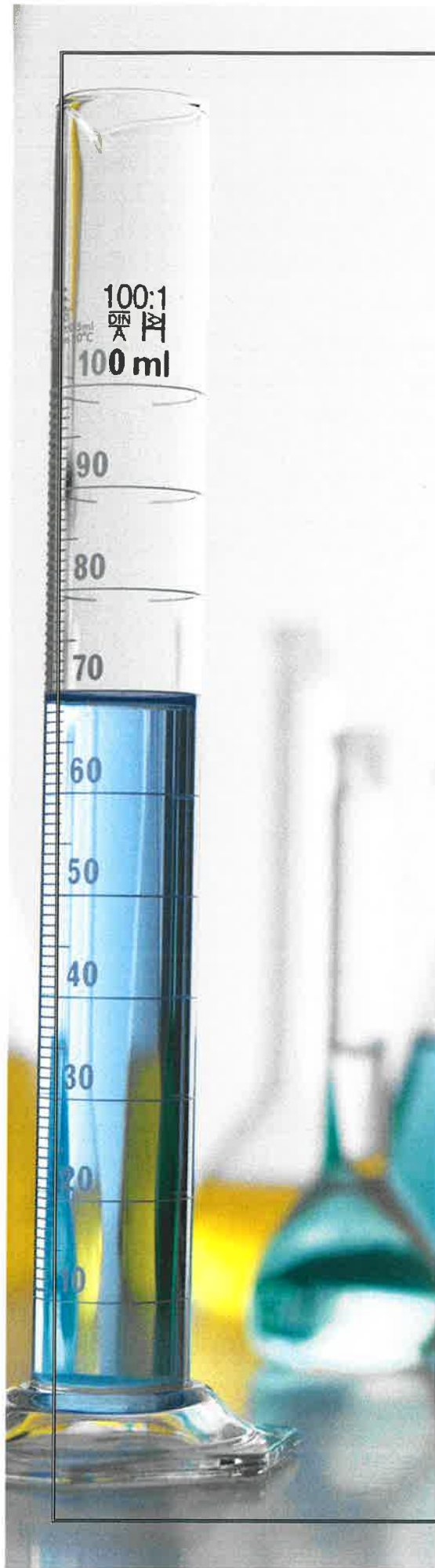


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INTRODUCTION



Concerns about poppy seed contaminated with morphine and codeine are not new. The plant that produces poppy seeds, *Papaver somniferum* (commonly known as opium poppy), also produces the opium latex that contains morphine, codeine and thebaine. These opiates are not present in the poppy seeds themselves; however poppy seeds can become contaminated with the opium latex during harvesting. It is well documented that consumption of poppy seed can produce a positive drug test result for opiates [1,2,3,4]. Traditional guidance has suggested that codeine concentrations exceeding 300 ng/mL coupled with morphine-to-codeine ratios <2 are indicative of codeine consumption and, therefore, exclude poppy seed consumption as a legitimate explanation for the test result. However, a recent scientific publication [5] suggests that a positive codeine only urine drug test can result from the ingestion of a particular poppy seed. These poppy seeds contain mostly codeine with only trace amounts of morphine.

FDA Authority

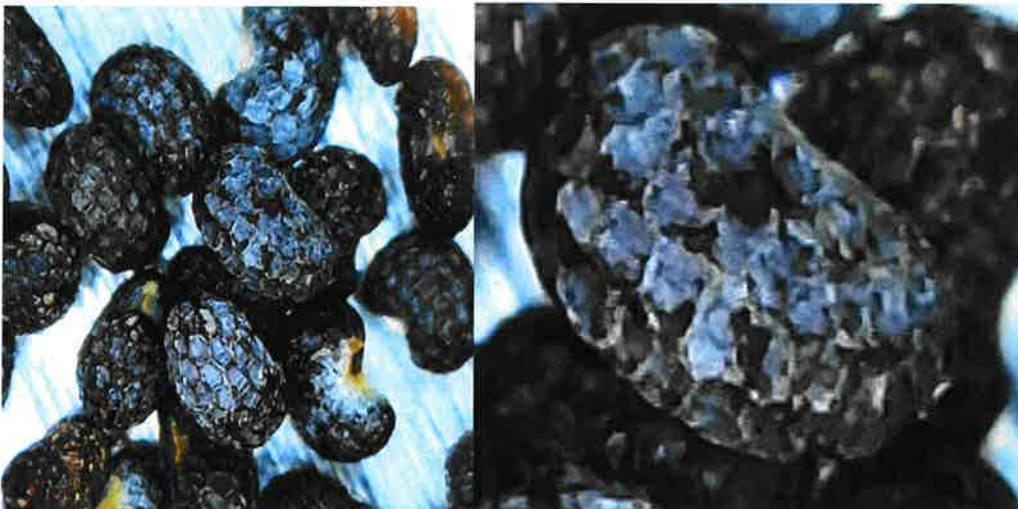
The FDA's authority to regulate contaminated poppy seeds derives from 21 U.S.C. § 331 and 21 U.S.C. § 342(a), which prohibit the sale of adulterated food and define a food as "adulterated:"(1) If it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health...or (4) if it has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. Opioid contamination in poppy seeds is an "added substance" because the opiates are not naturally present in the seeds and are instead the result of contamination that occurs during harvesting or processing. Such contamination renders the seeds "injurious to health" because opiates may cause a range of severe adverse health consequences, including respiratory depression, abdominal pain, addiction, and death.

Similarly, the FDA has authority under 21 U.S.C. § 342(a)(4) to ensure that poppy seeds are not “prepared, packed, or held under insanitary conditions ... whereby [they] may have been rendered injurious to health,” including by specifying good manufacturing practices and preventive controls needed to ensure poppy seeds are not contaminated with dangerous levels of opiates.

Finally, the FDA has general authority to issue regulations to prevent the sale of adulterated seeds under 21 U.S.C. § 371 which authorizes the agency to “promulgate regulations for the efficient enforcement of this chapter,” as well as the regulatory authorities conferred under 21 U.S.C. § 350g, which requires food facilities to conduct hazard analysis and set in place risk-based preventive controls,⁷⁴ and 21 U.S.C. § 384a, which requires importers to perform risk based foreign supplier verification activities for the purpose of ensuring the safety of imported food.

Poppy Seed and Opium Latex

Poppy seeds do not contain any opiate compounds, they are contaminated during harvesting with the opium latex which contains morphine, codeine and thebaine. A study in the Journal of Forensic Science showed poppy seeds from seven different origins contain a wide variation of morphine (2-251 µg/g) and codeine (0.4-57.1 µg/g). The poppy seeds are kidney shape with honeycomb-like outer shell which can easily trap and retain the opium latex as seen in the photo below.



DOD INTEREST



Morphine to Codeine Ratio

Morphine/codeine ratio is widely used in forensic medicine to differentiate between the consumption of codeine and morphine [8]. A morphine/codeine ratio below 1.0 is indicative of codeine only ingestion, whereas a morphine/codeine ratio above 1.0 is indicative of morphine or heroin ingestion. However, the ratio of 1.0 is not absolute in determining the source of morphine. About 3% of the population are CYP2D6 ultra-rapid metabolizers. In these individuals, the morphine/codeine ratio can be higher than 1.0 even in with the sole consumption of codeine.

Codeine Positives in the DoD Random Urinalysis Program

The DoD cutoffs for morphine and codeine are 4,000 and 2,000 ng/mL respectively. Recently, the DoD Military Drug Testing Laboratories have encountered numerous codeine positive urine samples with little or no morphine, where the service member has claimed poppy seed ingestion. Preliminary investigation by the DoD laboratories have shown that certain poppy seeds contain high amounts of codeine with little or no morphine. This is contrary to previous publications on the opiate content of contaminated poppy seeds, which showed a higher concentration of morphine than codeine with morphine to codeine ratios greater than 2.0 [7]. The obvious concern for the DoD is determining if the source of the codeine was passive ingestion of poppy seeds or illicit consumption.

Chesapeake Toxicology Resources Involvement

CTR laboratories was contracted to determine the concentration of codeine and morphine in two batches of poppy seeds provided by the Air Force Drug Testing Laboratory, San Antonio, TX.

CHESAPEAKE TOXICOLOGY RESOURCES STUDY



Three different brands of poppy seeds were analyzed for the concentration of codeine and morphine. Codeine and morphine were extracted from the seeds and analyzed by liquid chromatography tandem mass spectrometry. Total concentration and the percentage of codeine and morphine per gram of seed are calculated and reported.

PRODUCTS OBTAINED FOR THE STUDY

Costo BayState Poppy Seeds

McCormicks Poppy Seeds

Great Value Poppy Seeds



Reference Standards

Reference standards of morphine (1.0 mg/mL, FE03232010, Exp. 4/25), morphine-d6 (1.0 mg/mL, FE03172006, Exp 4/25), codeine (1.0 mg/mL, FE05052005, Exp. 6/25), and codeine-d6 (1.0 mg/mL, FE03162011, Exp. 4/25), were obtained from Cerilliant.

Instrumentation

SCIEX 4500 QTRAP Tandem Mass Spectrometer

Shimadzu Nexera X2 Liquid Chromatograph

Agilent Poroshell 120 EC-C18 (4.6 x 50mm, 2.7um) HPLC column

EXTRACTION AND QUANTITATION METHOD



Extraction

Approximately 0.5 grams of poppy seeds from each source were pulverized in the 2010 Geno/Grinder. Three separate measurements of ~50 mg of each poppy seed brand were weighed into clean labeled 12x75mm culture tubes. To each sample, 2.0 mLs of HPLC grade methanol was added. The samples were mixed for 15 minutes and then decanted to remove the poppy seed pulp. The methanol extract was dried in the TurboVap @ 40°C under nitrogen. The dried extract was reconstituted in 1.0 mL of methanol. One hundred microliters of the extracts and calibrators listed below were diluted first with 300 uL of ISTD solution and then diluted 1:5 with 95:5 mobile phase. Two microliters were injected.

Calibration Curve Preparation

Standard Spiking Solution was prepared from 1.0 mg/mL of codeine and morphine:

CCSS Preparation from Stock Ampoules

#	Analytes	Stock Concentration (µg/mL)	Spike Volume (µL)	Resulting Concentration (ng/mL)
1	Codeine	1000	50	10000
2	Morphine	1000	50	10000

Calibration Curve was prepared according to the following table:

Standard to Use	Prepared From CAL4			Prepared from CCSS Solution				
	CAL1	CAL2	CAL3	CAL4	CAL5	CAL6	CAL7	CAL8
Amount of CCSS to add (µL)				40	50	100	150	200
Amount From CAL4 (µL)	125	250	500					
Amount of Methanol to add (µL)	875	750	500	1960	950	900	850	800
Total Volume (µL)	1000	1000	1000	2000	1000	1000	1000	1000

Calibration Curve								
Analytes	CAL1	CAL2	CAL3	CAL4	CAL5	CAL6	CAL7	CAL8
Codeine	25	50	100	200	500	1000	1500	2000
Morphine	25	50	100	200	500	1000	1500	2000

Liquid Chromatography

Flow rate: 0.90 mL/min

Column Oven: 40°C

Mobile Phase A: Water w/0.1% formic acid

Mobile Phase B: Acetonitrile:Methanol (50:50) w/0.1% formic acid

Step	Time (min)	Module	%B
1	0.25	Pump B	5
2	5.00	Pump B	85
3	5.25	Pump B	95
4	6.05	Pump B	95
5	6.10	Pump B	5
6	6.50	Pump B.	5
7	7.00	Controller	STOP

Mass Spectrometer

Source: TurbolonSpray® ion source

Polarity: Positive

IonSpray Voltage Positive Polarity (IS): 4500 V

Curtain Gas (CUR): 30 psi

Temperature (TEM): 550°C

Ion Source Gas 1(GS1): 55 psi

Ion Source Gas 2 (GS2): 60 psi

Interface Heater (Ihe): On

Collision gas (CAD): medium

Target Scan Time: 0.30 sec

MRM Transition Parameters:

Analytes	Retention time (min)	Q1 (m/z)	Q2 (m/z)	DP (V)	EP (V)	CE (V)	CXP (V)
Morphine 1	1.40	286.1	152.1	46	10	89	8
Morphine 2	1.40	286.1	165.1	46	10	51	10
Morphine-d6 1	1.40	292.1	152.0	50	10	83	8
Codeine 1	1.81	300.2	152.1	106	10	63	10
Codeine 2	1.81	300.2	165.0	106	10	83	16
Codeine-d6 1	1.80	306.2	152.2	106	10	65	8

Curve Processing Parameters

MultiQuant software was used to process the calibration curve using 1000 ng/mL of codeine-D₆ and morphine-D₆ internal standard per sample. The curve was processed by a quadratic regression (weighting 1/x). Criteria for acceptable is ±20% MRM ratios, ±3% retention times, and >0.99 for coefficient of determination (R²).

RESULTS



Codeine				
McCormick's				
#	Weight (mg)	Measured Quant (ng/mL)	Codeine (ug/g)	% Codeine (w/w)
Mc_1	49.8	0.00	0.00	0.000%
Mc_2	50.0	0.00	0.00	0.000%
Mc_3	49.7	0.00	0.00	0.000%
	avg	0.00	0.00	0.000%
	stdev	0.00	0.00	0.0000%
	CV	#DIV/0!	#DIV/0!	#DIV/0!
Poppy seeds		Codeine		
10	grams		0.00	mg
50	grams		0.00	mg
100	grams		0.00	mg
Morphine				
McCormick's				
#	Weight (mg)	Measured Quant (ng/mL)	Morphine (ug/g)	% Morphine (w/w)
Mc_1	49.8	89.04	1.79	0.0002%
Mc_2	50.0	76.47	1.53	0.0002%
Mc_3	49.7	75.46	1.52	0.0002%
	avg	80.32	1.61	0.000%
	stdev	6.18	0.12	0.0000%
	CV	7.7%	7.7%	7.7%
Poppy seeds		Morphine		
10	grams		0.02	mg
50	grams		0.08	mg
100	grams		0.15	mg

Codeine				
Costco BayState				
#	Weight (mg)	Measured Quant (ng/mL)	Codeine (ug/g)	% Codeine (w/w)
BS_1	51.1	14855.32	290.71	0.029%
BS_2	52.9	16474.22	311.42	0.031%
BS_3	50.4	12015.22	238.40	0.024%
	avg	14448.25	280.18	0.028%
	stdev	1843.00	30.73	0.003%
	CV	12.8%	11.0%	11.0%

Poppy seeds		Codeine
10 grams		2.91 mg
50 grams		15.57 mg
100 grams		23.84 mg

Morphine				
Costco BayState				
#	Weight (mg)	Measured Quant (ng/mL)	Morphine (ug/g)	% Morphine (w/w)
BS_1	51.1	248.72	4.87	0.0005%
BS_2	52.9	371.45	7.02	0.0007%
BS_3	50.4	204.07	4.05	0.0004%
	avg	274.75	5.31	0.0005%
	stdev	70.77	1.25	0.0001%
	CV	25.8%	23.6%	23.6%

Poppy seeds		Morphine
10 grams		0.05 mg
50 grams		0.35 mg
100 grams		0.40 mg

Codeine				
Great Value				
#	Weight (mg)	Measured Quant (ng/mL)	Codeine (ug/g)	% Codeine (w/w)
GV_1	52.6	12030.78	228.72	0.023%
GV_2	49.7	11361.15	228.59	0.023%
GV_3	52.9	11889.50	224.75	0.022%
	avg	11760.48	227.36	0.023%
	stdev	288.20	1.84	0.000%
	CV	2.5%	0.8%	0.8%

Poppy seeds		Codeine
10 grams		2.29 mg
50 grams		11.43 mg
100 grams		22.48 mg

Morphine				
Great Value				
#	Weight (mg)	Measured Quant (ng/mL)	Morphine (ug/g)	% Morphine (w/w)
GV_1	52.6	25.54	0.49	0.0000%
GV_2	49.7	23.70	0.48	0.0000%
GV_3	52.9	26.78	0.51	0.0001%
	avg	25.34	0.49	0.0000%
	stdev	1.27	0.01	0.000001%
	CV	5.0%	2.5%	2.5%

Poppy seeds		Morphine
10 grams		0.00 mg
50 grams		0.02 mg
100 grams		0.05 mg

[1]TM, Opfermann G, Schänzer W. Urinary Concentrations of Morphine and Codeine After Consumption of Poppy Seeds. *J Anal Toxicol* (January-February 2003) 27(1): 53-56

[2]DW Lachenmeier, C Sproll, F Musshoff. Poppy seed foods and opiate drug testing—where are we today? *Therapeutic Drug Monitor*. 2010 Feb; 32(1): 11-18.

[3]Moeller MR, Hammer K, Engel O. Poppy seed consumption and toxicological analysis of blood and urine samples. *Forensic Sci Int*. 2004 Jun 16; 143(2-3): 183-186

[4]C Meadway, S George, R Braithwaite. Opiate concentrations following the ingestion of poppyseed products—evidence for the "poppy seed defense." *Forensic Sci Int* . 1998;96:29-38

[5]G.M. Reisfield, S.A. Teitelbaum, J.T. Jones, Poppy Seed Consumption May Be Associated with Codeine-Only Urine Drug Test Results, *Journal of Analytical Toxicology*, 01 October 2022
<https://doi.org/10.1093/jat/bkac079>

[6]MG Pelders 1, JJ Ros, Poppy seeds: differences in morphine and codeine content and variation in inter- and intra-individual excretion. *J Forensic Sci*. 1996 Mar;41(2):209-12.

[7]ML Smith, DC Nichols, P Underwood, Z Fuller, MA Moser, C LoDico, DA Gorelick, MN Newmeyer, M Concheiro, MA Huestis Morphine and Codeine Concentrations in Human Urine following Controlled Poppy Seeds Administration of Known Opiate Content, *Forensic Sci Int*, 2014 Aug, 241:87-90.

[8]G Ceder, AW Jones. Concentration ratios of morphine to codeine in blood of impaired drivers as evidence of heroin use and not medication with codeine. *Clin Chem*. 2001;47(11):1980–4

Poppy Seed Consumption May Be Associated with Codeine-Only Urine Drug Test Results

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Abstract

Consumption of poppy seed-containing food products can result in opiate-positive urine drug test results and may pose challenges in distinguishing poppy seed consumption from opiate administration. In this context, guidance has suggested that codeine concentrations exceeding 300 ng/mL coupled with morphine-to-codeine ratios <2 are indicative of codeine consumption and, therefore, exclude poppy seed consumption as a legitimate explanation for the test result. In recent years, we performed independent medical examinations of three individuals who produced codeine-positive/morphine-negative (300 ng/mL) forensic urine drug test results but denied codeine administration, attributing their test results to the consumption of specific poppy seed-containing food products. In the present study, 11 participants consumed one of the 10 unique poppy seed-containing food products, including the three implicated food products. Six of 33 non-baseline urine samples (18%)—representing three food products—were positive for codeine and negative for morphine at 300 ng/mL cut-offs (and therefore featured morphine-to-codeine ratios <2). This study adds to a small literature indicating that consumption of poppy seed-containing food products cannot reliably be distinguished from codeine administration based on previously published urinary opiate concentrations and ratios. An important caveat is that in none of these cases did maximum urinary codeine concentrations exceed 1,300 ng/mL.

Introduction

Poppy seeds used in food products are derived from the opium-producing poppy *Papaver somniferum* L., the latex of which contains numerous alkaloids, including morphine and codeine (1). Although the seeds themselves do not contain opiates, they may be contaminated with them, via the poppy latex, during the harvesting process (1). Importantly, following poppy seed consumption, urinary opiate concentrations may exceed the common 300 ng/mL cut-off concentration (2). Such urine drug test results can pose challenges in distinguishing opiate (codeine, heroin and morphine) administration from poppy seed consumption (2, 3).

Two of us (G.M.R. and S.A.T.) performed forensic independent medical examinations (IMEs) for Florida's professional health programs, which provide nondisciplinary monitoring and advocacy services for contracted health care professionals with substance use disorders. Contractees in these programs are required to maintain abstinence from potentially impairing substances, and their abstinence is monitored by means of random drug tests. Regarding opiates, contractees are admonished to avoid poppy seed-containing food products because confirmed opiate-positive urine drug test results prompt a reflexive IME for the evaluation of opiate abuse or unauthorized use. Since 2020, we have encountered three cases in which contractees produced codeine-positive/morphine-negative urine drug test results but denied using codeine, instead attributing their drug test results to consumption of specific poppy seed-containing food products.

In each of these cases, an opiate-positive immunoassay (IA)-based urine drug screen (300 ng/mL cut-off) was followed by a liquid chromatography–tandem mass spectrometry (LC–MS–MS)-based positive result for codeine (300 ng/mL cut-off) coupled with negative results for morphine (300 ng/mL cut-off) and the heroin metabolite 6-acetyl morphine (10 ng/mL cut-off). The implicated food products included New York Style™ Everything Bagel Crisps (urinary codeine 808 ng/mL), Publix Greenwise® lemon poppy seed mini-muffins (urinary codeine 328 ng/mL) and Thomas'® Everything Bagels (urinary codeine 548 ng/mL). In each case, the index urine sample was collected within 5 h of poppy seed consumption. And in each case, the contractee, on examination, evidenced no indicia of opiate abuse. In the third case, the contractee, following the production of a confirmed codeine-positive/morphine-negative urine drug test result, was administered—and passed—a polygraph examination focused on the intentional administration of codeine.

In interpreting these urine drug test results, we initially consulted the current edition of the Medical Review Officer Handbook, which did not appear to support our contractees' poppy seed defense (4). As the scientific studies cited were decades old, we elected to identify a pertinent review article via a search of the PubMed database using the terms codeine AND poppy seeds AND urine and filtered for review articles and English language. This returned two citations. El Sohly and Jones (1989), based on a review of the extant literature, published guidelines on source differentiation of opiates

in biological fluids (5). With regard to codeine, the authors suggested that a urinary codeine concentration exceeding 300 ng/mL together with a morphine-to-codeine ratio <2 is indicative of codeine use and rules out poppy seeds as the cause of the test result. More recently, Tenore (2010), in a non-systematic review of the literature, confirmed that a morphine-to-codeine ratio <2 is consistent with codeine administration and cannot be explained on the basis of poppy seed consumption (6).

In order to assess the current validity of these guidelines, we queried the PubMed database using the search terms poppy AND (seed OR seeds) AND (codeine OR morphine OR opiates) and filtered for human studies and English language. The search returned 54 citations. After reviewing the abstracts and, when necessary, the complete papers, we eliminated 15 studies that did not involve poppy seed administration, six that did not present original research, four in which urinary codeine concentrations were not measured, three that involved opiate IA testing exclusively and two that did not involve urine drug testing. The remaining 24 publications were relevant to this question.

Twenty-one of the 24 publications presented data supportive of the ElSohly guideline (7–27). Three publications, however, presented data that contravened the guideline. Lo and Chua (1992) fed 25 participants poppy seed-containing curry meal(s) and collected urine samples for up to 48 h. Hydrolyzed urine specimens were analyzed for morphine and codeine by gas chromatography–mass spectrometry. The authors presented selected data, specifically each participant's maximum urinary morphine concentration and the synchronic urinary codeine concentration. The data included two urine samples (8% of the total) in which urinary codeine concentrations exceeded 300 ng/mL (730 and 340 ng/mL, respectively) and the morphine-to-codeine ratio was <2 (1.74 and 0.88, respectively) (28).

Chang et al. (2012), in a letter to the editor, reported a case involving a workplace urine drug test result of codeine 575 ng/mL and morphine <50 ng/mL (hydrolyzed specimen, LC–MS–MS analysis). The employee denied codeine use and attributed her drug test result to the consumption of poppy seed-containing bread. A subsequent n-of-1 experiment was conducted in which a volunteer consumed the bread, with urine samples collected at baseline and at regular intervals for the following 7.5 h. Urinary codeine concentrations exceeded urinary morphine concentrations at every time point. In all specimens except for the first, codeine concentrations exceeded 300 ng/mL, reaching a maximum of 874 ng/mL at 6.5 h. Conversely, morphine concentrations never exceeded 300 ng/mL (maximum 125 ng/mL). The authors stated that similar results were obtained from a second volunteer who consumed poppy seed bread from a different supplier (29).

Most recently, Lewis et al. (2021) reported a study of 17 participants, each of whom consumed one Costco Wholesale® poppy seed muffin and provided urine samples for analysis at baseline and at 4–6 and 21–25 h post-consumption. Opiate-positive samples by IA (300 ng/mL cut-off) were hydrolyzed and subjected to LC–MS–MS analysis. At 4–6 h, the mean (maximum) urinary codeine concentration was 988 ng/mL (1,281 ng/mL) and the mean urinary morphine concentration was 105 ng/mL (30).

The aim of this study was to characterize the urinary opiate profile associated with the consumption of 10 unique

poppy seed-containing food products—including the three aforementioned food products that served as the impetus for this research. We hypothesized that the consumption of these three food products—and possibly others—would be associated with codeine-positive/morphine-negative (and, by definition, morphine-to-codeine ratios <2) urine drug test results at a common 300 ng/mL cut-off.

Methods

Participants

Individuals were recruited by flyers, word-of-mouth and participants' referrals. Participants were ages 18–90, inclusive. Exclusion criteria included past-4-week use of codeine, morphine or heroin and allergy or intolerance to poppy seeds.

All participants provided written informed consent. The study protocol (IRB20210956) was approved by the University of Florida Institutional Review Board. Participants were compensated \$50 for their involvement in the study.

Study design and procedure

Ten unique poppy seed-containing food products (and 11 participants) were involved in this study.

Potential participants were requested to avoid consuming poppy seed-containing food products during the 48 h before the study day. The study days began in the morning, and the potential participants were requested to refrain from eating breakfast before reporting to the study site (31).

Upon reporting to the study site, and following the informed consent process, participants provided a baseline (hour 0) unobserved urine specimen for subsequent opiate analysis. The specimen container was marked with the participant's numeric identifier and the date and time of collection and stored at -20°C . Participants then proceeded with the observed consumption of a specific poppy seed-containing food product. See Table I for details on food products and serving sizes.

Participants were then dismissed from the study site with three urine sample collection cups (marked with their numeric identifier), a permanent marker, three zip locking specimen laboratory transport bags and an insulated foam container. They were requested to avoid the consumption opiates or poppy seed-containing food products for the following 12 h. They were instructed to collect urine samples at hours 4, 8 and 12; mark each cup with the collection time; place each cup in a zip locking bag and place the bag in their freezer. They were requested to return their urine samples to the study site, in the insulated container, within 72 h.

Upon receipt, the urine samples were stored at -20°C . Shortly before transport to the laboratory, specimens were thawed; 10 mL from each specimen was pipetted to a test tube, marked with the numeric identifier and the date and time of collection and transported to the laboratory with dry ice cooling.

Specimen analysis

Urine specimens were analyzed at the United States Drug Testing Laboratories (USDTL, Des Plaines, IL, USA).

Table I. Study Product Details and Portion Sizes

Product	Manufacturer-suggested serving size	Study portion size
Lenny and Larry's Lemon Poppy Seed Cookies	0.5 cookie (220 cal)	2 cookies (880 cal)
McCormick Poppy Seeds	Not specified	5 mL
Publix GreenWise Mini Lemon Poppy Seed Muffins	4 muffins (440 cal)	12 muffins (1,320 cal)
Stern's Bakery Poppy Seed Cake	2 oz slice (180 cal)	5 slices (900 cal)
Snack Factory Everything Pretzel Crisps	10 crackers (110 cal)	1 package (770 cal)
Mary's Gone Crackers Super Seed Everything Crackers	12 crackers (150 cal)	1 package (650 cal)
New York Style™ Everything Bagel Crisps	6 chips (130 cal)	1 package (910 cal)
New York™ Everything Flatbreads	1.5 pieces (70 cal)	1 package (630 cal)
Thomas'® Everything Bagels	1 bagel (290 cal)	4 bagel tops (580 cal)
Publix GreenWise Everything Bagels	1 bagel (280 cal)	4 bagel tops (560 cal)

Creatinine

Urinary creatinine concentrations were measured on an Olympus AU640 using the DRI Creatinine-Detect Test (Microgenics, Fremont, CA, USA), an FDA-cleared IVD reagent for the measurement of creatinine concentration in human urine. The assay uses an alkaline picric acid (Jaffe reaction) to form a reddish complex, the absorbance of which is proportional to the creatinine concentration. The assay is linear from 0.78 to 420 mg/dL.

Liquid chromatography–tandem mass spectrometry (LC–MS–MS)

Urine samples were quantified by LC–MS–MS for codeine, morphine, hydrocodone and hydromorphone. Briefly, 100 μ L aliquots of urine were fortified with 50 μ L of an acetonitrile mixture of internal standards (codeine- d_3 , morphine- d_3 , hydrocodone- d_3 and hydromorphone- d_3 ; 0.3 μ g/mL) and 200 μ L of B-One® recombinant β -glucuronidase (Kura Biotech, Los Angeles, CA, USA). The aliquots were incubated at room temperature for 30 min to hydrolyze the glucuronide conjugates. Hydrolysis was monitored by inclusion of a certified control containing morphine-3- β -D-glucuronide with each batch. The specimens were transferred to 2 mL glass autosampler vials and forwarded for LC–MS–MS analysis.

Separation was achieved with an Agilent 1,200 liquid chromatograph (Agilent, Palo Alto, CA, USA) fitted with a Kinetex® phenyl-hexyl column (2.6 μ m, 50 \times 4.6 mm; Phenomenex, Torrance, CA, USA) held at 40°C. Mobile phase A was 10 mmol ammonium formate with 0.05% formic acid, and mobile phase B was 0.05% formic acid in methanol. The solvent program began with 10% mobile phase B and was increased to 100% at 4.5 min and held for 1 min. Mobile phase B was decreased to 10% and allowed to equilibrate for

2 min before the introduction of the next specimen. The flow rate was 600 μ L/min.

Total codeine, morphine, hydrocodone and hydromorphone were detected with a Sciex 5500 Tandem Mass Spectrometer equipped with a Turbo Spray source (Sciex, Concord, Ontario, Canada). Data were acquired using multiple reaction monitoring in positive ionization mode. The curtain gas was 20 psi, Gas 1 was 50 psi, Gas 2 was 60 psi, ion spray voltage was 2,500 V, source temperature was 650°C and scan speed was 10 Da/s. Additional mass spectrometry parameters are listed in Table II.

Analyte concentrations were calculated using a nine-point calibration curve with calibrator concentrations of each analyte ranging from 20 to 5,000 ng/mL. The identification criteria used for this procedure included four components: retention time, signal to noise, baseline resolution and relative ion intensity. The relative retention time of each analyte was required to be within 2.5% of the relative retention time established by the mean of the multipoint calibrators. A signal-to-noise ratio of greater than 3:1 was required of each chromatogram. A minimum of 90% return to baseline was required to consider a peak to be adequately resolved from a co-eluting peak. The mass transition ratios for each analyte were required to be within 20% of the corresponding mass transition ratio that was established by the mean of the multipoint calibrators. The data were processed using Sciex Analyst 1.6.3. software.

The assay was validated according to the recommendations of the Standard Practices for Method Validation in Forensic Toxicology (32). The limit of detection was 10 ng/mL, and the limit of quantitation was 20 ng/mL. The analytic measurement range for these compounds was 20–5,000 ng/mL. Precision and bias determinations were evaluated at control levels of 50, 125 and 800 ng/mL and were all <15% with the exception of the codeine precision measurement for the 50 ng/mL control which was 20%.

Results

Ten unique poppy seed-containing food products were included in this study. Because one of the food products was used twice, 11 participants were enrolled in, and completed, the study.

The data are presented in Table III. Note that the lower limit of quantitation of the assay (20 ng/mL) was an order of magnitude lower than the laboratory's clinico-forensic reporting threshold of 300 ng/mL. For ease of referencing results that are directly responsive to the study question, those for which codeine concentrations \geq 300 ng/mL were coupled with morphine concentrations <300 ng/mL have been bolded. No samples were positive for hydrocodone or hydromorphone, minor metabolites of codeine and morphine, respectively (data not shown) (33).

A total of 44 urine samples were collected, 11 of which were baseline samples. Eleven of the 33 non-baseline samples (33%)—representing six unique food products—were positive for codeine at a cut-off concentration of 300 ng/mL. Six of these samples (18% of all non-baseline samples; 54% of codeine-positive samples)—representing three unique food products—were negative for morphine at a cut-off of 300 ng/mL (and, therefore, were associated with morphine-to-codeine ratios <2).

Table II. Mass Spectrometry Parameters for Opiate Analysis

Analyte	Q1 (m/z)	Q2 (m/z)	DP (V)	CE (V)	CXP (V)	EP (V)
Codeine- <i>d</i> ₃	303.1	165.0	6	53	20	10
	303.1	152.0	6	73	20	10
Codeine	300.1	215.1	100	35	12	10
	300.1	165.0	100	50	12	10
Morphine- <i>d</i> ₃	289.1	153.0	41	57	12	10
	289.1	165.0	41	59	12	10
Morphine	286.0	152.0	90	75	12	10
	286.0	165.0	90	50	12	10
Hydrocodone- <i>d</i> ₃	303.1	199.0	1	45	32	10
	303.1	141.0	1	61	16	10
Hydrocodone	300.1	199.0	100	50	12	10
	300.1	128.0	100	70	10	10
Hydromorphone- <i>d</i> ₃	289.0	185.0	16	45	4	10
	289.0	157.0	16	57	12	10
Hydromorphone	286.1	185.0	100	39	10	10
	286.1	157.0	100	51	8	10

CE = collision energy, CXP = collision cell exit potential, DP = declustering potential, EP = entrance potential, m/z = mass/charge ratio, Q1 = first quadrupole, Q2 = second quadrupole.

The maximum urinary codeine concentration was 1,045 ng/mL, in Participant 8 (hour 8).

Of the six participants with ≥ 1 positive urinary codeine result at the 300 ng/mL cut-off, the maximum codeine concentrations were achieved at hour 4 in Participants 5, 8, 9, 10 and 11 and at hour 8 in Participant 4.

Baseline codeine-negative (at 300 ng/mL), but quantifiable, results were observed in Participant 3 (106 ng/mL) and 6 (156 ng/mL). These results could be attributable to recent, pre-study poppy seed consumption or codeine administration. In each case, the issue was moot, however, because in neither case did post-poppy seed consumption urinary opiate concentrations ever approach the 300 ng/mL cut-off.

Discussion

This study was prompted by a series of three codeine-positive/morphine-negative (300 ng/mL cut-off) forensic urine drug test results in monitored health care professionals who were contractually obligated to refrain from unauthorized opiate use. In each case, the positive drug test result triggered a reflex IME to assess for codeine abuse or unauthorized use. In each case, the contractee denied the intentional administration of codeine and attributed their positive drug test result to the consumption of a unique poppy seed-containing food product—the so-called “poppy seed defense.” In no case, did the contractee exhibit indicia of opiate abuse. In one case, a contractee was administered—and passed—a polygraph examination focused on intentional opiate administration.

The present study examined 10 poppy seed-containing food products, including the three poppy seed-containing food products implicated in the aforementioned cases, for evidence of an association of these products with codeine-positive/morphine-negative urine drug test results.

Two of the implicated food products tested in this study—Publix Greenwise® Poppy Seed Muffins and Thomas® Everything Bagels—were indeed associated with codeine-positive/morphine-negative urine drug test results, thereby supporting the contractees’ poppy seed defense. The third product, New York Style™ Everything Bagel Crisps, did not fit this urinary opiate profile. The study participant

who consumed the same branded product produced a single codeine-positive result (301 ng/mL); however, at all non-baseline time points, the morphine-to-codeine ratio was >3 . These results do not support the contractee’s poppy seed defense, but neither do they definitively disprove it. The study results associated with this product could be explainable by variations in opiate content between sources, or even within batches, of poppy seeds (9, 16, 34) or, hypothetically, by cytochrome P-450 (CYP) 2D6 ultra-rapid metabolizer (UM) status of Participant 8 (35).

In the six participants who produced one or more codeine-positive results at the 300 ng/mL cut-off, the maximum urinary codeine concentrations were achieved at hour 4 in five participants and at hour 8 in one participant. Of note, however, in Participant 4, urinary codeine concentration remained >300 ng/mL and morphine-to-codeine ratios remained <2 in the final, hour 12, urine sample.

This study confirms and extends the findings of three previous publications that consumption of poppy seed-containing food products may result in urinary opiate profiles that were long thought to be indicative of codeine administration (28–30). Specifically, previous guidance, suggesting that urinary codeine >300 ng/mL coupled with a morphine-to-codeine ratio <2 evidences codeine consumption, is incorrect. Following poppy seed consumption, urinary codeine concentrations may exceed 300 ng/mL and, more importantly, may exceed urinary morphine concentrations. An epiphenomenon is that, when urinary codeine concentrations are present at clinically relevant concentrations (i.e., hundreds of ng/mL), urinary morphine may be reported as negative. An important note, based on this and previously published research, is that, with poppy seed consumption, maximum urinary codeine concentrations are unlikely to exceed 1,300 ng/mL.

This study has some limitations. Portion sizes used in this study were larger, in most cases by multiples, than suggested serving sizes listed on the nutrition labels. Our rationale for this was 2-fold. First, we sought to maximize the potential for identifying poppy seed-containing products capable of producing codeine concentrations exceeding the 300 ng/mL threshold. Second, people often fail to comprehend, or adhere to, serving size suggestions, and we sought

Table III. Urine Drug Test Results following the Consumption of Poppy Seed-Containing Food Products

Subject	Food product	Time (h)	Creatinine (mg/dL)	I.C-MS-MS (ng/mL)		
				Codeine	Morphine	Morphine:codeine
1	Lenny and Larry's Lemon Poppy Seed Cookies	0	53	—	—	
		4	96	135	40	0.30
		8	93	66	22	0.33
		12	152	79	21	0.26
2	Lenny and Larry's Lemon Poppy Seed Cookies	0	115	—	—	
		4	136	43	46	1.07
		8	184	39	38	0.97
		12	240	33	28	0.24
3	McCormick Poppy Seeds	0	100	106	—	
		4	89	43	—	
		8	162	44	—	
		12	208	100	—	
4	Publix GreenWise® Mini Lemon Poppy Seed Muffins	0	106	—	—	
		4	106	136	—	
		8	191	1,045	46	0.04
		12	148	526	35	0.07
5	Stern's Poppy Seed Cake	0	88	—	—	
		4	98	634	1,661	2.7
		8	130	571	1,923	3.4
		12	163	538	1,248	2.3
6	Snack Factory "Everything" Pretzel Crisps	0	129	156	—	
		4	38	163	103	0.63
		8	90	149	123	0.82
		12	58	53	43	0.81
7	Mary's Gone Crackers Super Seed "Everything" Crackers	0	128	—	—	
		4	82	—	71	
		8	37	—	—	
		12	35	—	—	
8	New York Style™ Everything Bagel Crisps	0	170	—	—	
		4	184	301	1,184	3.93
		8	185	280	965	3.45
		12	244	136	507	3.73
9	New York™ Everything Flatbreads	0	20	—	—	
		4	91	314	1,456	4.64
		8	148	136	528	3.88
		12	177	93	439	4.72
10	Thomas'® Everything Bagels	0	28	—	—	
		4	75	808	24	0.03
		8	77	347	—	<0.06
		12	51	282	—	<0.07
11	Publix GreenWise® Everything Bagels	0	204	—	—	
		4	249	967	60	0.06
		8	186	531	21	0.04
		12	172	232	—	<0.09

Results in which codeine concentrations >300 ng/mL were coupled with morphine concentrations >300 ng/mL have been bolded.

to generate data reflective of this reality (36). It is notable, therefore, that the single urinary codeine concentration that exceeded 1,000 ng/mL was associated with the consumption of three suggested serving sizes. This was a single "dose" study. Had participants consumed these products multiple times per day or over multiple days, we expect that we might have seen more codeine-positive (and, perhaps, morphine-negative) samples (21). Finally, this study was not designed to estimate the prevalence of poppy seed-containing food products associated with codeine-positive/morphine-negative urine drug test results. In this regard, it is important to note that, although 3 of the 10 products studied were associated with codeine-positive/morphine-negative urine drug test results, two of these products were selected based on

self-reports of individuals who produced such forensic test results and implicated these products in their poppy seed defense, thereby introducing a sort of (intentional) sampling bias in product selection. A prevalence study would involve analyses of a large number of poppy seed-containing food products, the identification of high-codeine (and high codeine-to-morphine) products and a human urine drug testing study of these selected products.

Conclusions

Three tested poppy seeding-containing food products were associated with urinary opiate profiles in which codeine, but not morphine, reached a 300 ng/mL threshold. This

adds to a small literature demonstrating that urinary codeine concentrations (at least those below $\sim 1,300$ ng/mL) and morphine-to-codeine ratios cannot reliably distinguish poppy seed consumption from codeine administration. In assessing the credibility of poppy seed defenses, therefore, it may be useful to interpret urine drug test results in the context of the specific food product; the serving size and pattern of consumption; the timing of consumption relative to urine sample collection and, if feasible, poppy seed analysis.

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Data availability statement

The data underlying this article is available in the article.

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Letter to the Editor



Interpreting Urine Drug Test Results in the Context of Chronic Opioid Analgesic Therapy and Poppy Seed Consumption

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Dear Editor,

Argoff and colleagues' article [1] illuminates the need for a scientifically supported consensus on appropriate use of urine drug monitoring in chronic opioid analgesic management. We are writing to highlight an additional factor of importance in drug monitoring that supports the use of definitive testing (gas chromatography-mass spectrometry [GC-MS], liquid chromatography-mass spectrometry [LC-MS], or liquid chromatography tandem-mass spectrometry [LC-MS/MS]) as best practice. Specifically, dietary consumption of poppy seeds may limit the ability of traditional enzyme immunoassay urine drug screens (UDS) to detect medication diversion or overuse in the context of chronic opioid prescription management.

Consumption of poppy seeds has been long reported to result in true opiate positives on urine drug screens [2]. The influence of poppy seed consumption on UDS results is especially relevant in the setting of chronic opioid management, where the screening and confirmation cutoffs are much lower than in the setting of workplace drug testing [3]. The trust underlying therapeutic relationships between patients and providers depends on reliable measures of opioid-use compliance, a notion that is central to the recommendations proffered by Argoff et al. [1].

Literature on this topic is difficult to apply clinically for at least two reasons. First, seed contamination by opiate alkaloids is thought to have varied in recent decades, with changes in harvesting methods favoring an increase in concentration, but increasing scrutiny by regulatory agencies more recently favoring a decrease [4]. This may limit the clinical utility of much of the original research on this subject, which dates back to the 1980s [4]. Second, the opiate alkaloid content of poppy seeds varies widely by both source and the methods used to prepare the seeds for consumption, such as baking [4]. This variability limits the clinical applicability of the literature to any individual patient. Rather, to preserve trust with their patients, clinicians attempting to interpret UDS in the context of poppy seed consumption are more likely to be interested in whether a realistic dose of commercially available, baked poppy seeds, such as the quantity present in "one poppy seed muffin," could plausibly result in a positive UDS.

In light of this, we hypothesized that the consumption of a realistic dose of poppy seeds would result in a true positive opiate UDS and could therefore complicate UDS interpretation in the setting of chronic opioid analgesic therapy. To aid in such interpretation, with approval from the Washington State University institutional

review board, we sought to provide a straightforward, clinically relevant two-measurement urine elimination profile for morphine and codeine following the consumption of poppy seeds. Seventeen gainfully employed, opioid-naïve adult volunteers were recruited from the Northwest Spine and Pain Medicine and Northwest Center for Regenerative Medicine employee pool. All participants provided written consent to participate with the understanding that no compensation would be provided. For the purposes of this study, opioid naivety was defined as avoidance of opioid medication or drug use for 30 days prior to participation. Participants also abstained from poppy seed consumption of any kind for 2 weeks before the study. After providing a negative baseline urine specimen, the time was documented and participants consumed a single poppy seed muffin from Costco, a large chain grocery warehouse. Per Costco's website, poppy seed muffins have an average mass of 156 grams. Bakery employees provided information on the quantity of poppy seeds included in a complete batch of muffins, and from this information, we estimate that on average, a single muffin contained roughly 7.6 grams of poppy seeds.

The participants provided one urine specimen between 4 and 6 hours after poppy seed consumption ($t=4$ to $t=6$) and a second specimen between 21 and 25 hours after consumption ($t=21$ to $t=25$). Urine specimens were analyzed by enzyme immunoassay (EIA), and results were confirmed by liquid chromatography tandem-mass spectrometry (LC-MS/MS). The urine samples were screened by Thermo Scientific's DRI Opiate Assay on a Mindray BS-480. The qualitative cutoff for the homogeneous EIA was 300 ng/mL for opiates in general. The specificity per the package insert is listed as 300 ng/mL, 340 ng/mL, 270 ng/mL, and 150 ng/mL for morphine, morphine-3-glucuronide, morphine-6-glucuronide, and codeine, respectively. Urine opiate concentrations were then confirmed by LC-MS/MS and corrected for creatinine. The creatinine-corrected results are reported as the concentration of opiate alkaloid per gram of creatinine. Metabolites, including morphine-3 glucuronide, morphine-6-glucuronide, and codeine-6-glucuronide values, were assumed to be included in the LC-MS/MS results. Our lab extraction methodology undergoes a hydrolysis step with an enzymatic efficiency of >90% for the aforementioned metabolites. Testing for sulfonated morphine and sulfonated metabolites was not performed.

All specimens screened positive for opiates by EIA at $t=4$ to $t=6$ hours, and 53% screened positive for opiates at $t=21$ to $t=25$ hours. Mean codeine and morphine concentrations by LC-MS/MS at $t=4$ to $t=6$ hours were 987.5 (663.9) $\mu\text{g/g}$ creatinine and 105.3 (85.59) $\mu\text{g/g}$ creatinine, respectively (Figure 1). At $t=21$ to $t=25$ hours, codeine remained detectable in the urine of 13 of the 17 participants by LC-MS/MS (Figure 1A).

These results suggest that in the setting of opioid prescription management, acute consumption of a realistic

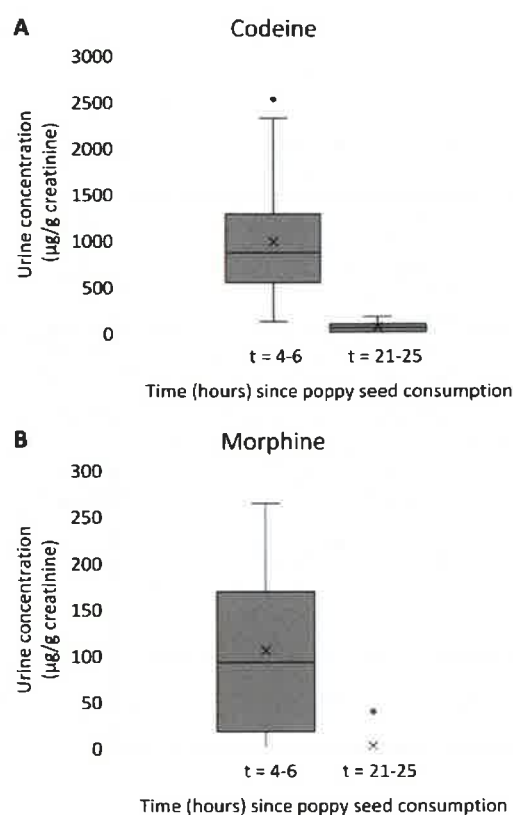


Figure 1. Creatinine-corrected urine codeine and morphine concentrations following consumption of a poppy seed muffin. The boxplots show in aggregate the creatinine-corrected urine concentrations of (A) codeine and (B) morphine measured by LC-MS/MS for 17 participants following consumption of a poppy seed muffin. "x" represents the mean for each plot. Specimens were collected 4–6 hours ($t=4$ –6 hours) and 21–25 hours ($t=21$ –25 hours) after consumption. (A) Mean concentrations for codeine at $t=4$ –6 hours and $t=21$ –25 hours were 987.5 (663.9) $\mu\text{g/g}$ creatinine and 66.08 (53.37) $\mu\text{g/g}$ creatinine, respectively. (B) Mean concentrations for morphine at $t=4$ –6 and $t=21$ –25 hours were 105.3 (85.59) $\mu\text{g/g}$ creatinine and 2.308 (9.518) $\mu\text{g/g}$ creatinine, respectively. Prior to eating a muffin, all participants provided a negative urine specimen.

dose of poppy seeds is a viable reason for an opiate-positive UDS. Whether intentionally or inadvertently, patients may mask medication diversion or overuse by consuming poppy seeds prior to providing urine specimens for drug screening. Confirmatory methods such as LC-MS/MS are indicated for more reliable interpretation of UDS results, for such testing can distinguish the contributing drugs or metabolites. A limitation of confirmatory testing in this context is that it may not provide benefit if a patient is truly prescribed morphine or codeine rather than a synthetic or semisynthetic opioid, which would be distinguished from poppy seed consumption by LC-MS/MS. Moreover, for patients prescribed other opioids, it may be difficult to determine whether morphine or codeine in the urine is more consistent with poppy seed consumption or use of unprescribed medications. Despite these limitations, confirmatory testing

remains important in that it recognizes an inconsistency that may be undetectable by UDS alone, thereby enabling subsequent provider–patient discussion.

Distinguishing poppy seed consumption from use of unprescribed medication with confirmatory testing is further complicated by the wide variation in the morphine and codeine content of poppy seeds. Much of the literature on this topic suggests that a ratio of morphine to codeine in the urine of less than 2 is inconsistent with poppy seed consumption [5] and more likely to suggest codeine use [6]. However, while higher concentrations of morphine than codeine in the urine are typically emphasized after poppy seed consumption [2, 5], our results demonstrate that this ratio is not always applicable. Clinical UDS results demonstrating this pattern should be interpreted with care. Further research comparing the urine concentrations of morphine and codeine in patients prescribed morphine and codeine with the urine concentrations of these substances in patients consuming poppy seeds may provide some guidance as to how to interpret urine drug testing results in this context but may be limited by the wide variation in the alkaloid content of poppy seeds.

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NORTHWEST
SPINE & PAIN MEDICINE

January 25, 2023

CAPT Erin Wilfong, Ph.D., USN
Director, Office of Drug Demand Reduction
Office of Force Resiliency
Office of the Under Secretary of Defense (Personnel and Readiness)
Pentagon 5A668

Dear Dr. Wilfong:

I, Jamie L. Lewis, M.D., grant permission for you, Erin R. Wilfong, Ph.D. to share the raw data from a poppy seed muffin study published in the Pain Management Journal, Volume 22, Issue 11, November 2021, Pages 2776-2778, <https://doi.org/10.1093/pm/pnab082>, with the Department of Defense.

I, Jamie L. Lewis, M.D., attest that the raw data provided that details the levels of codeine and morphine after ingestion of poppy seed muffins is the raw data used for submission of a 2021 Letter to the Editor in Pain Management.

Codeine and morphine calculations were in units of ng/ml and samples were collected at (A) 0 hr. (before ingestion of poppy seed muffin), (B) 4-6 hrs. (after ingestion), and (C) 21-24 hrs. (after ingestion).

Sincerely,

Jamie L. Lewis, M.D.
Board Certified: Physical Medicine and Rehabilitation
Board Certified: Pain Medicine
Clinical Assistant Professor: WSU Elson S. Floyd College of Medicine

SID	Sample #	Collection Time	Screen_Urine_Creatinine	Screen_Opiate	Conf_Morphine	Conf_Codeine	Weight	Gender
102057901	A	9:05	196.2 NEG		0	0	99	99
	B	15:00	248.6 POS		176.8	1654.7		
	C	8:00	216.5 POS		0	204.8		
102057902	A	9:04	36.7 NEG		0	0	99	99
	B	14:17	295.8 POS		0	371.6		
	C	8:37	41 NEG		0	50.3		
102057903	A	7:48	182 NEG		0	0	148	1
	B	14:41	308.5 POS		608.2	2680.3		
	C	7:13	98.7 POS		0	91		
102057904	A	7:10	240 NEG		0	0	179	0
	B	14:09	289.2 POS		765.2	1493.9		
	C	7:06	166.4 POS		65.3	136.8		
102057905	A	8:40	93.4 NEG		0	0	150	0
	B	14:50	121.3 POS		122.3	1329.8		
	C	9:15	59.6 NEG		0	56.8		
102057906	A	8:55	271.2 NEG		0	0	205	0
	B	15:00	295.8 POS		242.5	1709.8		
	C	8:45	170.4 NEG		0	0		
102057907	A	9:30	148.8 NEG		0	0	115	1
	B	14:00	198.8 POS		498.4	2105.2		
	C	11:00	130 POS		0	58.4		
102057910	A	8:45	168.9 NEG		0	0	190	1
	B	14:05	67.3 POS		116.5	881.1		
	C	10:30	92.6 NEG		0	0		
102057911	A	9:58	31.5 NEG		0	0	147	1
	B	14:19	13 POS		0	328.3		
	C	9:28	138 POS		0	93.7		
102057912	A	8:01	24.3 NEG		0	0	160	1
	B	14:15	238.2 POS		0	340.5		
	C	7:48	17.8 NEG		0	0		
102057913	A	9:36	195.7 NEG		0	0	185	0
	B	14:51	238.2 POS		190.2	1152.7		
	C	9:05	231 POS		0	65.1		
102057914	A	7:30	159.5 NEG		0	0	240	0
	B	15:15	204.1 POS		188.6	1430.9		
	C	8:30	93.2 NEG		0	53.3		
102057915	A	7:26	254.2 NEG		0	0	200	1
	B	14:06	78.5 POS		114.8	812.8		
	C	10:15	187.1 NEG		0	0		
102057916	A	8:04	274.5 NEG		0	0	190	1
	B	15:18	244.8 POS		322.6	1463.2		
	C	9:23	102.7 NEG		0	55.5		
102057917	A	9:34	260.3 NEG		0	0	125	1
	B	15:36	200.1 POS		71.5	2537.3		
	C	9:32	235.6 POS		0	363		
102057918	A	10:30	47.1 NEG		0	0	160	1
	B	15:29	35 POS		0	522.8		
	C	7:40	281.6 POS		0	149.6		
102057925	A	7:32	68.1 NEG		0	0	143	1
	B	14:54	41.7 POS		68.7	967.8		
	C	8:04	48 POS		0	84.9		

T0 POS 0%
T4 POS 100%
T24 POS 47%

Female=1
Male=0
99=not answered