

Letters

RESEARCH LETTER

Substances in Counterfeit Prescription Pills Seized by Law Enforcement, 2017-2022

Counterfeit prescription pills are designed to replicate legitimate pharmaceutical pills in appearance and pharmacologic effects. However, the pharmacology of the active ingredients may be different, and the dose can be uncertain or irregular.



Supplemental content

In addition, counterfeit prescription pills can be contaminated with fentanyl and, more recently, with xylazine. Thus, counterfeit prescription pills have been associated with adverse outcomes, including fatal overdose.^{1,2} Counterfeit drugs obtained during law enforcement seizures undergo comprehensive confirmatory toxicology testing.

Results are generally not shared with the public. This descriptive study reports substances identified during testing of counterfeit prescription pills seized by law enforcement in Rhode Island; such documentation can help characterize the local street market.

Methods | Data were obtained from law enforcement drug seizures reported by the Rhode Island forensic drug chemistry laboratory from January 2017 to December 2022. The number of pills obtained during seizure incidents range from a single pill to thousands; the numbers of incidents and of pills obtained cannot be reported. A representative sample was tested from each incident. If pills of 1 imprint or type were obtained, 1 pill was tested. If there were multiple imprints or types, then 1 of each imprint or type was analyzed. Pills were

Table 1. Laboratory-Identified Counterfeit Pills by Markings in Rhode Island, 2017-2022^a

Category, pill marking	Counterfeit pills tested, No. (%)						Total
	2017	2018	2019	2020	2021	2022	
Alprazolam							
B 707	0	0	0	1 (1.4)	43 (32.8)	26 (41.9)	70 (22.4)
G 372 2	1 (7.7)	0	2 (7.4)	2 (2.9)	2 (1.5)	3 (4.8)	10 (3.2)
GG 249	3 (23.1)	0	1 (3.7)	4 (5.7)	4 (3.1)	1 (1.6)	13 (4.2)
R 0 3 9	0	0	5 (18.5)	21 (30.0)	20 (15.3)	4 (6.5)	50 (16.0)
S 90 3	4 (30.8)	0	8 (29.6)	26 (37.1)	48 (36.6)	18 (29.0)	104 (33.3)
V 2090	4 (30.8)	0	0	0	1 (0.8)	5 (8.1)	10 (3.2)
XANAX	1 (7.7)	9 (100)	11 (40.7)	16 (22.9)	13 (9.9)	5 (8.1)	55 (17.6)
Total, No.	13	9	27	70	131	62	312
Amphetamine/dextroamphetamine							
AD 30	2 (100)	0	6 (85.7)	16 (33.3)	33 (42.3)	20 (51.3)	77 (44.3)
b 974 30	0	0	0	9 (18.8)	29 (37.2)	13 (33.3)	51 (29.3)
dp 30	0	0	1 (14.3)	3 (6.3)	8 (10.3)	5 (12.8)	17 (9.8)
E 404	0	0	0	20 (41.7)	8 (10.3)	1 (2.6)	29 (16.7)
Total, No.	2	0	7	48	78	39	174
Clonazepam							
R 34	0	0	1 (50.0)	0	0	0	1 (50.0)
TEVA 832	0	0	1 (50.0)	0	0	0	1 (50.0)
Total	0	0	2	0	0	0	2
Oxycodone							
A 215	17 (29.8)	32 (45.7)	32 (32.3)	18 (21.4)	36 (15.9)	21 (14.0)	156 (22.7)
M 30	26 (45.6)	25 (35.7)	27 (27.3)	33 (39.3)	153 (67.7)	105 (70.0)	369 (53.8)
V 4812	9 (15.8)	11 (15.7)	27 (27.3)	25 (29.8)	28 (12.4)	15 (10.0)	115 (16.8)
Other	5 (8.8)	2 (2.9)	12 (12.1)	8 (9.5)	9 (4.0)	9 (6.0)	45 (6.6)
Multiple listed	0	0	1 (1.0)	0	0	0	1 (0.1)
Total, No.	57	70	99	84	226	150	686
Unknown							
200	0	0	1 (50.0)	0	0	0	1 (50.0)
Fragments (unmarked)	0	0	1 (50.0)	0	0	0	1 (50.0)
Total, No.	0	0	2	0	0	0	2

^a Pills markings are the imprint or text found on a pill.

Table 2. Twelve Substances Most Commonly Found in Laboratory-Identified Counterfeit Pills by Pill Type for Alprazolam, Amphetamine/Dextroamphetamine, and Oxycodone in Rhode Island, 2017-2022

Category, substance	Active substances, No. (%)						Total
	2017	2018	2019	2020	2021	2022	
Alprazolam							
Total pills, No.	13	9	27	70	131	62	312
Etizolam ^a	11 (84.6)	5 (55.6)	4 (14.8)	27 (38.6)	63 (48.1)	8 (12.9)	118 (37.8)
Clonazolam ^a	0	0	2 (7.4)	19 (27.1)	45 (34.4)	35 (56.5)	101 (32.4)
Flualprazolam ^a	0	1 (11.1)	13 (48.1)	19 (27.1)	14 (10.7)	6 (9.7)	53 (17.0)
Cocaine	0	0	0	4 (5.7)	21 (16.0)	13 (21.0)	38 (12.2)
Caffeine	0	0	0	5 (7.1)	22 (16.8)	10 (16.1)	37 (11.9)
Methamphetamine	0	0	0	1 (1.4)	11 (8.4)	10 (16.1)	22 (7.1)
Alprazolam	7 (53.8)	6 (66.7)	4 (14.8)	0	0	0	17 (5.4)
Lidocaine	0	0	0	0	15 (11.5)	2 (3.2)	17 (5.4)
Flubromazolam ^a	2 (15.4)	1 (11.1)	3 (11.1)	3 (4.3)	4 (3.1)	2 (3.2)	15 (4.8)
Bromazolam ^a	0	0	0	0	2 (1.5)	12 (19.4)	14 (4.5)
Fentanyl	2 (15.4)	0	0	0	3 (2.3)	3 (4.8)	8 (2.6)
Tramadol	0	0	0	0	4 (3.1)	4 (6.5)	8 (2.6)
Amphetamine/dextroamphetamine^b							
Total pills, No.	2	0	7	48	78	39	174
Methamphetamine	1 (50.0)	0	7 (100)	46 (95.8)	76 (97.4)	34 (87.2)	164 (94.3)
Caffeine	0	0	2 (28.6)	16 (33.3)	60 (76.9)	26 (66.7)	104 (59.8)
Amphetamine	0	0	0	3 (6.3)	9 (11.5)	8 (20.5)	20 (11.5)
Eutylone	0	0	0	3 (6.3)	4 (5.1)	0	7 (4.0)
Cocaine	0	0	0	0	1 (1.3)	1 (2.6)	2 (1.1)
MDMA	0	0	0	0	2 (2.6)	0	2 (1.1)
Trazodone	1 (50.0)	0	0	0	0	0	1 (0.6)
Oxycodone							
Total pills, No.	57	70	99	84	226	150	686
Fentanyl	44 (77.2)	59 (84.3)	90 (90.9)	79 (94.0)	222 (98.2)	149 (99.3)	643 (93.7)
Tramadol	3 (5.3)	4 (5.7)	8 (8.1)	10 (11.9)	95 (42.0)	52 (34.7)	172 (25.1)
Acetaminophen	16 (28.1)	19 (27.1)	32 (32.3)	20 (23.8)	44 (19.5)	31 (20.7)	162 (23.6)
Xylazine	0	0	12 (12.1)	6 (7.1)	59 (26.1)	58 (38.7)	135 (19.7)
Diphenhydramine	0	0	24 (24.2)	25 (29.8)	68 (30.1)	14 (9.3)	131 (19.1)
Para-fluorofentanyl	0	0	0	0	57 (25.2)	67 (44.7)	124 (18.1)
Lidocaine	0	0	6 (6.1)	7 (8.3)	52 (23.0)	25 (16.7)	90 (13.1)
Cocaine	0	0	8 (8.1)	6 (7.1)	46 (20.4)	24 (16.0)	84 (12.2)
Caffeine	0	0	9 (9.1)	12 (14.3)	33 (14.6)	17 (11.3)	71 (10.3)
Other fentanyl analogs and U-49900 ^c	15 (26.3)	16 (22.9)	20 (20.2)	4 (4.8)	1 (0.4)	1 (0.7)	57 (8.3)
Heroin	1 (1.8)	6 (8.6)	2 (2.0)	10 (11.9)	14 (6.2)	23 (15.3)	56 (8.2)
Acetyl fentanyl	1 (1.8)	5 (7.1)	14 (14.1)	1 (1.2)	8 (3.5)	13 (8.7)	42 (6.1)

Abbreviation: MDMA, 3,4-methylenedioxyamphetamine.

^a Etizolam, clonazolam, flualprazolam, flubromazolam, and bromazolam are novel benzodiazepines not approved by the US Food and Drug Administration for use in the US.

^b Only 7 substances were detected in counterfeit amphetamine/dextroamphetamine pills.

^c From 2017 to 2020, fentanyl analogs were detected in 30 pills without fentanyl present. Carfentanil was detected 11 times from 2018 to 2020.

characterized based on markings. Any pill that yielded a result other than the expected active ingredients as marked was considered counterfeit and included in the data set. Testing of each counterfeit pill was recorded by year based on the date results were finalized by the laboratory, which varied from the date of seizure by weeks to 6 to 9 months. The largest drug seizures and interstate investigations have evidence tested at Drug Enforcement Agency laboratories and were not included. Testing was performed using comprehensive gas

chromatography/mass spectrometry screening. Commercially available and in-house reference libraries were used for initial screening, with positive identification of controlled substances made after comparison with certified reference standards when analyzed within 24 hours under identical conditions. We characterized the type of counterfeit prescription pills tested and determined the presence of active substances in counterfeit pills. Basic descriptive statistical analysis was conducted using Microsoft Excel, version 16.82.

Results | There were 1176 counterfeit pills tested. Based on the markings indicating the expected active substance, counterfeit pills were classified into 5 categories: oxycodone (n = 686), alprazolam (n = 312), amphetamine/dextroamphetamine (n = 174), clonazepam (n = 2), and unknown (n = 2) (Table 1). Substances identified were generally in the same class as the markings on the pills (Table 2). Fentanyl was not detected in any counterfeit amphetamine/dextroamphetamine pills. In counterfeit oxycodone pills, fentanyl analogues were present without fentanyl in 30 of 310 pills (9.6%) from 2017 to 2020. However, by 2022, 149 of 150 pills (99.3%) contained fentanyl and 67 (44.7%) contained para-fluorofentanyl as the dominant fentanyl analogue. Counterfeit alprazolam pills contained 9 novel benzodiazepines not approved in the US. Eight counterfeit alprazolam pills (2.6%) contained fentanyl. Of 137 pills containing xylazine, 135 (98.5%) were counterfeit oxycodone pills. Xylazine was detected with fentanyl in 136 of 137 pills (99.3%).

Discussion | Although the substances identified in counterfeit prescription pills seized by law enforcement in Rhode Island generally were in the same class as the markings on the pills, fentanyl and xylazine were increasingly found in counterfeit oxycodone, and some counterfeit alprazolam contained fentanyl and unapproved benzodiazepines. If counterfeit pills contain novel substances or pharmacologically different active ingredients (ie, dose, duration of effects) than the expected substance, management of withdrawal and treatment of substance use can be more difficult.

Most knowledge of counterfeit pills comes from community drug-checking programs, such as the use of fentanyl test strips, which have methodologic limits, or high-level government reports without comprehensive toxicology included. Comprehensive laboratory testing is an important complement to identify the range of substances found in counterfeit pills.^{3,4} Study limitations include lack of quantitative testing and information on the numbers of drug seizures and pills tested. The exclusion of federal cases, limited number of pills per seizure tested, and data limited to Rhode Island suggest the results may not be representative or generalizable. Who used counterfeit pills and whether use was associated with adverse events is not known. Given the rapidly evolving nature of the drug supply, these data may not represent the current market. The disclosure of data from other states in a timely fashion is needed to inform public health interventions.

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