Changing Composition of Street Drugs in Latin America and The Risk of Fentanyl

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Illicit Drugs are Rarely Pure

Diluents

- Inert substances added to illicit drugs to bulk out the drug and decrease the amount of active ingredient.

Adulterants

- Pharmacologically active ingredients added to illicit drugs to give bulk, complement or enhance the effects, or produce synergistic effects

Morbidity Perspective

Chemical Profile of Cocaine Samples in Sao Paulo – Nov. 2014 (1144 samples)

Adulterants	Crack	HCl
Phenacetin	60%	6%
Aminopyrine	25%	1%
Levamisole	1%	50%

Chemical Profile of Cocaine Samples in the Southern Cone - 2012

	Brazil	Chile	Paraguay	Uruguay	Argentina
No. Samples Tested:	40	20	20	9	15
Average Purity (Range)	(29.7% -89.6%)	(15.8% - 92.2%)	(4.6% – 84.6%)	(35.8% - 82.4%)	(17.4% - 18.4%)
Number (%) with Adulterants	30 (75%)	8 (40%)	17 (85%)	9 (100%)	15 (100%)
Phenacetin	26 (65%)	1 (5%)	13 (65%)	2 (22%)	15 (100%)
Levamisole	1 (3%)		1 (5%)	2 (22%)	
Other	3 (7%)	7 (35%)	3 (15%)	5 (55%)	
Aminopyrine + Phenacetin	16 (40%)	-	8 (40%)	1 (11%)	

Drug Adulterant Testing Results

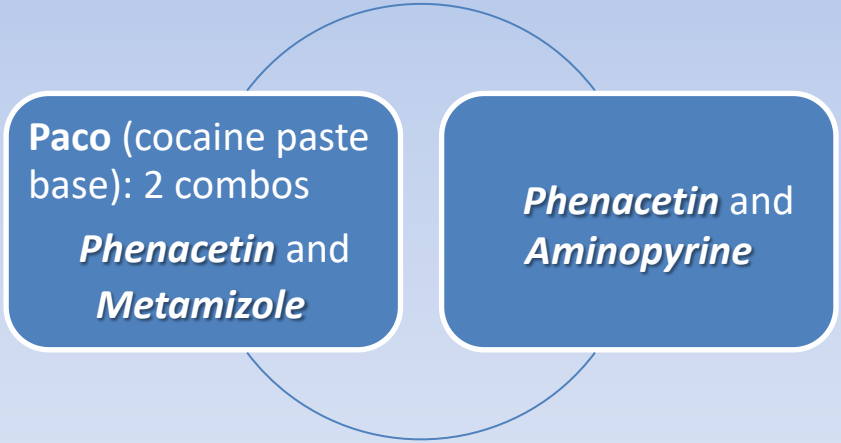
Peru

PCB (cocaine paste base): 1 combo

Phenacetin

Drug Adulterant Testing Results

Argentina



Ecuador

New street drug called **"H"**

-- Heroin cut with ***diltiazem***, ***phenacetin***, and ***cocaine***

Cocaine HCl

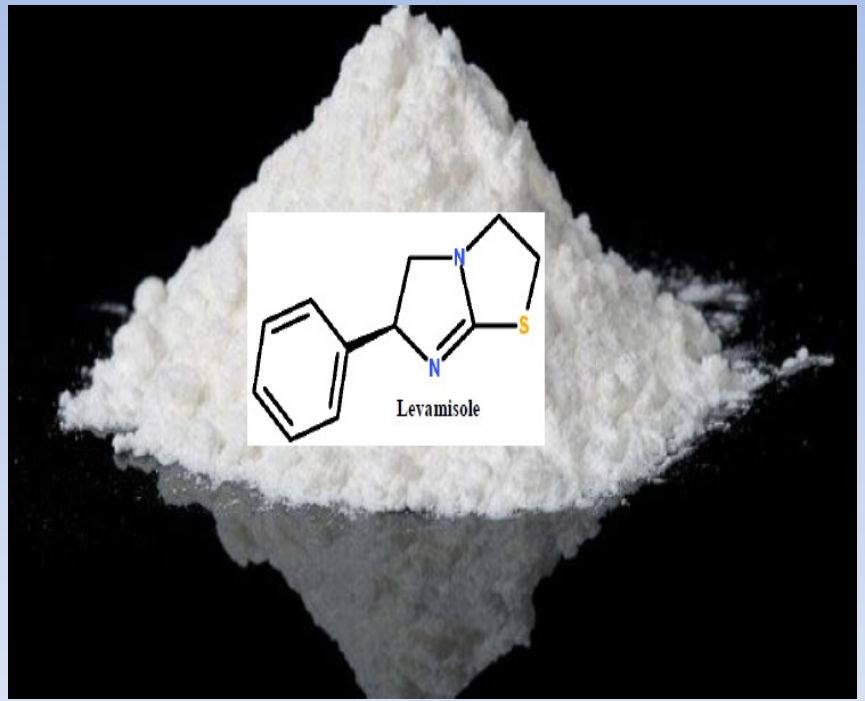
-- cut with ***levamisole*** and ***lidocaine***

Drug Adulterant Testing Results

Honduras

Cocaine HCl

Levamisole



Benzocaine

- Benzocaine, a local anesthetic, is often used as a cocaine adulterant
- Methemoglobinemia – ***reduced oxygen levels in blood****
- ***South Africa*** crack substitute: Benzocaine + Phenacetin
- ***Honduras*** crack substitute: Benzocaine + Levamisole

*Phillips et al. Cardiac complications of unwitting co-injection of quinine/quinidine with heroin in an intravenous drug user. J Gen Intern Med 2012; 27(12): 1722-5.

Levamisole is Toxic

Levamisole is a veterinary pharmaceutical used primarily to treat worm & parasitic infestations in livestock.

It has also been used experimentally and historically to treat various autoimmune disorders and cancers in humans.

Withdrawn from the Canadian (2003) and USA (1999) markets due to **toxicity.**

Results in a decrease of white blood cells that can **lower immunity and increase opportunist infections (e.g., CV-19).**

Levamisole is Toxic

- An accumulating body of literature has described a clear link between levamisole-adulterated cocaine use and the occurrence of **neutropenia** and **agranulocytosis, vasculitis, retiform purpura** and other forms of **skin necrosis, vasculopathy, arthralgia,** and **leukoencephalopathy***
- Chronic exposure to levamisole-contaminated cocaine is associated with **broad cognitive and neuroanatomical impairments** (e.g., executive function deficits and pronounced thinning of the lateral prefrontal cortex)**
- Levamisole is also linked to **neurotoxic effects** with regular use of levamisole-contaminated cocaine**

*Brunt TM, et al, Adverse effects of levamisole in cocaine users: a review and risk assessment. Arch. Toxicol. 91, 2303-2313 (2017).

*Lee KC, et al, Complications associated with use of levamisole-contaminated cocaine: an emerging public health challenge. Mayo Clin. Proc. 87, 581-586 (2012).

**Vonmoos M, et al, Cognitive and neuroanatomical impairments associated with chronic exposure to levamisole-contaminated cocaine. Translational Psychiatry (2018)8:235.

Levamisole: Role as an Adulterant

- It is suggested that levamisole increases the number of D1 dopamine receptors in the brain and potentiates the euphoria, psychostimulant effects, and intense “high” of cocaine.*

- Levamisole has at times been detected in up to 79% of the cocaine street supply in the U.S. and overseas.

*Hofmaier T, et al, Aminorex, a metabolite of the cocaine adulterant levamisole, exerts amphetamine like actions at monoamine transporters. Neurochem Int (2014) Jul; 73(100): 32-41.

*Tallarida CS, et al, Levamisole and cocaine synergism: a prevalent adulterant enhances cocaine’s action in vivo. Neuropharmacology, 2014 Apr;79:590-5.

*Katarzyna M, et al, Acute coronary syndrome after levamisole-adulterated cocaine abuse. Journal of Forensic & Legal Medicine, 21 (2014) 48-52.

*Larocque A & Hoffman RS, Levamisole in cocaine: Unexpected news from an old acquaintance. Clin Toxicol, 2012 Apr;50(4):231-41.

Phenacetin

- Phenacetin induces hemolytic anemia, a disorder in which red blood cells are destroyed prematurely, affecting oxygen transfer*
- Respiratory depression & cardiac arrest may ensue from lack of oxygen
- The chronic use of phenacetin is associated with nephrotoxicity and analgesic nephropathy (kidney damage)**
- In one prospective study, phenacetin was associated with an increased risk of death due to renal diseases, cancers, and cardiovascular diseases***

*Millar J, et al, Phenacetin-induced hemolytic anemia. Can Med Assoc J (1972) Apr 8; 106(7): 770–775

** C. Cole, Liverpool John Moores University, Centre for Public Health, CUT: A Guide to Adulterants, Bulking Agents and Other Contaminants Found in Illicit Drugs, Centre for Public Health, Faculty of Health and Applied Social Sciences, Liverpool John Moores University, Liverpool, 2010

***Dubach et al (1991) An epidemiologic study of abuse of analgesic drugs. Effects of phenacetin and salicylate on mortality and cardiovascular morbidity (1968 to 1987). *N Engl J Med*. 324 (3): 155–60

Aminopyrine

Banned analgesic & anti-inflammatory

Dramatic decrease in white blood cells, leading to increased susceptibility to infection, suppressing immune function and the body's ability to fight off even minor infections*

People who smoke coca paste or crack cocaine contaminated by aminopyrine can experience overwhelming, rapidly-developing, life threatening infections* (**e.g., CV-19**)

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*Gilman AG, et al (eds.). Goodman and Gilman's *The Pharmacological Basis of Therapeutics*. 8th ed. New York, NY. Pergamon Press, 1990., p. 655.

Metamizole/Dipyrone

Metamizole is a pain reliever, fever reducer, and spasm reliever

Side effect of **agranulocytosis** (a dangerously suppressed immune system that places user at very high risk for serious infections due to a severely lowered white blood cell count)*

Combining dipyrone with opiates like heroin results in analgesic potentiation and produces supra-additive effects**

* Brack A, Rittner HL, Schäfer M (March 2004). "Nichtopioidanalgetika zur perioperativen Schmerztherapie" [Non-opioid analgesics for perioperative pain therapy. Risks and rational basis for use]. Der Anaesthesist (in German). 53 (3): 263–80.

** Hernandez-Delgadillo G & Cruz S. (2004). Dipyrone potentiates morphine-induced antinociception in dipyrone-treated and morphine-tolerant rats. Eur. J. of Pharmacol. 502, 67-73.

Diltiazem

- Diltiazem is a medication belonging to a class of calcium-channel blockers and it is commonly used to treat high blood pressure
- Double-depressant effect with heroin
- As an adulterant, it can cause severe adverse cardiovascular reactions, including angina, bradycardia, hypotension, and arrhythmia*
- Potentiates cocaine toxicity & toxic cardiac effects (possibly due to hypoxemia – low oxygen concentrations in blood)*

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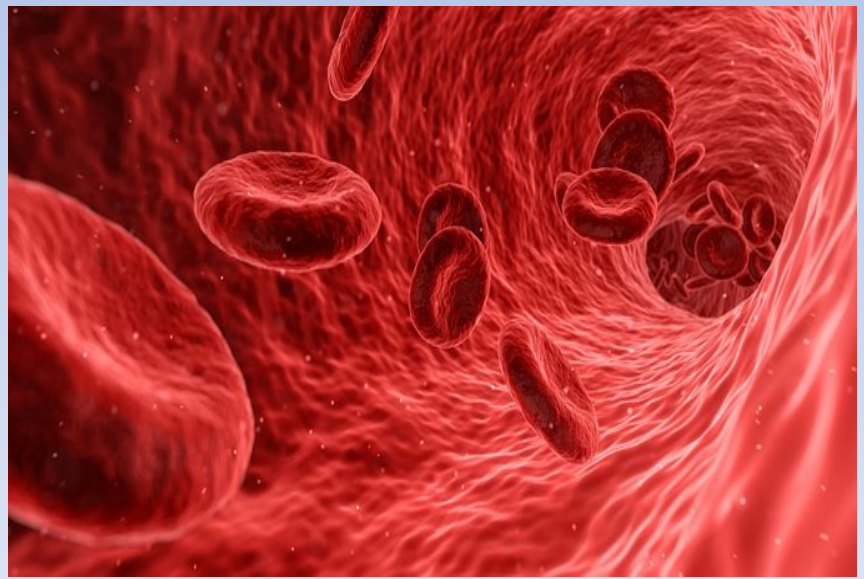
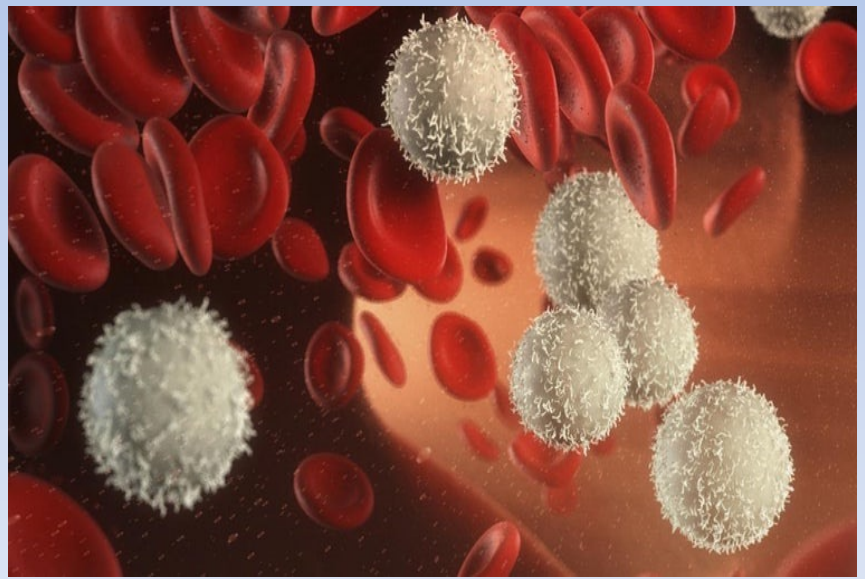
*Brunt T. Monitoring illicit psychostimulants and related health issues. Oisterwijk, The Netherlands: BOXPress, 2012.

Adulterant Effects on Health

Phenacetin Depletes Red Blood Cells, Damages Kidneys, and Bladder Cancer



Levamisole, Metamizole & Aminopyrine Deplete White Blood Cells



Severe Health Problems Accelerated with Adulterated Drugs versus Adulterated Aspirin

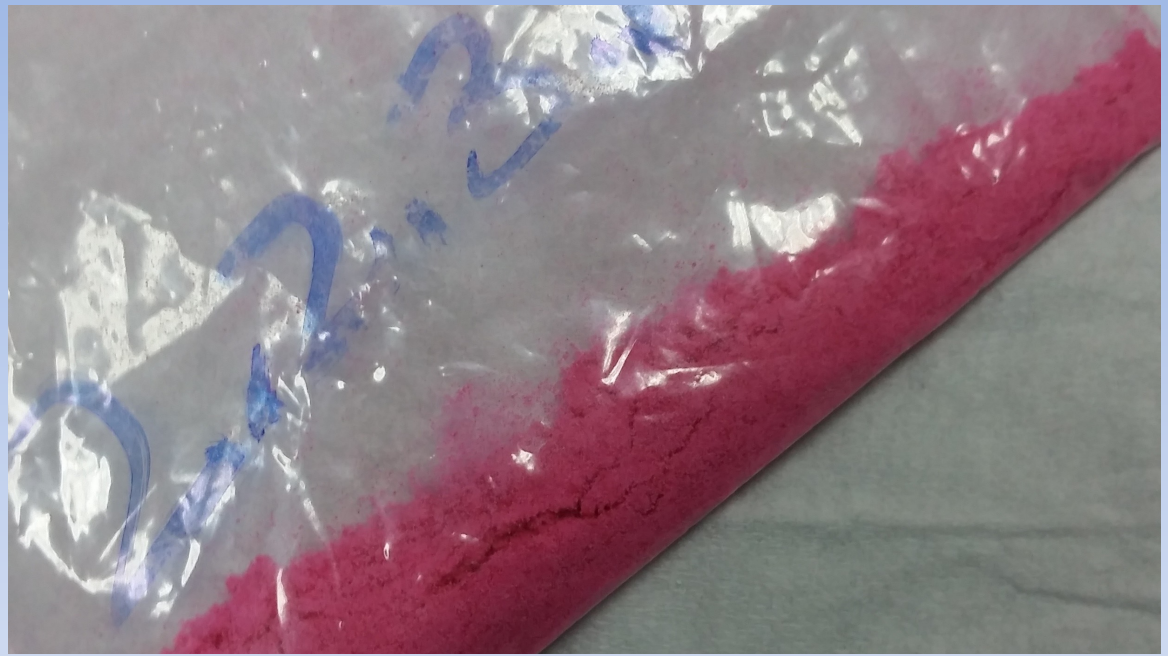
Health Problems from Aspirin Containing Phenacetin Took Years to Appear. Aspirin was Taken as needed for Pain in the 1960s

Crack Used 15-30 X day X 7 days/week X 6 months

Today Health Problems Appear within Months

Unique Stimulants in Latin America

- Pink cocaine in the form of the powerful stimulant/hallucinogenic **2C-B**
- Dragonfly cocaine: a **cocaine, ketamine, and MDMA** mixture
- New toxic cocaine in the form of **translucent flakes or fly wings**



Pink Cocaine (aka 2C-B): Honduras

- Wholesale Seizure at Airport
- Tested Positive for Pure 2C-B
- Destined for Mexico & United States

2C-B


Synthetic analog of mescaline related to the phenylethylamine family synthesized in 1974 by Alexander Shulgin, a biochemist and pharmacologist
A powerful stimulant and hallucinogenic drug whose effects are a cross between ecstasy and LSD
Seized in Chile, Colombia, Panama, Costa Rica, Honduras, Spain, United States
Detected in Honduras in August 2017
Other analogs: FLY, Dragonfly, Bromo-Dragonfly

- DEA reporting indicates Colombian DTOs are responsible for most of the manufacture, transportation, and distribution of ***2C-B*** in Colombia and the United States.*

- ***2C-B*** is typically sold as a **dyed-pink powder** to distinguish it from both MDMA and cocaine.*

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*U.S. Department of Justice, Drug Enforcement Administration. (2017). 2017 National Drug Threat. DEA-DCT-DIR-040-17. Washington, DC: DEA. Available: https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf

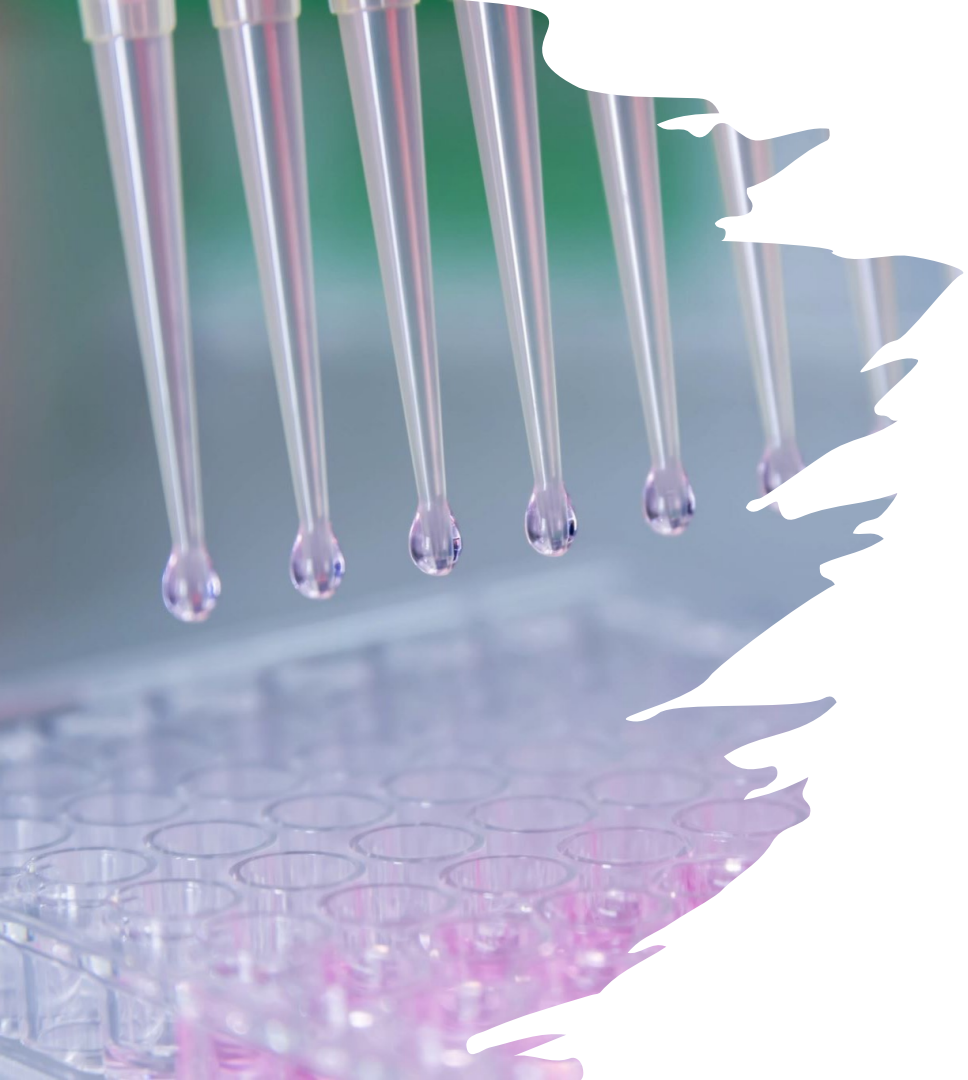
Health Threat of Pink Cocaine

United States: Dyed Cocaine HCl

Dosage: 30 - 60 mg

Honduras: 2C-B

Dosage: 5 - 9 mg



Health Threat of Pink Cocaine

- Users typically insufflate (snort) 60 mg of Cocaine HCl.* However, the typical dose of 2C-B is 9 mg.**
- At doses over 30–40 mg the 2C-B user may experience ***frightening hallucinations***, as well as ***tachycardia***, ***hypertension***, and ***hyperthermia***.***

*"Erowid 2C-B Vault: Dose/Dosage" (http://www.erowid.org/chemicals/2cb/2cb_dose.shtml).

**Jeffcoat AR, et al. (1989). Cocaine disposition in humans after intravenous injection, nasal insufflation (snorting), or smoking. Drug Metab. Dispos, 17 (2): 153 – 159.

***Carmo H, et al. (2005). Metabolic pathways of 2C-B: Analysis of phase I metabolism with hepatocytes of six species including human. Toxicology. 206 (1): 75 – 89.

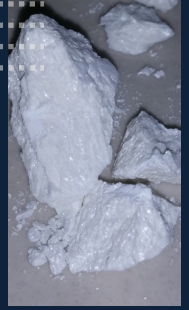
Dragonfly Cocaine – El Salvador

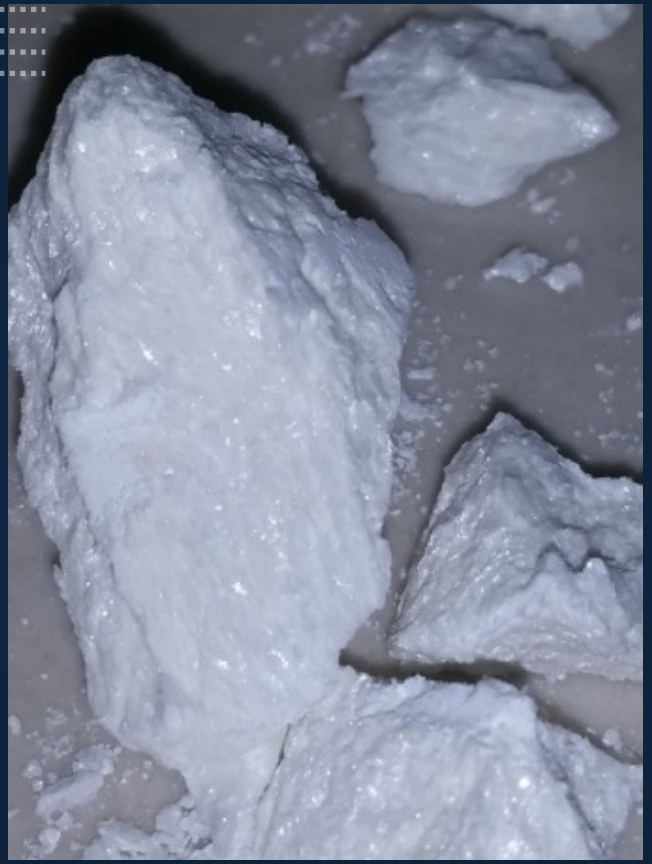
- **Combination of:**
  - *Cocaine*
  - *MDMA/Ecstasy*
  - *Ketamine*

- **Used as substitute for 2C-B**

New Form of Cocaine Detected in Southern Cone of South America

- First Powder
- Then Rock/Crack
- Now Translucent Scales





Brazil
(Scama or Fish Scales)

Argentina
(Alita de Mosca or Little Fly Wing)

Paraguay & Chile
(Alita de Mariposa or Butterfly Wings)

- **80% Cocaine HCl**
- **20% Phenacetin**

Severe Health Problems Reported in Argentina from Little Fly Wing

- Translucent flake appearance
- *High purity Cocaine HCl* cut with *Phenacetin*
- Wash powdered forms of cocaine and phenacetin in a gaseous solution of sulfuric acid & table salt to form translucent flakes
- Intra-nasal Use
- ER reports of respiratory depression and cardiac arrest
- ER reports of convulsions and abnormal muscle movements
- Fly Wing users snort amounts similar to crack/paco smokers

Mortality Perspective

Fentanyl

The fentanyls are a class of *highly potent* narcotic analgesics.

Fentanyl itself is solely used as a surgical anesthetic or as a narcotic to treat chronic, severe, or cancer pain that cannot be controlled by other medications.

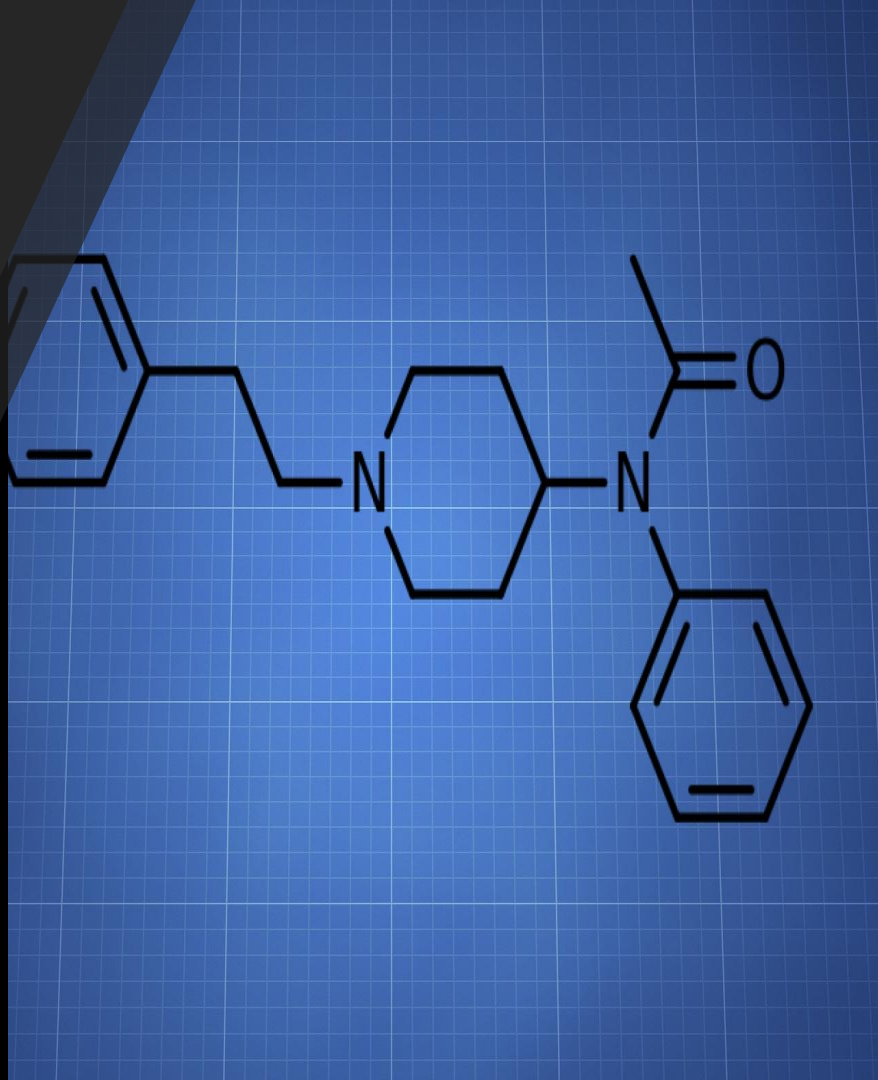
It is the *most potent* opiate available for medical treatment.

Fentanyl analogs such as Carfentanil are used to *immobilize* large animals such as elephants.

Fentanyl

- ***Fentanyl*** is 80 to 100 times stronger than morphine and 50 times more potent than heroin
- ***Acetyl Fentanyl*** (15 X morphine)
- ***Butyrfentanyl*** (7 X morphine)
- ***Carfentanil*** is estimated to be 10,000 X stronger than morphine and 5,000 X more potent than heroin

  (or 100 X stronger than fentanyl)
- Fentanyl's effects include ***respiratory depression*** and ***arrest***

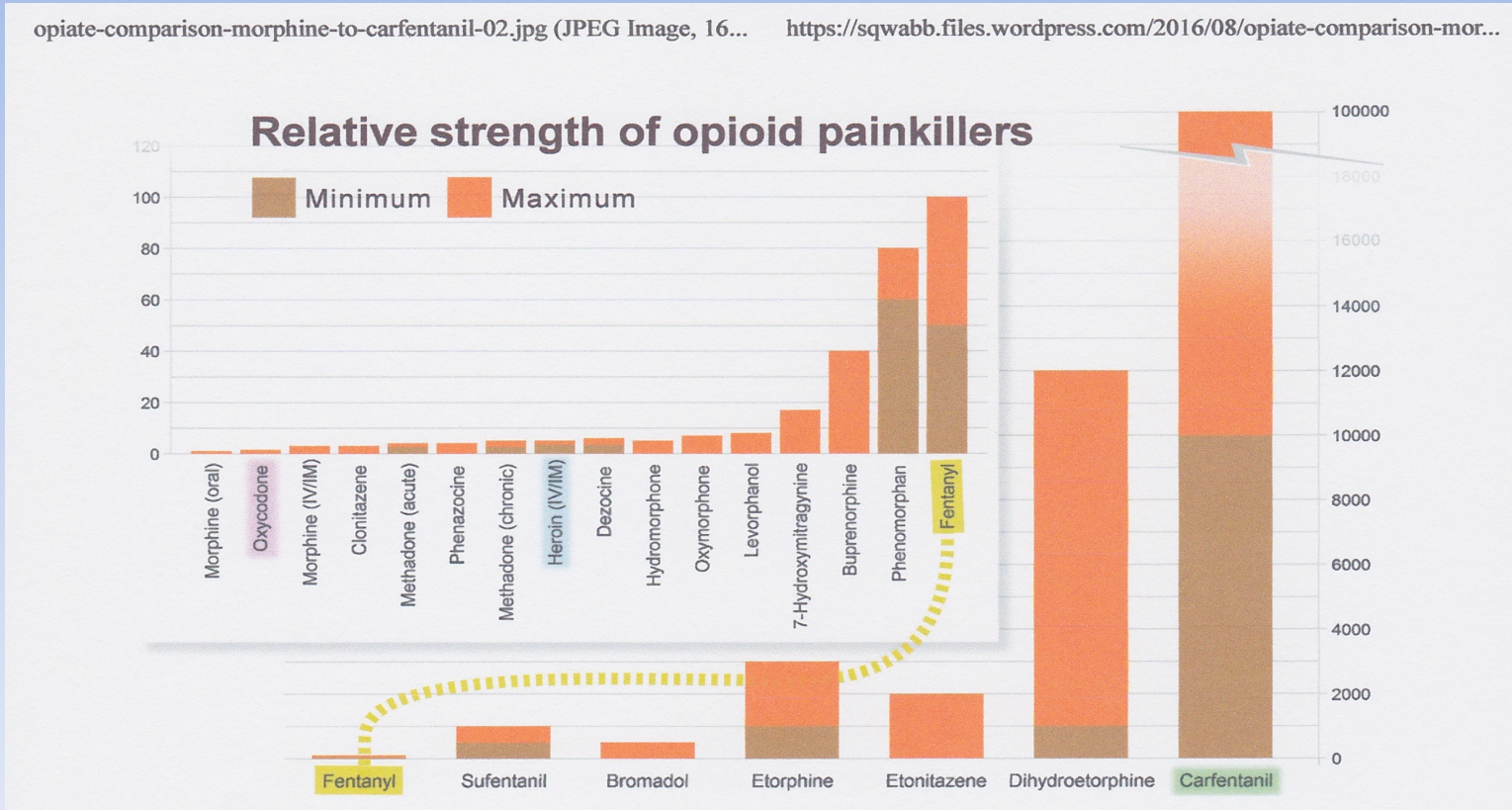


FENTANYL ANALOGS

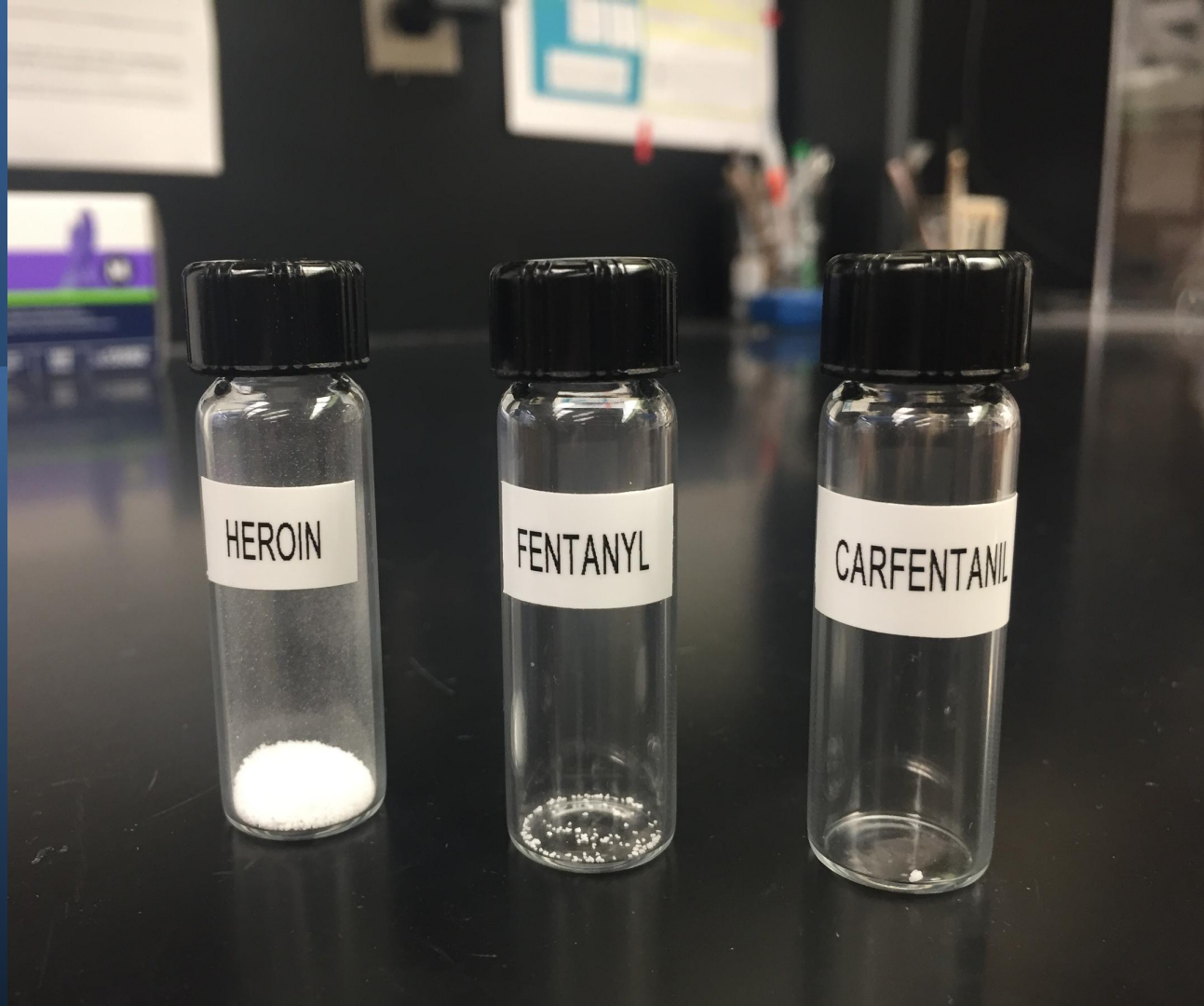
- **Only 200+ have been synthesized and studied**
- **There is potential for more than 1400 analogs of fentanyl to exist**

Illicit Forms of Fentanyl

Fentanyl vs Carfentanil vs Opioid Painkillers



Lethal Dose: Heroin vs Fentanyl(s)



Equivalency to Table Salt

FENTANYL

10 grains

CARFENTANIL

1/10 grain