

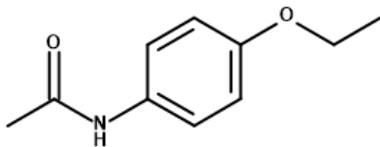


**PUBLIC HEALTH ALERT**

Substance abuse treatment providers, clinicians, outreach workers, and public health clinics should be aware of the following information. Phenacetin is commonly used as an adulterant in illicit drug products, most often in cocaine exhibits, but has also been identified in samples containing heroin and/or fentanyl or multicomponent seized material products. The addition of phenacetin to illicit drugs may be due to its minor euphoric effects, influence on some side-effects of cocaine due to its analgesic action, or to disguise the bitter taste of cocaine without compromising the physical properties of the product - both have similar melting points. Phenacetin is a **known carcinogen and has associated adverse effects on cardiovascular, renal and urologic systems.** Exposure to phenacetin is associated with nephrotoxicity, nephropathy, hemolytic anemia, methemoglobinemia, and kidney and bladder cancer.

**Background:** Phenacetin, a pain-relieving and fever-reducing drug, was discovered as an analgesic in 1887. It was one of the first synthetic fever reducers on the market and one of the first non-opioid analgesics without anti-inflammatory properties. Due to its hazardous side effects, including carcinogenic and kidney-damaging properties, the Food and Drug Administration (FDA) ordered its withdrawal from drug markets in 1983. Since being withdrawn phenacetin has become a common adulterant of illicit substances. In a 9-year longitudinal study of cocaine powders in the Netherlands, the percentage of samples containing phenacetin increased from 1.6 to 40.6 with a peak of 48% in 2006. Additionally, phenacetin was the most frequently identified adulterant in the samples.

**Phenacetin**



**Recommendations for Clinicians**

- Be aware that illicit drugs may contain toxic adulterants that can complicate the clinical presentation.
- Be familiar with the signs and symptoms associated with phenacetin toxicity.
- Be aware that routine hospital drug tests will not disclose the presence of phenacetin, which requires a special test.

**Frequent Indicators of Toxicity of Street Drugs Containing Phenacetin**

- Headache
- Nausea
- Shortness of breath
- Cyanosis
- Ataxia
- Lethargy
- Confusion
- Hallucinations
- Methemoglobinemia

**Recommendations for MEs & Coroners**

- Conduct testing for phenacetin in suspected stimulant or opioid-related fatalities.

**Recommendations for Forensic and Clinical Laboratories**

- Include phenacetin in the scope of testing.
- Develop sensitive confirmatory procedures for common adulterating agents, including phenacetin.
- Consider laboratory analysis of seized drug samples taken from suspected drug overdose investigations.
- Share data on adulterants in drug seizures in your jurisdiction with local health departments, medical examiners and coroners.

**Phenacetin Positivity in Seized Drug Testing in the US**

• An ongoing project at the FRFF (2017-present), supported by the Colombo Plan and MJM Technologies, is the analysis of seized drug exhibits for the presence of toxic adulterants. A summary of the phenacetin findings by state is shown below. Phenacetin was commonly identified in samples containing cocaine, but also in cases with heroin and/or fentanyl. Data collected from the same states over the four years of the project has found widespread use of phenacetin as an adulterant and a trend of increasing frequency of detection.

| State                 | Phenacetin Positives | % Positivity |
|-----------------------|----------------------|--------------|
| New Hampshire (n=200) | 120                  | 60.0%        |
| California (n=174)    | 88                   | 50.5%        |
| Florida (n=200)       | 85                   | 42.5%        |
| Pennsylvania (n=357)  | 84                   | 23.5%        |
| Vermont (n=509)       | 116                  | 22.7%        |
| Maryland (n=32)       | 4                    | 12.5%        |
| Illinois (n=399)      | 48                   | 12.0%        |
| Ohio (n=190)          | 22                   | 11.5%        |
| Texas (n=600)         | 22                   | 3.7%         |
| Kentucky (n=398)      | 13                   | 3.3%         |

**Phenacetin Reported Internationally**

- Countries reporting illicit drug products adulterated with phenacetin as part of the International Toxic Adulterants Database (ITAD) program and/or during The 2nd International Symposium of Forensic Drug Testing Lab Directors in Singapore.





**Health Impacts:** Concomitant use of phenacetin and illicit drugs can enhance the toxicity of the illicit drug. Phenacetin use has been associated with a higher likelihood of reported adverse effects in drug consumers, including cardiac arrhythmias and hallucinations. Effects in the case of an overdose related to phenacetin consumption may include confusion, ataxia, lethargy, headache or methemoglobinemia. Chronic use of phenacetin is associated with nephrotoxicity leading to renal failure and back and flank pain. Intranasal administration may result increased toxicity due to a lack of CYP1A2 in the nasal mucosa, which is known to metabolize phenacetin *in vivo*. Phenacetin is metabolized to paracetamol (acetaminophen), which is also a pharmacologically active substance and detectable with laboratory testing.

In a study reviewing cocaine adulterants in blood samples (n=97), phenacetin was identified in 19% of the samples. Ante-mortem blood concentrations range from 14-166 ng/mL and 28-1151 ng/mL in post mortem samples. In a case resulting in death from the rupture of packages of cocaine containing phenacetin in a body packer, phenacetin blood concentrations reached 20,000 ng/mL, however, the cause of death was attributed to cocaine overdose. Phenacetin was quantitated in the packages at a concentration of 30% with cocaine quantitated at a concentration of 20%. Phenacetin is known to be redistributed after death.

Health providers should consider the possibility of exposure to phenacetin in patients who maybe experiencing cocaine toxicity and have cyanosis, methemoglobinemia, and/or chronic renal effects, which may be due to papillary necrosis and urothelial cancer.

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**Phenacetin Adulterated Drug  
Exposure – Diagnosis and Treatment**

**Signs & Symptoms of Intoxication/Chronic Use**

| Physical                             | Behavioral  |
|--------------------------------------|---|
| Cyanosis<br>Flushed face<br>Headache | Behavioral effects are likely attributed to illicit substance co-ingested with phenacetin. Phenacetin-related behavioral effects are rare |

**Provider Response**

| Physical   | Behavioral   |
|--|--------------|
| Measure methemoglobin if cyanotic<br>Measure electrolytes and renal function<br>Measure CBC with differential<br>Check apap level of LFTs<br>Administer IV fluids<br>Correct abnormalities in lab findings on CBC and electrolytes<br>Administer sodium bicarbonate if patient is acidotic<br>Consider administering oral activated charcoal if phenacetin is ingested | No treatment |

**FURTHER TREATMENT NEEDED?**  
Once patient's behavior and physical responses are stable, then determine further treatment is needed.

- YES**
1. If methemoglobin >20% or if patient is symptomatic even if <20%, call the poison center or medical toxicologist. Note: Phenacetin is contraindicated in patients with G6PD. Severe G6PD deficiency is more common in SE Asia and Mediterranean populations.
  2. Recheck methemoglobin concentrations every 2-4 h until normalizing
  3. Correct acidosis with sodium bicarbonate
  4. Administer IV saline solutions

**NO**  
In most cases, further treatment is not required.