



**Disclosures** 

I am a paid employee of the Orange County Crime Lab.  
 The views expressed here are solely mine and do not reflect that of the Orange County Crime Lab.




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**Learning Objectives** 

- History
- Drug trends
- Pharmacokinetics
- Behavioral effects
- Psychomotor effects / Driving Effects
- Analytical challenges
- Testing scopes




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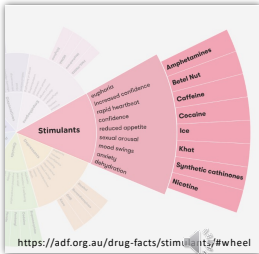
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**Central Nervous System Stimulants** 

Activate Sympathetic Nervous System:

- Increase alertness
- Induce euphoria (potentially)
- Autonomic stimulation
  - Tachycardia
  - Hypertension



<https://adf.org.au/drug-facts/stimulants/#wheel>

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**Central Nervous System Stimulants** 

- \_\_\_\_ Cocaine/Cocaethylene
- \_\_\_\_ Methamphetamine/Amphetamine
- \_\_\_\_ MDMA/MDA
- \_\_\_\_ Ephedrine/Pseudoephedrine
- \_\_\_\_ Cathinone/Synthetic Cathinone
- \_\_\_\_ Methylphenidate
- \_\_\_\_ Phentermine
- \_\_\_\_ Adderall
- \_\_\_\_ Nicotine
- \_\_\_\_ Caffeine



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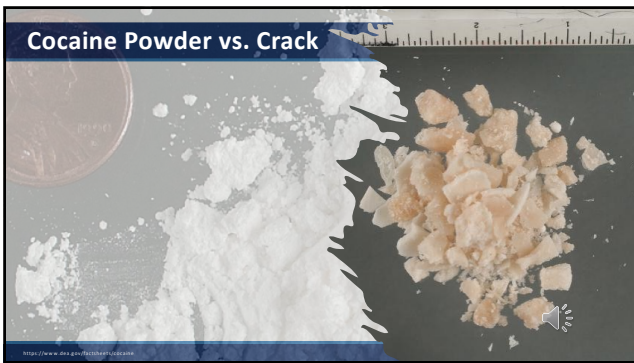
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**Cocaine - History** 

**Source**  
Natural alkaloid extracted from leaves of the coca plant *Erythroxylon coca*

**Historic usage**  
Increase endurance, relieve hunger, and promote a sense of well-being.

**Legal use**  
Local anesthetic

**Present use**  
Commonly abused for euphoric effects and increased mental alertness



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**Cocaine - Information**

**Also known as**  
Methylbenzylecgonine, coke, snow, dust

**Metabolites**  
Benzoylcocaine, ecgonine methyl ester

**Cocaethylene**  
Formed in the liver with the presence of cocaine and ethanol

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**Historic Trends - Cocaine**

The timeline shows the following events:

- 6th Century:** Indigenous people in South America chewed the leaves to increase endurance.
- 1860s:** Cocaine was isolated from the coca leaves.
- 1879:** Used to treat morphine addiction.
- 1884:** Used as a local anesthetic.
- 1886:** Used in Coca-Cola's first recipe.
- 1886:** Cocaine abused was recognized.
- 1914:** Cocaine was replaced by amphetamine due to cost and duration of effects.
- 1930s:** Cocaine is back as the recreation drug due to strict regulations placed on amphetamine.
- 1960s:** Classified as Schedule II.
- 1970:** Cocaine continued to be the top illicit drug to abuse.
- 1977:** (End of timeline)

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**Salt or Base?**

Cocaine Hydrochloride	Cocaine Base
~ 30% purity	~ 90% purity
Schedule II	Schedule I
Has medical usage	No medical usage
Converted from base with diluents	Extracted from coca leaves

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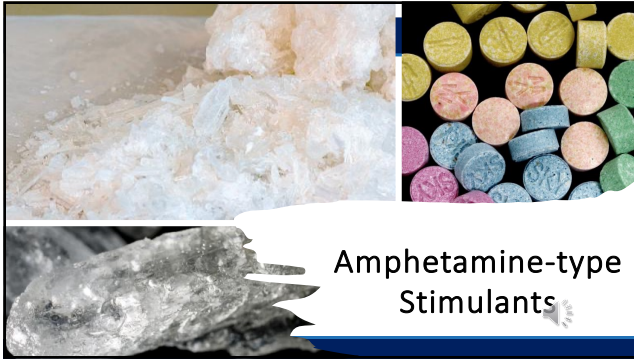
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**Amphetamines - Information** 

- Phenethylamine compounds with sympathomimetic activity
- Amphetamines
  - Amphetamine, dextroamphetamine, methamphetamine
- Sympathomimetic amines
  - Phenylpropanolamine, ephedrine, pseudoephedrine
  - methylenedioxyamphetamine (MDA), methylenedioxymethamphetamine (MDMA).
- U.S. Controlled Substance
  - Schedule II

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**Historic Trends - Amphetamines** 

Year	Event
1887	Amphetamine was synthesized in Germany
1893	Methamphetamine was synthesized from Ephedrine
1930s	Prescription amphetamine was created for treatment for narcolepsy and depression
WWII	Methamphetamine and amphetamine were abused by soldiers and factory workers
1970	Categorized as a Schedule II drug with high abuse potential
1981	Phenyl-2-propanol and methylamine placed as Schedule II compounds
1994	Pharmaceutical sales of ephedrine were subjected to record keeping by the DEA
2006	Pseudoephedrine and phenylpropanolamine had limited availability for sales

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**Amphetamines - History** 

**Source**  
Synthesized in 1887, medically used in 1930s

**Historic usage**  
Treatment of narcolepsy and depression, used to alleviate fatigue, elevate mood, produce euphoria.

**Legal use**  
Decongestant, treatment of ADHD, and appetite suppressants

**Present use**  
Nonrefillable prescription for ADHD and short-term weight-loss treatments.  
Ephedrine/pseudoephedrine and phenylpropanolamine are commonly used for the production of methamphetamine.

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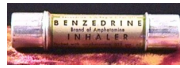

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**Amphetamine isomers** 

d-isomer	l-isomer	Mixture of both
Dexedrine	Benzedrine	Adderall
		

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**Methamphetamine isomers** 

d-isomer	l-isomer	Mixture of both
Desoxyn and "Street" Meth	Metabolite of Selegiline Nasal Decongestant	"Street" Meth
		

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**OTC and Prescription Drugs** 

- Evekeo®**
  - Treat ADHD
  - Amphetamine
- Adderall**
  - Treat hyperactivity
  - Amphetamine + Dextroamphetamine
- Sudafed®**
  - Decongestant
  - Pseudoephedrine
- Suprenza**
  - Treat obesity
  - Phentermine
- Ritalin**
  - Treat ADD and ADHD
  - Methylphenidate

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**Other stimulants** 

MDMA/MDA  
 Cathinone/Synthetic Cathinones  
 Ephedrine/Pseudoephedrine  
 Nicotine and Caffeine



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**Current Trends – 2019 - 2022** 

	2019	2020	2021	2022
<b>Total Cases (Alcohol)</b>	8154	5905	6899	6219
<b>Total Cases (Alcohol + Drugs)</b>	4333 (53%)	3323 (56%)	3676 (53%)	3392 (55%)
<b>Percent of cases (Drugs + BAC &gt; 0.08% (w/v))</b>	38%	38%	38%	41%
<b>Average BAC % (w/v) for all cases</b>	0.16	0.17	0.17	0.17

Data from Orange County Crime Lab, Southern California, USA

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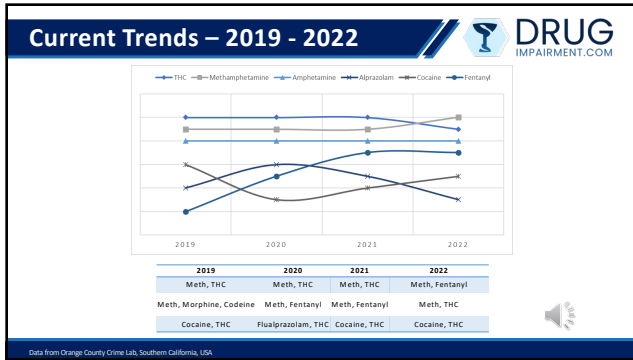
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### Global Trends - Cocaine

From the UNODC Executive Summary 2023

- It is estimated that in 2021, 22 million had used cocaine

↑ Users   ↑ Demand   ↑ Prevalence rates

- 0.32% of general population in 2004 to 0.42% in 2021
- Cocaine seizures have also grown significantly, reaching 2,026 tons (unadjusted for purity) in 2021. In the long term, the growth in seizures has outpaced that in production, and therefore to a certain extent contained the net supply available for consumption.
- With the global market for cocaine centralizing in Americas and Western and Central Europe, there is also an increase in market growth in Africa, Asia, and South-Eastern Europe.

[https://www.unodc.org/unodc/en/data-and-analysis/Exsum\\_wdr2023.html](https://www.unodc.org/unodc/en/data-and-analysis/Exsum_wdr2023.html)

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### Global Trends - Methamphetamine

From UNODC Executive Summary 2023

- Reported in first place by 13% of countries.
- Mostly seen in East and South-East Asia, and recently increased in South-Eastern Europe.
- Global methamphetamine manufacture, trafficking, and use remains concentrated in East and South-East Asia and North America, with the two subregions accounting for almost 90% of methamphetamine seized globally in the period 2017–2021.
- It is estimated that in 2021, 36 million people had used amphetamines, and 20 million had used “ecstasy”-type substances in the past year.
- The proportion of female users is higher in the case of amphetamine-type stimulants (45% of users are women) and non-medical use of pharmaceuticals (between 45 and 49% of users are women), whereas the highest share of men is found in users of opiates (75%) and cocaine (73%).

[https://www.unodc.org/unodc/en/data-and-analysis/Exsum\\_wdr2023.html](https://www.unodc.org/unodc/en/data-and-analysis/Exsum_wdr2023.html)

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**Newsletter** DRUG IMPAIRMENT.COM

**School prevalence of stimulant therapy for ADHD associated with higher rates of prescription stimulant misuse among teens**  
 New study signals importance of monitoring and screening for prescription stimulant misuse in schools

April 16, 2023

Researchers have identified a strong association between prevalence of prescription stimulant therapy for attention-deficit/hyperactivity disorder (ADHD) and rates of prescription stimulant misuse

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**Behavioral Effects** DRUG IMPAIRMENT.COM

**Irritability**

- Paranoia
- Fatigue
- Severe depression
- Aggressive
- Fallen asleep

**Elevated mood**

- Induce euphoria
- Increase alertness
- Improve task performance
- Restlessness

Levine, B., Principles of Forensic Toxicology, 4th Edition  
 Wilson, B., A Primer of Drug Action, 5th Edition  
<https://nda.nih.gov/publications/infacts/methamphetamine>

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**DRE Matrix** DRUG IMPAIRMENT.COM

	OAS Depressants	OAS Stimulants	Hallucinogens	Dissociative Anesthetics	Narcotic Analgesics	Inhalants	Cannabis
<b>HGN</b>	Present	None	None	Present	None	Present	None
<b>VGN</b>	Present (High Dose)	None	None	Present	None	Present (High Dose)	None
<b>LOC</b>	Present	None	None	Present	None	Present	Present
<b>Pupil Size</b>	Normal	Dilated	Dilated	Normal	Constricted	Normal	Dilated
<b>Reaction to Light</b>	Slow	Slow	Normal	Normal	Little	Slow	Normal
<b>Pulse Rate</b>	Down	Up	Up	Up	Down	Up	Up
<b>Blood Pressure</b>	Down	Up	Up	Up	Down	Up/Down	Up
<b>Body Temperature</b>	Normal	Up	Up	Up	Down	Up/Down/Normal	Normal

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**Effects on psychomotor performance** DRUG IMPAIRMENT.COM

Withdrawal following extended meth use can manifest as severe depression, extreme fatigue, lethargy, and disturbed sleep. Logan et al., 1996

Combination of cocaine and alcohol resulted in aggressive driving, more likely to occur with the present of alcohol than with cocaine. Wayne County, MI 1996-98

Stimulant effects may increase certain behaviors on the road like speeding, running red lights, aggressive driving. After the "high", follows extreme fatigue and sleepiness. Parekh, 2019

Cocaine showed correlation to poor concentration and judgement and overconfidence in driving skills. Blandino, et al., 2022

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**Typical oral dosage** DRUG IMPAIRMENT.COM

Drug	Oral dose (mg)
Cocaine	40 – 100
Amphetamine	5 – 30
Methamphetamine	5 – 20
MDMA	50 – 150
Ephedrine	25 – 150
Pseudoephedrine	30 - 60
Phentermine	18.75 - 37.5

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**Method of Admin** DRUG IMPAIRMENT.COM

Topically applied	Orally	Intravenously (IV)	Smoke (SM)	Intranasal (IN)
Cocaine	Methamphetamine Amphetamine	Methamphetamine Amphetamine Cocaine	Methamphetamine Cocaine	Methamphetamine Cocaine

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**Pharmacokinetics - Absorption** 

- Intranasal**
  - Cocaine: dosage dependent, 25 – 94%
  - Methamphetamine: 90% bioavailability
- Intravenous**
  - Cocaine: 100% bioavailability
  - Methamphetamine: 100% bioavailability
- Oral**
  - Cocaine: 20% bioavailability
  - Methamphetamine: 67% bioavailability
- Smoking**
  - Cocaine: dosage dependent, 57 – 70%
  - Methamphetamine HCl: occasionally, 67% - 90%

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**Duration of Effects** 

- Intranasal**
  - Cocaine: 45 – 60 minutes
  - Methamphetamine: 4 – 8 hours
- Intravenous**
  - Cocaine: 15 – 30 minutes
  - Methamphetamine: 4 – 8 hours
- Oral**
  - Cocaine: 1 -2 hours
  - Methamphetamine: ~ 3 hours
- Smoking**
  - Cocaine: 5 – 15 minutes
  - Methamphetamine: ~ 2.5 hours

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**Chronic use** 

**Cocaine**

- Loss of smell
- Respiratory distress
- Severe bowel decay
- Contracting bloodborne diseases

**Methamphetamine**

- “Meth mouth” – tooth decay and tooth loss
- Intense itching
- Paranoia
- Contracting bloodborne diseases

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### Half-life



DRUG	BLOOD HALF-LIFE
Cocaine	0.5 – 1.5 hours
d-Methamphetamine	6 – 15 (urine pH-dependent)
Amphetamine	7 – 34 (urine pH-dependent)
MDMA	4 – 12
Ephedrine	4 – 10
Pseudoephedrine	3 – 16 (urine pH-dependent)
Cathinone	2.7 – 6.0
Methylphenidate	1.4 – 6.2
Phentermine	19 – 24
Nicotine	0.5 – 1.5 (urine pH-dependent)
Caffeine	2 – 12

Source: R. Disposition of Toxic Drugs and Chemicals in Man, 13<sup>th</sup> Ed

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### Pharmacokinetics - Distribution



Drug	V <sub>d</sub> (L/kg)
Cocaine	1.6 – 2.7
d-Methamphetamine	3.0 – 7.0
l-Methamphetamine	3 – 5
Amphetamine	3.2 – 5.6
MDMA	3 – 7
Ephedrine	2 – 5
Pseudoephedrine	2.0 – 3.0
Cathinone	1.9 – 3.5
Methylphenidate	11 – 33
Phentermine	3 – 4
Nicotine	1.0 – 3.0
Caffeine	0.4 – 0.6

Source: R. Disposition of Toxic Drugs and Chemicals in Man, 13<sup>th</sup> Ed

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### Blood to Plasma Ratio



Drug	Ratio
Cocaine	~ 1.0
Amphetamine	30 - 110
Ephedrine	68 – 100
MDA	Not available
MDMA	Not available
Methamphetamine	0.65 (N=1)
Methylphenidate	10 – 60
Pseudoephedrine	500 – 770

Source: R. Disposition of Toxic Drugs and Chemicals in Man, 13<sup>th</sup> Ed

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### Cocaine Metabolism

1. Ecgonine methyl ester  
2. Norcocaine  
3. Benzoylecgonine  
4. Ethylcocaine  
5. Methyl-ecgonidine

1. Plasma pseudochoolinesterase, liver benzoylsterase  
2. P450  
3. Chemical hydrolysis, liver methylesterase  
4. Liver methylesterase, ethyl alcohol  
5. Smoking

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### Methamphetamine Metabolism

Enzymes for metabolism

- CYP2D6
- Dopamine β-hydroxylase
- Flavin-containing Monooxygenase 3
- Butyrate-CoA ligase
- Glycine N-acyltransferase

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### Therapeutic concentrations

Drug	Therapeutic (ng/mL)	Fatal (ng/mL)
Cocaine	50–90	1000–20000
Amphetamine	30–110	>200
Ephedrine	68–100	3500–21000
MDA	No therapeutic use	1800–26000
MDMA	No therapeutic use	>350
Methamphetamine	10–50, up to 200	150–1000
Methylphenidate	10–60	From 2000
Pseudoephedrine	500–770	From 1600

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**Tolerance** 

- Tolerance: To produce same level of pleasure, higher doses are taken.
- Behavioral hyperactivity by methamphetamine seen minimal development on tolerance level.
- Plasma/blood cocaine concentrations is hard to interpret due to tolerance.
- As tolerance of cocaine increases, the risk of overdosing is high due to the toxicity of the drug.



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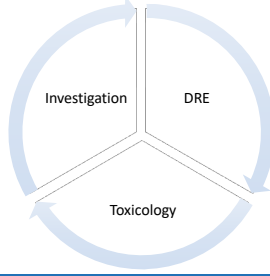
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**Interpretation of concentrations** 



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**Pharmacokinetics - Excretion** 

- Only 1% of cocaine unmetabolized excreted in urine, 26-39% for benzoylecgonine, and 18-22% for ecgonine methyl ester.
- 30-40% of oral dose as unchanged methamphetamine and 10 – 23% as unchanged amphetamine.
- Urine pH affects the half-lives of amphetamines.



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### Recommended Testing Scope

Drug	Blood Screen	Blood Confirm	Urine Screen	Urine Confirm	Oral Fluid Screen	Oral Fluid Confirm
Meth	20	20	200	50	20	20
Amp	20	20	200	50	20	20
MDMA	-	20	-	50	20	20
MDA	-	20	-	50	20	20
Cocaine	-	10	-	20	15	8
BE	50	50	150	50	15	8
CE	-	10	-	20	-	8

All units are ng/mL

Recommendations for Toxicological Investigation of Drug-Impaired Driving and Motor Vehicle Fatalities—2021 Update

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### Stability

- Recommended storage in -20 °C and sodium fluoride to preserve drugs in biological samples.
- Cocaine rate of metabolism increases as the sample storage temperature and evidence collection time increases.
- Methamphetamine is stable with high probability of confirmation upon reanalysis.

<https://pubmed.ncbi.nlm.nih.gov/31118862/>  
Winters et al., Drug Abuse and Forensic Toxicology, Wiley Forensic Sci, 2022      Georg DA, Mackerell JL. A 5-year stability study of common illicit drugs in blood. J Anal Toxicol. 1995

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### Analytical Challenges

- Isomers
  - Methamphetamine and phentermine
  - Ephedrine and pseudoephedrine
  - d and l-isomeric forms of methamphetamine and amphetamine
- OTC and Prescription medications
  - Selegiline metabolizes into l-methamphetamine and l-amphetamine
  - Sudafed false positive on immunoassay panel
  - Vick's inhaler with l-methamphetamine

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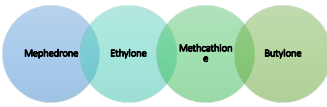
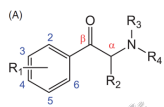
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**Novel Psychoactive Substances** DRUG IMPAIRMENT.COM

**Synthetic Cathinones or 'Bath salts'**

Labeled "not for human consumption" or "plant food" or "research chemicals"  
 Substituted cathinones  
 Administration: oral, snorting  
 Adverse effects: hallucinations, paranoia, panic attacks

Synthetic cathinones

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**Methamphetamine vs Cocaine** DRUG IMPAIRMENT.COM

Methamphetamine versus Cocaine

Methamphetamine	Cocaine
Stimulant	Stimulant and local anesthetic
Man-made	Plant-derived
Smoking produces a long-lasting high	Smoking produces a brief high
50% of the drug is removed from the body in 12 hours	50% of the drug is removed from the body in 1 hour
Increases dopamine release and blocks dopamine re-uptake	Blocks dopamine re-uptake
Limited medical use for ADHD, narcolepsy, and weight loss	Limited medical use as a local anesthetic in some surgical procedures

<https://nda.fda.gov/publications/research-reports/nda-an-pubs/nda/nda-how-methamphetamine-differs-from-other-stimulants-such-cocaine>

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**Drug-facilitated sexual assaults** DRUG IMPAIRMENT.COM

**ANSI/ASB 121, 1<sup>ST</sup> Ed, 2021 - Recommended testing scopes for urine**

25 ng/mL: amphetamine, methamphetamine, MDMA, MDA  
 50 ng/mL: benzoyllecgonine

**References**  
 Jansen KL, Theron L. Ecstasy (MDMA), methamphetamine, and date rape (drug-facilitated sexual assault): a consideration of the issues. *J Psychoactive Drugs*. 2006 Mar;38(1):1-12. doi: 10.1080/02791072.2006.10399822. PMID: 16681170.  
 EMCDDA 2008, Technical datasheets, Sexual assaults facilitated by drugs or alcohol

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**Summary** 

- Central nervous system stimulants acts on the sympathetic system and autonomic nervous system to which increase alertness and body processes.
- Cocaine and methamphetamine are commonly abused due to the euphoria and increased awareness.
- Stimulant effects may increase certain behaviors on the road like speeding, running red lights, aggressive driving. After the “high,” extreme fatigue and sleepiness follow.



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**Thank You!** 

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