Hallucinogens

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Introduction

- Definitions and Terminology
- *Hallucinogen* means “producer of hallucinations”. Many drugs, when taken in sufficient quantity, are psychoactive and can cause auditory and/or visual hallucinations.
- Such hallucinations may be present as part of a delirium, accompanied by disturbances in judgment, orientation, intellect, memory, emotion and level of consciousness.

- Hallucinogen, however, generally refers to compounds that alter consciousness without producing delirium, sedation, excessive stimulation or intellectual or memory impairment as prominent effects.

- This label actually is inaccurate because true LSD-induced hallucinations are rare; what are commonly seen are illusory phenomena.

- An illusion is a perceptual distortion of an actual stimulus in the environment.

- There are a variety of widely accepted synonyms for the hallucinogens, including the terms psychedelic & psychomimetic.

Classification of Hallucinogens

- 1.Hallucinogenic Amphetamines:

  MA, MDMA, MDA, MDEA ,DOM, Mescaline

- 2. Indolealkylamine Hallucinogens:

  LSD, DMT, Psilocybin, Psylocin

- 3.Cyclohexylamine derivatives:

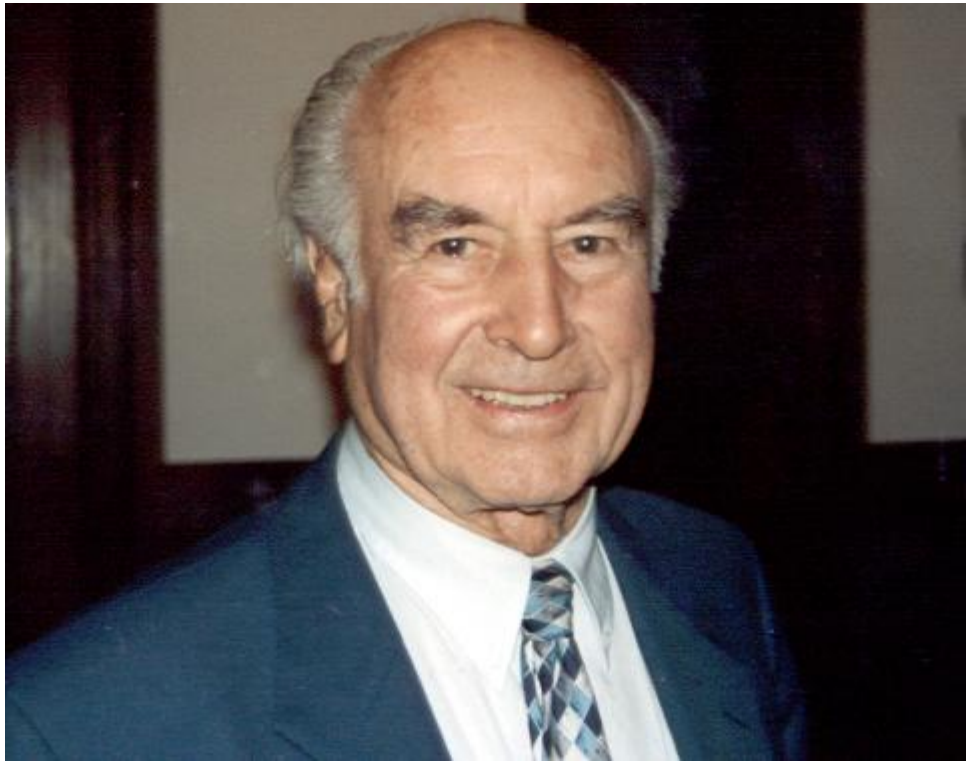
  Phencyclidine(PCP), Ketamine, PHP,PCC

- 4. Cannabinoids

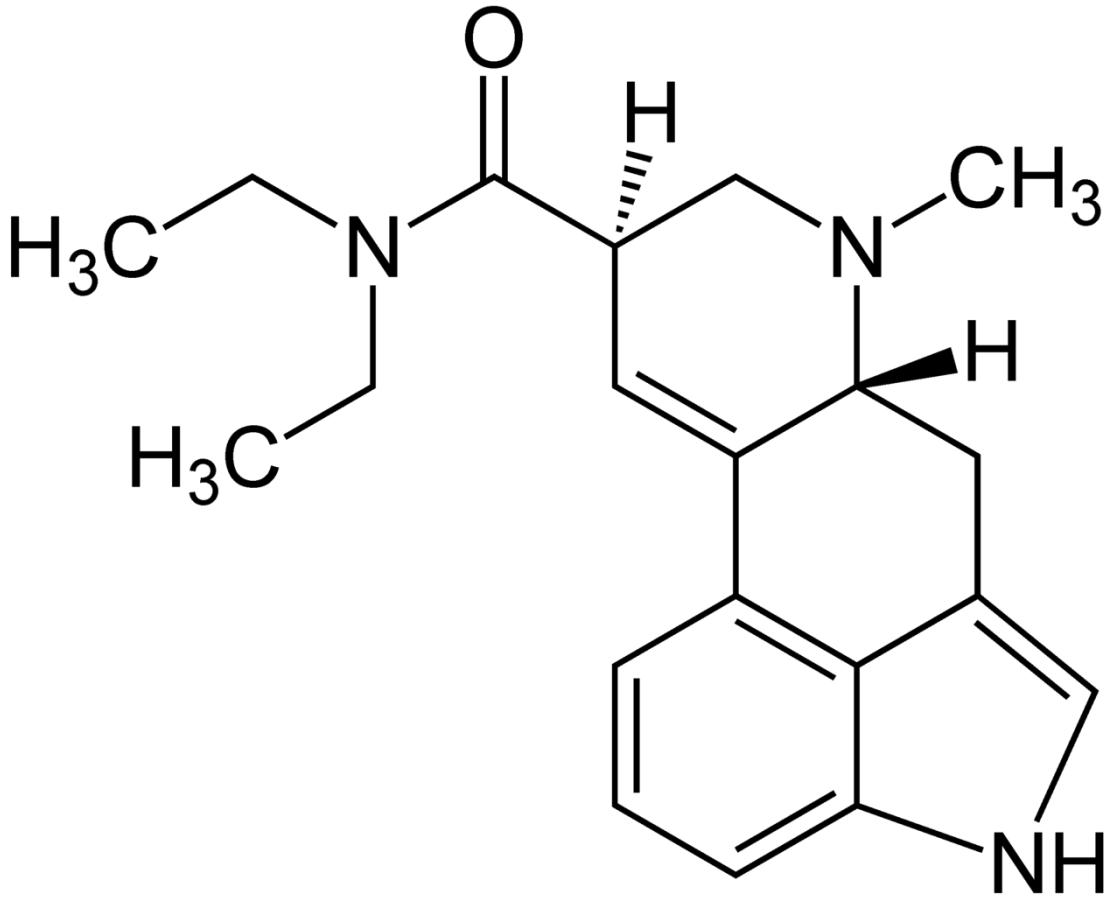
Lysergic Acid Diethylamide (LSD)

- LSD was first synthesized by *Dr. Hofmann* in 1938 in *Sandoz* Pharmaceutical Company.
- It was called LSD-25 because it was the 25th compound mad in this series of experiments on ergot derivatives.
- In 1943, *Hofmann* accidentally ingested some of the compound, and soon had the first LSD “trip”.

Dr. Albert Hofmann



LSD Chemical Structure



Epidemiology of LSD Abuse

- Use and availability of LSD decreased from the mid-1970s through the 1980s.
- In 1992, there was an increase in prevalence in the use of LSD by school-age children and young adults.
- In 1994, the annual prevalence rates for LSD use were 7% in high school students and 5% in college students.

Street Names

- Dots
- Microdot
- Acid
- Sugar
- Sugar Cubes
- Window Pane
- California sunshine
- Hippie
- Window glass
- Trip
- Zen
- Blotter
- Blotter Acid
- Paper Acid
- Cid
- Battery acid

Pharmacokinetics

- The absorption of LSD from GI occurs rapidly, with drug diffusion to all tissues, including the brain.
- The onset of psychological and behavioral effects occurs approximately 60 min. after oral administration and peaks 2 to 4 hours after administration, with a gradual return to the predrug state in 10 to 12 hours.

Potency of LSD

- LSD is one of the most potent hallucinogens known, with behavioral effects occurring in some individuals after doses as low as 20 mcg.
- In the past, typical street doses ranged from 50 to 300 mcg.
- Because of its high potency, LSD can be applied to paper blotters or the backs of postage stamps.

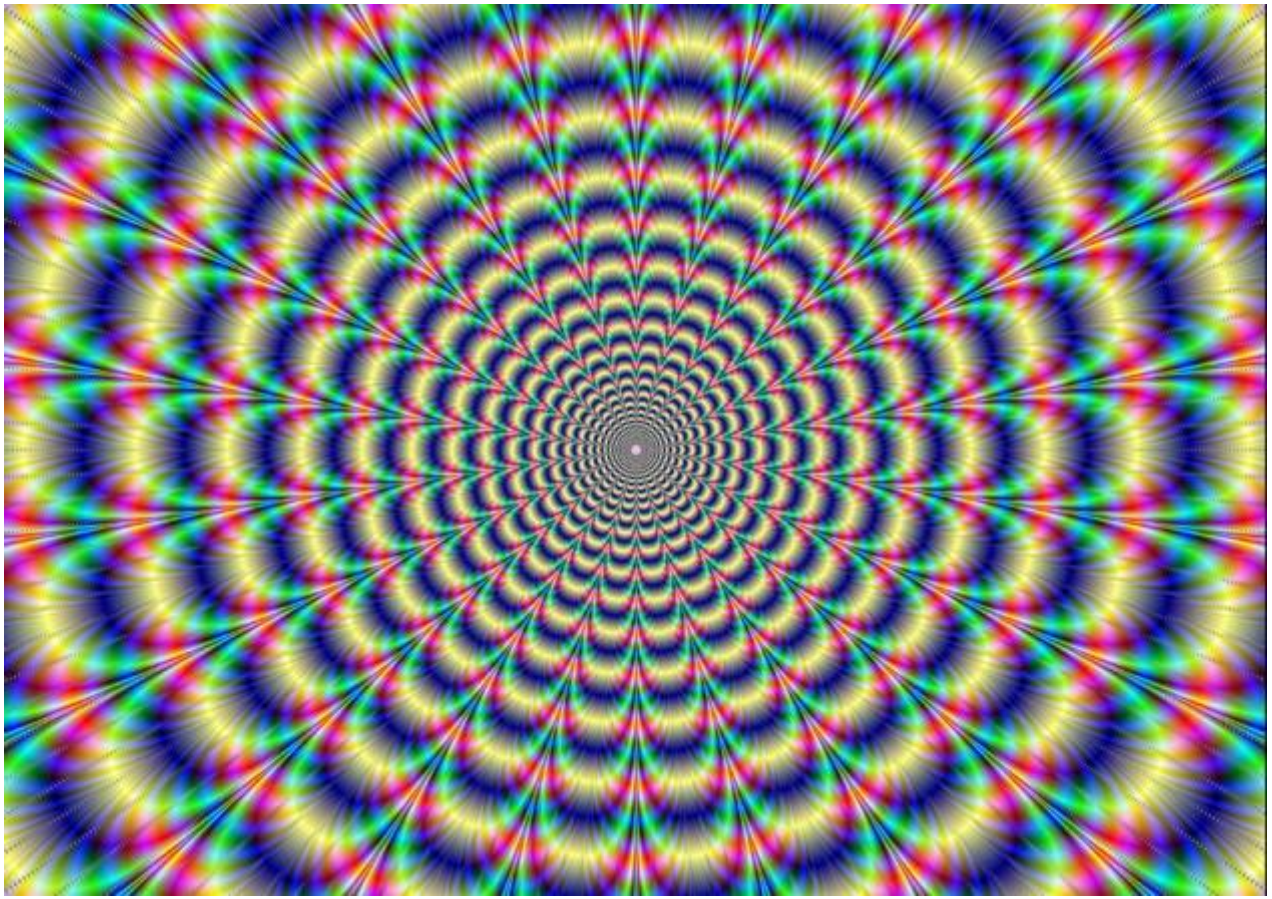
Mechanism of Action

- The exact mechanisms of action of LSD still remain unclear.
- Some of these mechanisms are:
- Affects on the electrical activity of neurons in the locus ceruleus and certain cortical regions.
- LSD is a antagonistic effects on 5-HT2A receptors.
- LSD inhibits the firing of serotonergic neurons in the dorsal raphe nucleus, most likely by interacting with presynaptic autoreceptors, now termed 5-HT1A.

Acute Psychological Effects

- The first 4 hours are sometimes called a “trip”.
- The subjective effects of LSD are dramatic, and can be divided into:
- Somatic (dizziness, paresthesias weakness, and tremor)
- Perceptual (altered visual sense and changes in hearing)
- Psychic (changes in mood, dream-like feelings, altered time sense, and depersonalization)

Music often induces colorful kaleidoscopic images that dance in synchrony with the music, especially with the eyes closed (Synethesia)



Autonomic and Other Effects

- Pupillary dilation, Hyperreflexia, Increases in Blood Pressure and Body Temperature, Tremor, Piloerection, Tachycardia, Nausea, vomiting.

Acute Adverse Reactions

- Acute anxiety, Panic Reactions so call “Bad trip”.

  Paranoid Ideation, Hallucinations, Psychosis.

- Treatment of acute adverse reactions:

  Treatment of acute adverse reactions to hallucinogens first must be directed toward preventing the patient from physically harming self or others.

  Lorazepam & Chlorpromazine or Haloperidol (Oral or IM)

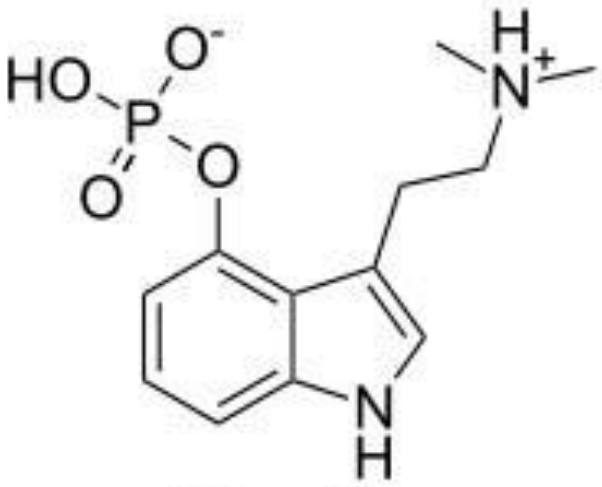
Long- Term Adverse Effects

Chronic adverse effects reactions include Psychoses, Depression, Paranoid states and Flashbacks.

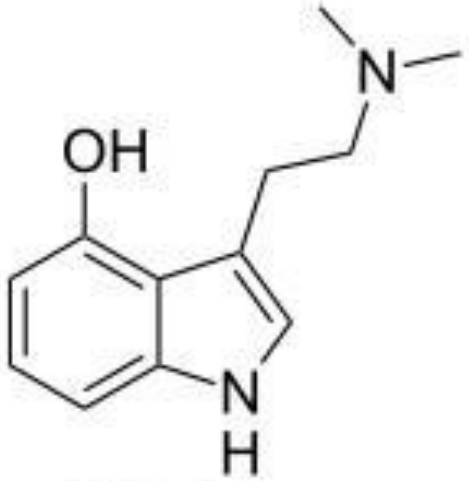
Psilocybin

- Psilocybin is a naturally occurring psychedelic prodrug compound produced by more than 200 species of mushrooms, collectively known as psilocybin mushrooms.
- As a prodrug, psilocybin is quickly converted by the body to **psilocin**.

Psilocybin *vs.* Psiclocin



Psilocybin



Psilocin

Natural occurrence

- The worldwide distribution of hallucinogenic mushrooms considered these to be distributed amongst the following genera: *Psilocybe* (116 species), *Gymnopilus* (14), *Panaeolus* (13), *Copelandia* (12), *Hypholoma* (6), *Pluteus* (6), *Inocybe* (6), *Conocybe* (4), *Panaeolina* (4), *Gerronema* (2) and *Agrocybe*, *Galerina* and *Mycena* (1 species each).
- The majority of these are found in Mexico (53 species), with the remainder distributed in the US and Canada (22), Europe (16), Asia (15), Africa (4), and Australia and associated islands (19).
- In general, psilocybin-containing species are dark-spored, gilled mushrooms that grow in meadows and woods of the subtropics and tropics, usually in soils rich in humus and plant debris.

Available forms

- Although psilocybin may be prepared synthetically, outside of the research setting, it is not typically used in this form.
- The psilocybin present in certain species of mushrooms can be ingested in several ways: by consuming fresh or dried fruit bodies, by preparing a herbal tea, or by combining with other foods to mask the bitter taste.
- In rare cases people have injected mushroom extracts intravenously.

Dried *Psilocybe* mushrooms showing the characteristic blue bruising on the stems

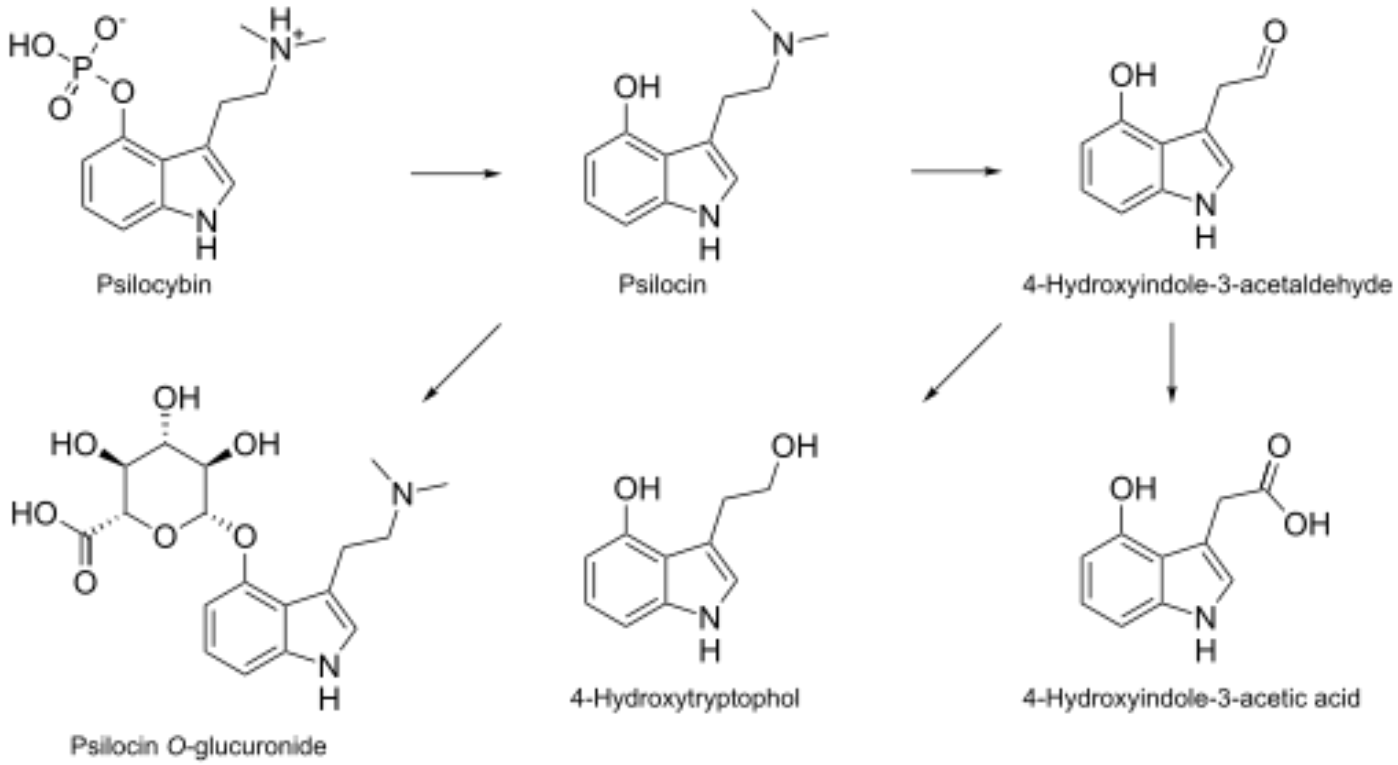
Pharmacodynamics

- Psilocybin is rapidly dephosphorylated in the body to psilocin, which is a partial agonist for several serotonin receptors.
- Psilocin has a high affinity for the 5-HT_{2B} and 5-HT_{2C} receptors in the human brain, and with a slightly lower affinity for the 5-HT_{2A} receptor. Psilocin binds with low affinity to 5-HT1 receptors, including 5-HT_{1A} and 5-HT_{1D}.
- Psilocin indirectly increases the concentration of the neurotransmitter dopamine in the basal ganglia, and some psychotomimetic symptoms of psilocin are reduced by haloperidol.
- Unlike LSD, psilocybin and psilocin have no affinity for the dopamine D2 receptors

Pharmacokinetics

- The effects of the drug begin 10–40 minutes after ingestion, and last 2–6 hours depending on dose, species, and individual metabolism.
- The half life of psilocybin is 163 ± 64 minutes when taken orally, or 74.1 ± 19.6 minutes when injected intravenously.
- A dosage of 4–10 mg is required to induce psychedelic effects. A typical recreational dosage is 10–50 mg psilocybin, which is roughly equivalent to 10–50 grams of fresh mushrooms, or 1–5 grams of dried mushrooms.
- A small number of people are unusually sensitive to psilocybin, such that a normally threshold-level dose of about 2 mg can result in effects usually associated with medium or high doses. In contrast, there are some who require relatively high doses to experience noticeable effects. Individual brain chemistry and metabolism play a large role in determining a person's response to psilocybin.

Psilocybin is converted in the liver to the pharmacologically active psilocin, which is then either glucuronated to be excreted in the urine or further converted to various psilocin metabolites.



Effects

- Most of the comparatively few fatal incidents reported in the literature that are associated with psychedelic mushroom usage involve the simultaneous use of other drugs, especially alcohol.
- Probably the most common cause of hospital admissions resulting from psychedelic mushroom usage involve "bad trips" or panic reactions, in which affected individuals become extremely anxious, confused, agitated, or disoriented.
- Accidents, self-injury, or suicide attempts can result from serious cases of acute psychotic episodes.

Investigation of Timothy Leary and colleagues at Harvard University (n= 175,1960s)

- Disorientation, Lethargy, Giddiness, Euphoria, Joy, and Depression. Anxiety , Paranoia.
- Low doses of the drug can induce hallucinatory effects. Closed-eye hallucinations may occur, in which the affected individual sees multicolored geometric shapes and vivid imaginative sequences.
- Some individuals report experiencing synesthesia, such as tactile sensations when viewing colors.
- Open-eye visual hallucinations are common, and may be very detailed although rarely confused with reality.

Physical effects

- Pupil dilation (93%); changes in heart rate (100%), including increases (56%), decreases (13%), and variable responses (31%); changes in blood pressure(84%),including hypotension (34%), hypertensio n (28%), and general instability (22%)
- Changes in stretch reflex (86%), including increases (80%) and decreases (6%); nausea (44%); tremor (25%); and dysmetria (16%).

Psychiatric Effects

- Panic reactions, violent behavior, suicidal thoughts, Schizophrenia-like psychosis, and convulsions have been reported in the literature.
- Other adverse effects less frequently reported include paranoia, confusion, prolonged derealization (disconnection from reality), and mania.
- Psilocybin usage can temporarily induce a state of depersonalization disorder. Usage by those with schizophrenia can induce acute psychotic states requiring hospitalization.
- Flashbacks can occur long after having used psilocybin mushrooms.
- Hallucinogen persisting perception disorder (HPPD) is characterized by a continual presence of visual disturbances similar to those generated by psychedelic substances.

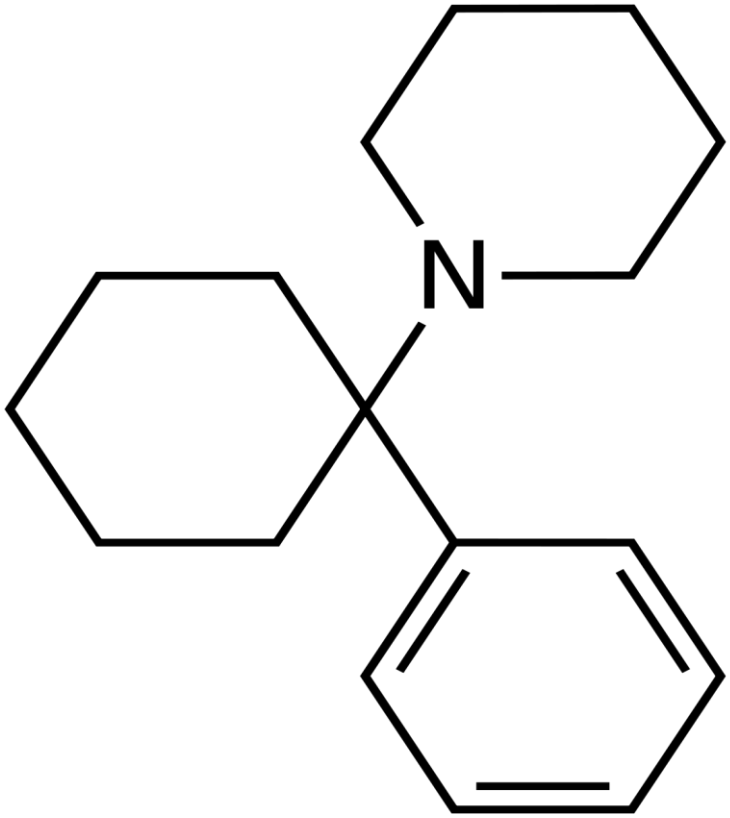
Perceptual distortions

- Psilocybin is known to strongly influence the subjective experience of the passage of time. Users often feel as if time is slowed down, resulting in the perception that "minutes appear to be hours" or "time is standing still".
- Users having a pleasant experience can feel a sense of connection to others, nature, and the universe; other perceptions and emotions are also often intensified. Users having an unpleasant experience (a "bad trip") describe a reaction accompanied by fear, other unpleasant feelings, and occasionally by dangerous behavior.

Phencyclidine (PCP)

- PCP is a tertiary amine with a three-ring structure, and is a stable, soluble, white crystalline solid at room temperature.
- PCP was originally marketed in the late 1950s by Parke Davis Pharmaceutical Company as a sedative and surgical anesthetic. Under trade name *Sernyl.*
- In 1967,PCP returned as *Sernylan* and was marketed as a veterinary tranquilizer.

PCP Chemical Structure



- PCP first emerged as a hallucinogenic in the late 1960s but did not become popular until the 1970s. Its popularity resulted in part from its easy synthesis.
- PCP is often added as an adulterant to marijuana or cocaine without the knowledge of the user.
- PCP was classified as a Schedule I agent in 1978, and sale of its chemical precursor (Piperidine) was restricted.

Street Names

- Angel Dust
- Hog
- Elephant
- PeaCe pill
- Horse tranquilizer

Pharmacokinetics

- PCP is a weak, alkaline salt, soluble in both water and ethanol and is rapidly absorbed after ingestion or inhalation or when it is administered IV, or per rectum.
- Absorption is minimal in the stomach but occurs rapidly in the upper small intestine.
- Onset of effects occurs in 30 min. when smoked.
- Acute symptoms and signs of toxicity usually last 4-6 hours and general resolve completely by 24-48 hours.

- PCP is a highly lipophilic weak base and thus is widely distributed into the tissues.
- It has an unusual entrogastric circulation, such that significant amounts of drug are actively secreted into the stomach and then reabsorbed in the small intestine.
- The concentration of PCP in the stomach may be up to 50 times higher than in the serum.
- PCP levels are highest in adipose tissue.

- The concentrations of PCP in brain and CSF may be up to 9 and 4 times higher than that in the plasma, respectively. PCP is metabolized mainly in the liver .
- Oxidative hydroxylation to the inactive monohydroxypiperidine is followed by glucuronidation.
- Significant first-pass liver metabolism also occurs when the drug is ingested orally.

Mechanism of Action

- PCP interacts with many types of receptors in CNS such as:
  - NMDA
  - GABA
  - Muscarinic Ach
  - Nicotinic Ach
  - Na/K Channel
  - Mu Opiate receptors
  - NE/DA/5-HT reuptake

Clinical Presentation

- Hallmarks:

  Nystagmus, Hypertension
- Sensorium:

  Unconscious, Lethargy/Stupor
- Anticholinergic effects:

  Mydriasis, Urinary retention
- Abnormal Vital Signs:

  Apnea/Respiratory arrest, Hyperthermia

- Motor Signs:

  Generalized rigidity, Localized Dystonia,

  Grand mal Seizure, Athetosis, Facial grimacing

- Cholinergic Signs:

  Diaphoresis, Bronchospasm, Hypersalivation, Bronchorrhea

- Behavior:

  Violent, Bizarre, Agitation, Hallucination, Nudism

Treatment

- Treatment is symptomatic and supportive.

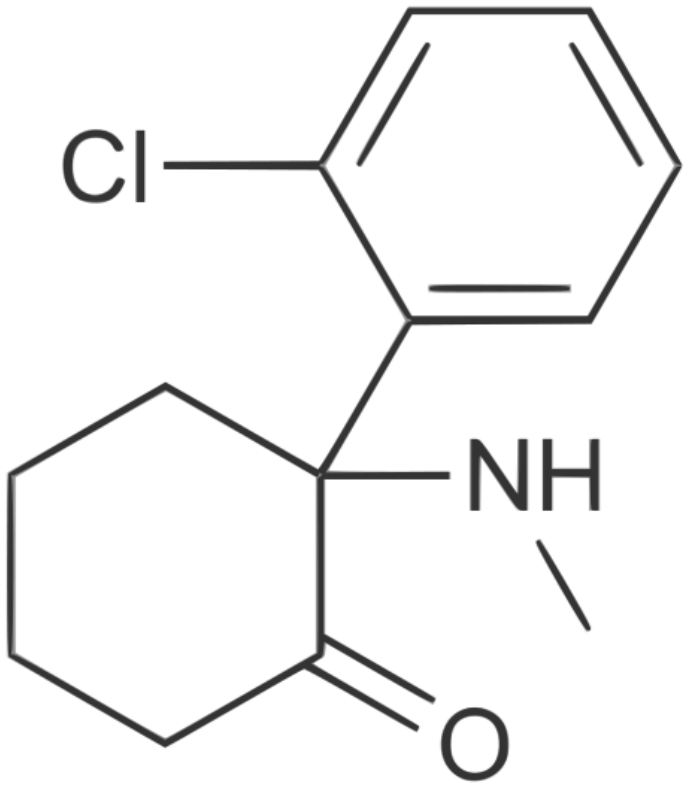
  ABC procedure is performed.
- Gastric lavage and emesis is not indicated in PCP smoking or nasal administration or if more than 1 hour has passed since the time of ingestion.
- PCP is actively secreted into stomach, multiple doses of activated charcoal may be benefit in binding free PCP.

- Patients should be observed in a quiet darkened environment. Auditory, tactile, or visual stimuli should be kept to a minimum to avoid provoking violent outburst.
- Lorazepam 0.1mg/kg or Haloperidol, 5-10mg, IM may be useful in management of such patients.

Ketamine

- In 1962, Calvin Stevens invented ketamine at the Park-Davis Pharmaceutical Company in Michigan.
- Ketamine is an analogue of PCP and in 1970, the FDA approved ketamine for human use for "dissociative anaesthesia".
- Street names: Special K, Vitamin K, Cat tranquilizer, K

Ketamine Chemical structure



A 1000 mg/10 mL vial of ketamine

Toxic Effects

- Ketamine is a NMDA antagonist and use of it has been with range of mental health problems including :

  Anxiety, Panic attacks, Flashbacks, Post-traumatic Stress Disorders (PTSD), Mania, Depression, Suicide, Insomnia, Nightmares, Persistent Hallucinations, Aggression, Catatonic Schizophrenia.

- Physical effects:

  Slurred Speech, Dizziness, Visual problems, Vertigo, Nausea, Vomiting Headache, Sweating, Muscle Spasms, Jerk Movements, Tremor, Heart Palpitation.

Treatment

Treatment has supportive/symptomatic

Bath Salts (Psychoactive bath salts, Monkey dust, Plant Food)

- BSs in general, are psychoactive synthetic drugs (designer drugs) made in large quantities in foreign drug labs.
- These drugs are all related to a broader group of chemical compounds known as synthetic cathinones, chemically similar to a substance found in the khat plant, which is known for its amphetamine-like stimulant effects.
- Some brand names of synthetic cathinones include Bliss, Vanilla Sky, Lunar Wave, Cloud Nine, and White Lightning.

Flakka

- A synthetic street drug called "Flakka" was in the news in late 2014 and 2015. Hospitals, doctors, police, and fire rescue crews in Florida saw patients with symptoms and signs that included bizarre behavior, agitation, Paranoia and delusions.
- Flakka can be smoked, vaped with an e-cigarette, snorted, injected, or swallowed. When heated up, it gives off a foul-smelling smoke characterized as smelling like dirty socks.

- Flakka is just a newer-generation version of a type of synthetic drug called bath salts.
- Flakka is the street name for the synthetic cathinone called alpha-pyrrolidinopentiophenone (Alpha-PVP).

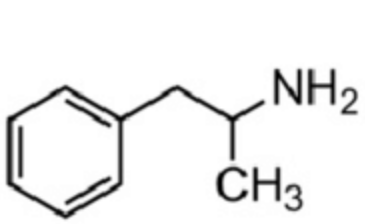
Bath Salts Forms

- The white powder, granules, or crystals.
- The drugs' packaging often states "not for human consumption" in an attempt to circumvent drug prohibition laws.
- Additionally, they may be mislabeled as plant food, powdered cleaner, and other such products.

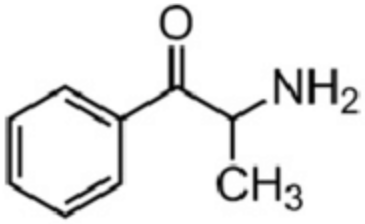

DEA

Pharmacology

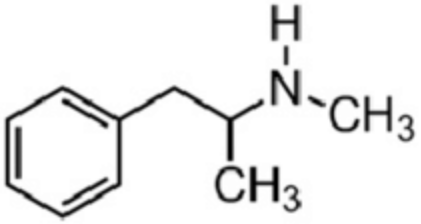
- Bath salts usually contain a cathinone, typically methylenedioxypyrovalerone (MDPV), methylone or mephedrone.
- They are similar to amphetamines in that they cause stimulant effects by increasing the concentration of monoamines such as dopamine, serotonin, and norepinephrinein synapses.
- They are generally less able to cross the blood brain barrier than amphetamines due to the presence of a beta-keto group that increases the compound's polarity.



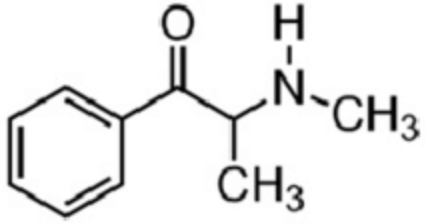
Amphetamine



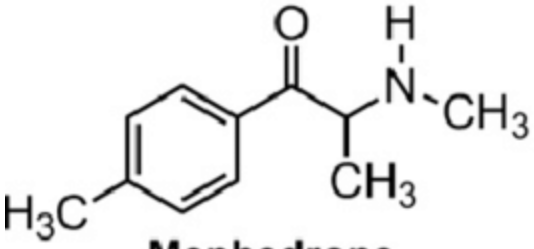
Cathinone



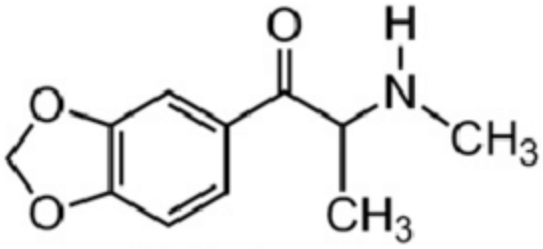
Methamphetamine



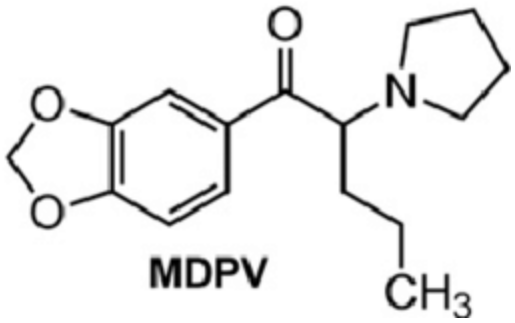
Methcathinone



Mephedrone



Methylone



MDPV

- Bath salts can be ingested orally, snorted, smoked, or injected. Bath salts can be detrimental to human health and can potentially cause erratic behavior, hallucinations, and delusions.
- This is often due to their wakefullness-promoting effect, leading to insomnia.

Side Effects of BS

- Bath salt users have reported symptoms that include headache, heart palpitations, nausea, cold fingers, hallucinations, paranoia, and panic attacks.
- Violent behavior, heart attack, kidney failure, liver failure, suicide, an increased tolerance for pain, dehydration, and breakdown of skeletal muscle tissue.
- Furthermore, there is evidence to support the claim that a psychoactive compound could catalyze psychosis in a person who is already susceptible to psychotic disorders.
- Contrary to popular belief, investigators found no connection to bath salts in the *Miami cannibal attack* (2012).
- Visual symptoms similar to those of stimulant overdoses include dilated pupils, involuntary muscle movement, rapid heartbeat, and high blood pressure.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