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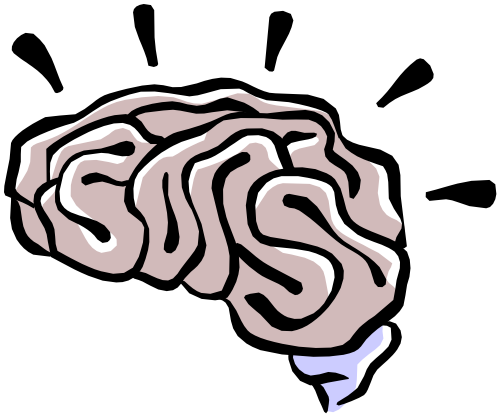
Subject: Pharmacology-I (BP 404T)
Unit: V
Topic: Pharmacology of Hallucinogens

Hallucinogens



- Hallucinogens are substances that alter sensory processing in the brain,

causing perceptual disturbances,

changes in thought processing, and depersonalization

The Nature of Hallucinogens

- Many drugs can exert hallucinogenic effects related to neurotransmitters:
- **Serotonin**: LSD, psilocybin, DMT
- **Norepinephrine**: amphetamine related, mescaline, MDMA
- **Acetylcholine**: atropine, scopolamine
- **Dissociative anesthetics**: PCP, ketamine

Names for Hallucinogens

- Psychedelic
- Psychotogenic
- Psychotomimetic

Sensory and Psychological Effects

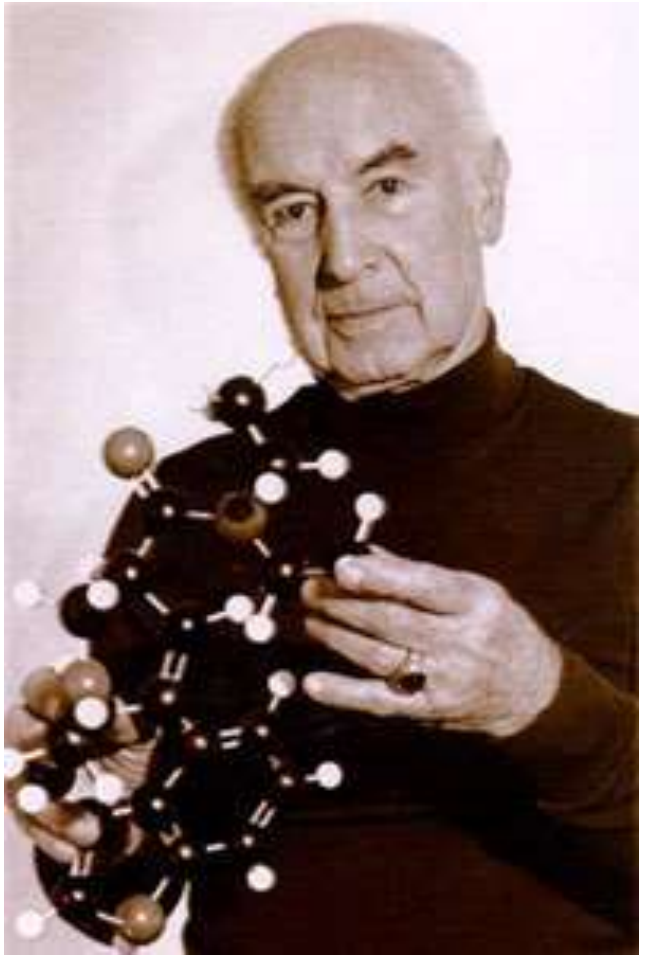
- Altered perception.
- - Synesthesia: blending of the senses. Perceptual changes.
- Self-reflection
- - “Make conscious the unconscious”
- Loss of identity and cosmic merging
- - “Mystical-spiritual aspect of the drug experience”
- Aldous Huxley: *Doors of Perception.*

LSD class drugs

- LSD, mescaline,
- psilocybin, DMT, bufotenine
- Primarily act on Serotonin receptors
- Frontal cortex and limbic system
- Also act on raphe nucleus which functions to filter incoming sensory stimuli
- Disrupts the sorting process
- Flood of sensations and perceptions

LSD-class Hallucinogens

- LSD Types of Agents
- These drugs cause predominantly psychedelic effects.
- Of high school seniors sampled:
- - 1999—12.2% had used LSD sometime during life
- - 2002—8.4% had used LSD sometime during life



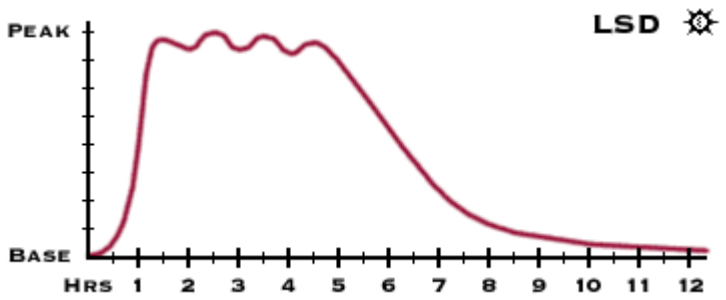
Albert Hofmann and LSD model

LSD Physical Effects

- LSD Types of Agents
- Physiological effects:
- - Massive increase in neural activity in some brain regions
- - Activates sympathetic nervous system (rise in body temperature, heart rate, and blood pressure)
- - Parasympathetic nervous system (increase in salivation and nausea)

LSD Timeline

- About half of the substance is cleared from the body within 3 hours, and more than 90% is excreted within 24 hours.
- Effects of this hallucinogen can last 2–12 hours.
- Tolerance to the effects of LSD develops very quickly.



Psilocybin

- Psilocybin—its principal source is the Psilocybe mexicana mushroom.
- It is not very common on the street.
- Hallucinogenic effects produced are quite similar to LSD.
- Cross-tolerance among psilocybin, LSD, mescaline.
- Stimulates the autonomic nervous system, dilates the pupils, increases the body temperature

Psilocybe Mushrooms

- Small brown mushrooms that stain blue to the touch
- Illicit cultivation but also foraged from temperate climates

Psilocybe Mushrooms:

Religious Use

Various Mushroom Stones (approx 1 ft tall - 1000 B.C. to 500 A.D.)

Religious use continues in Oaxaca, Mexico

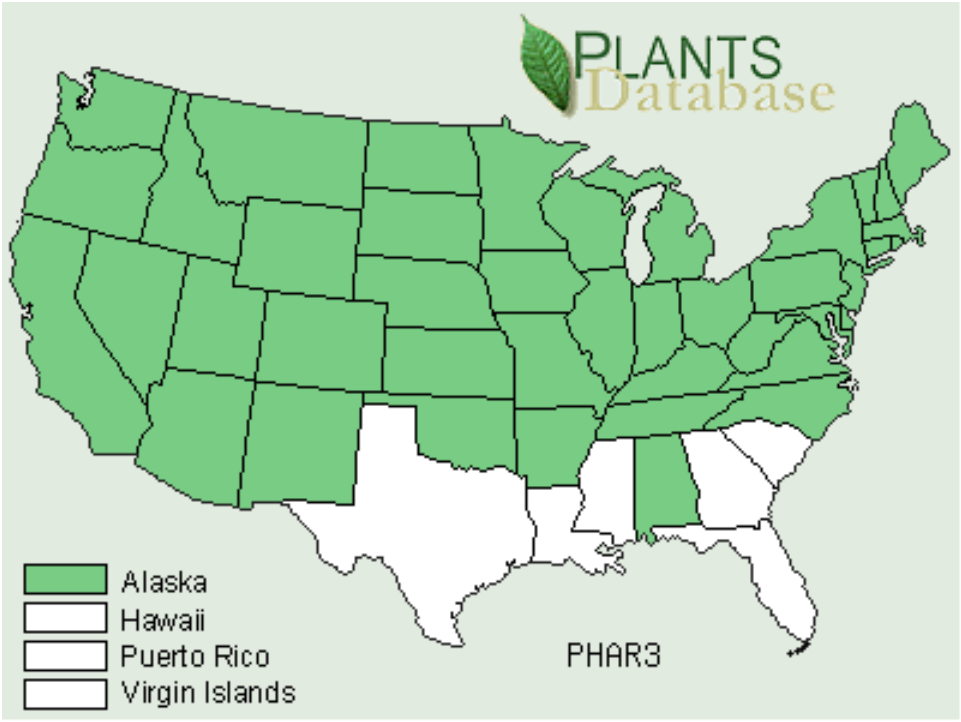
Dimethyltryptamine (DMT)

- Dimethyltryptamine (DMT)
- - A short-acting hallucinogen
- - Found in seeds of certain leguminous trees and prepared synthetically.
- - It is inhaled and similar action as psilocybin.
- - High doses can be quite intoxicating.
- - Can also cause unpleasant reactions/\.

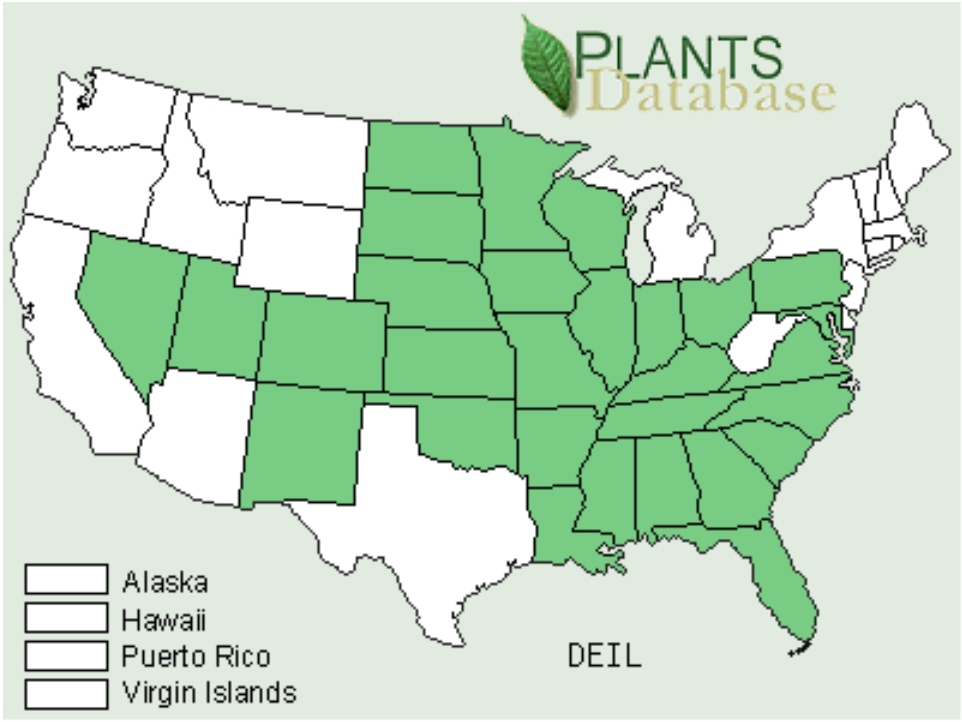
DMT…it's as common as crabgrass…

- "Canary" grass; *Phalaris aquatica, P. arundinacea, P. canariensis, P. tuberosa*
- *Desmanthus illinoensis;* Prairie Bundleflower
- Many other sources; mostly S. America.

Phalaris (DMT source)



Desmanthus illinoesis (DMT Source)



Bufo Frogs…

- Contains bufontinin but intoxication primarily from 5-Meo-DMT
- The toad is NOT licked but glands are milked for poison

Amphetamine Class

- Mescaline
- Synthetic amphetamine derivatives (DOM, MDA, MDMA)
- Act on dopamine and serotonin

Amphetamine Hallucinogens

- Drugs are chemically related to amphetamines.
- They have varying degrees of hallucinogenic and CNS stimulant effects.
- - Release serotonin are dominated by their hallucinogenic action
- - Release dopamine are dominated by their stimulant effects

Amphetamine Hallucinogens

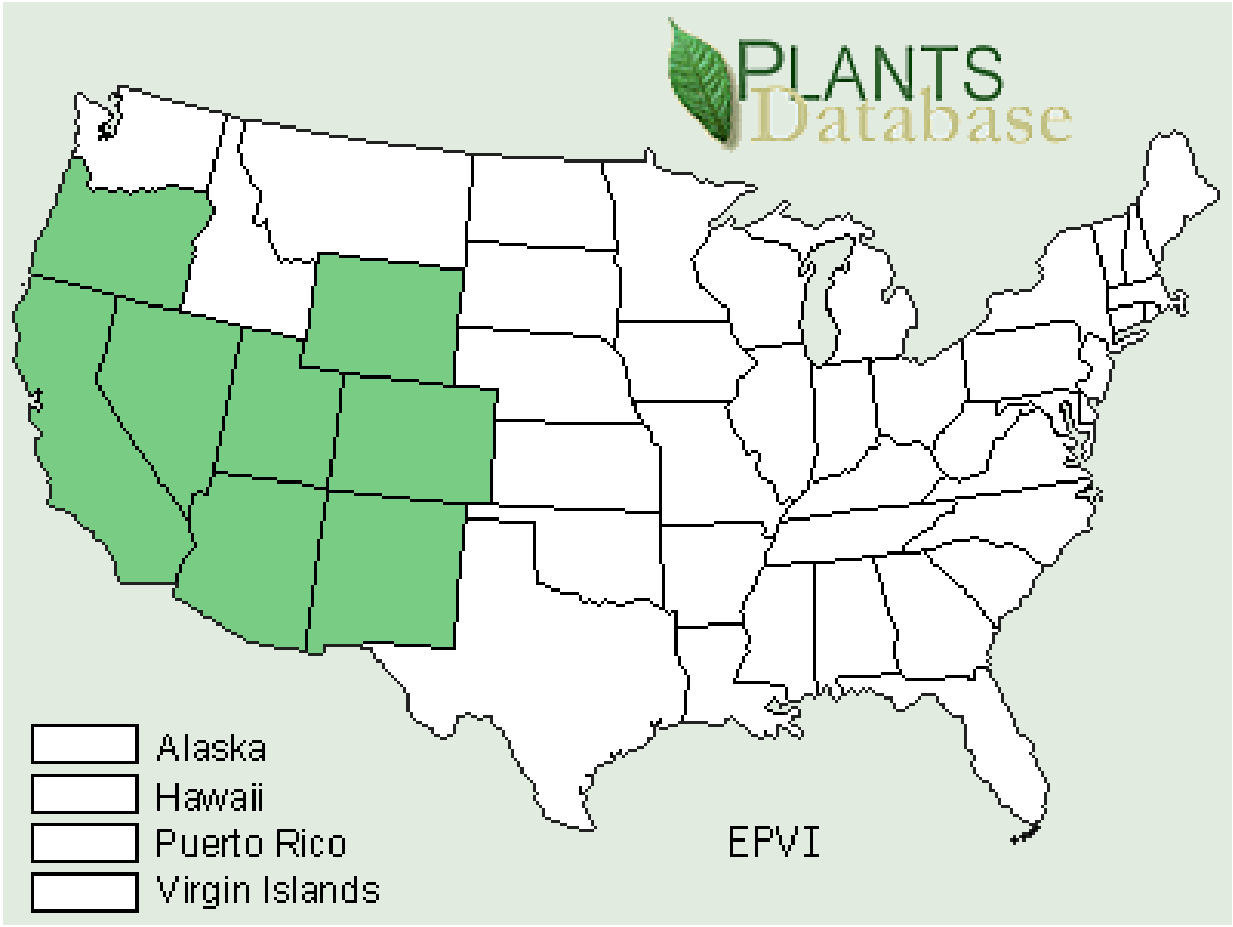
- Mescaline
- “Designer” amphetamines
- 3,4 Methylenedioxyamphetamine (MDA)
- Methylenedioxymethamphetamine
- (MDMA, Ecstasy)

Ephedra of the US

E. trifurca, *E. viridis*, *E. torreyana, E. nevadensis* and *E. californica*

- 100 gm dried ephedra could contain anywhere from 0 to 2.6 gm of ephedrine.

Ephedra grows in the deserts of the Southwest

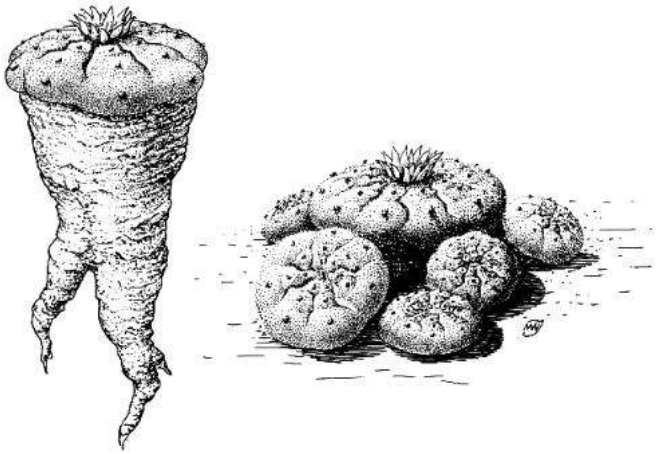


Mescaline

- Mescaline is the most active drug in **peyote cactus**; it induces intensified perception of colors and euphoria

- - Effects include dilation of the pupils, increase in body temperature, anxiety, visual hallucinations, and alteration of body image, vomiting, muscular relaxation.
- Very high doses may cause death.
- - Street samples are rarely authentic.

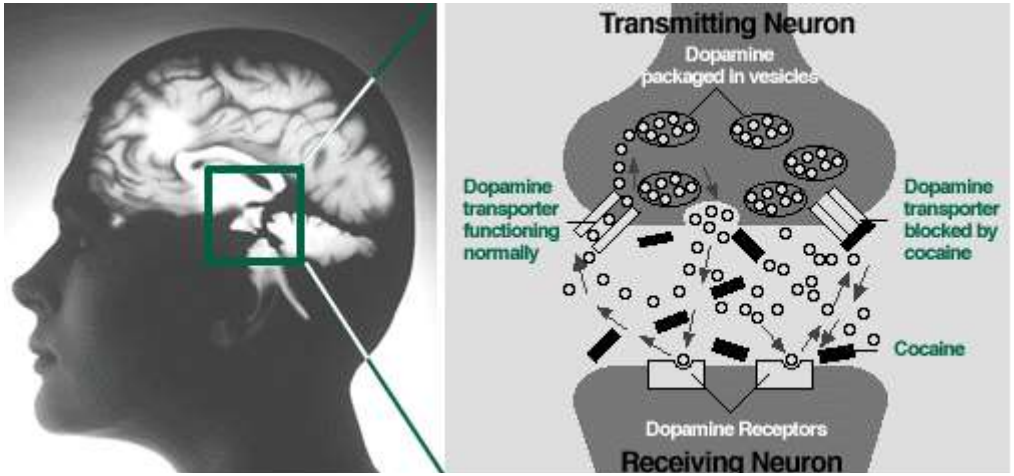
Peyote



- *Lophophoria williamsii* contains 1.5% mescaline (β-3,4,5-trimethoxyphenethylamine)
- 3mg/kg potent intoxication
- Up to 8 to 10 hour duration
- Continued religious use in North America
- Other cacti used in South America and also…

Psychostimulants

The most common psychostimulants (cocaine, MDMA and amphetamine) act on the synapse to increase the activity of dopamine, noradrenaline and serotonin.



Cocaine blocks pre-synaptic reuptake

MDMA ('Ecstasy')

- A synthetic amphetamine derivative, usually sold as small tablets or capsules
- Many tablets sold as ecstasy also contain other chemicals including: ketamine, GHB, amphetamine, caffeine.
- A recent study (Baggott et al 2000) found that:
  - 63% contained MDMA
  - 29% contained other substances (e.g. caffeine, psuedoephedrine)
  - 8% contained no MDMA

MDMA ('Ecstasy'): Effects

- Immediate sought after-effects, 4-6 hours in duration
  - euphoria, increased confidence, increased perception of closeness to others, visual hallucinations

- Negative effects
  - jaw clenching, anxiety, paranoia, insomnia, dry mouth, increased body temperature

Party drug culture

- High levels of activity: hydration and hyperthermia
- Poly-drug use, illicit and misuse of prescribed substances:
  - Viagra used primarily within the gay community
  - Anti-depressants and benzodiazepines thought to increase the ‘high’ or relieve the ‘come down’ associated with party drug use

Risks of Ecstasy

- Toxicity: MDMA overdose is rare
  - associated with intense sympathomimetic responses and active hallucinations as well as thermoregulatory, neurologic, cardiovascular, hepatic and electrolyte disturbances (Gowing et al 2002).
- Risks of adulterants
- Dependence syndrome (occasionally)
- Some evidence of cognitive impairment as a result of long term use (Kalant, 2001)
- Association between long-term MDMA use and emotional disturbance (depression).

Anticholinergics

- Attach to Ach receptors and act as antagonists
- Found in Belladonna, Nightshade, Jimsonweed and Mandrake plants

Ach Antagonists

- Plants containing scopolamine
- Low doses produce amnesia, fatigue, mental confusion, dreamless sleep and loss of attention
- High doses: Hallucinations, paralysis of respiratory system, coma, and death.
- Side Effects: increase in sympathetic activity
- Hot as a hare, dry as a bone, red as a beet, and mad as a hen

Datura stramonium

- Leaves typically cut and smoked
- Contains atropine, scopalomine
- Ancient ceremonial use in the U.S.
- Occasional report of death by ingestion of root
- Many other sources for atropine and scopalomine
- Member of Nightshade family
- "Jimson weed"

Dissociative Drugs

Dissociative Drugs

PCP (phencyclidine)

Ketamine

Dextromethorphan

• Phencyclidine (PCP)

- It was developed as an intravenous anesthetic,
- but found to have serious adverse side effects.
- It differs from the other traditional hallucinogens.
- It is a general anesthetic in high doses.
- It causes incredible strength and extreme violent behavior.
- Management of the severe psychological reactions requires drug therapy.

PCP physiological effects

- - Hallucinogenic effects, stimulation, depression, anesthesia, analgesia
- - Large doses can cause coma, convulsions, and death.
- PCP psychological effects
- - Feelings of strength, power, invulnerability;
- perceptual distortions, paranoia, violence,
- Potential for psychotic break.

Ketamine (“Special K”)

- Anesthetic developed to replace PCP, manufactured by Pfizer
- Used in human and veterinary medicine
- Injected or dried and snorted
- Feelings of floating, or sometimes terrifying “bad trip” called “K hole”
- “Vitamin K”
- “K”
- “Bump”

DXM **(dextromethorphan)**

Cough suppressant

- (Also used to boost effects of analgesics for severe pain)
- Typical dose 15-30 mg. for cough
- 4 or more ounces may cause distorted visual perceptions, similar effects to PCP and Ketamine
- “Robo”
- Internet groups to discuss “Robo-ing”