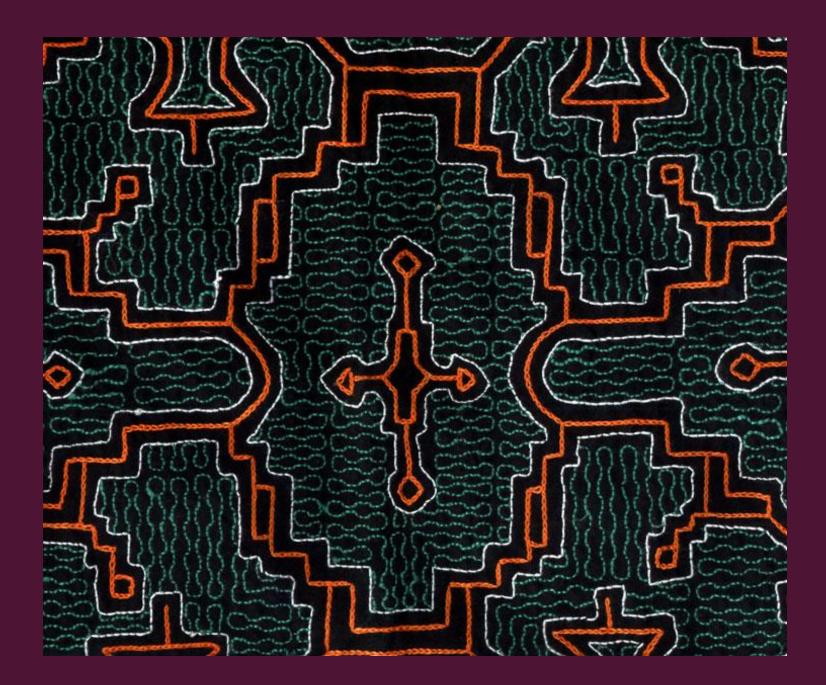
OVERVIEW ON THE HISTORY OF PSYCHEDELICS AND MDMAAS TREATMENTS FOR PSYCHIATRIC DISORDERS

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NATIONAL ACADEMIES WORKSHOP ON PSYCHEDELICS



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- Scientific Advisory Panel
 - Lobe Sciences

Disclaimer: None of my slides and/or handouts contain any advertising, trade names or productgroup messages. Any treatment recommendations I make will be based on clinical evidence or guidelines.

CONVERGENT EVOLUTION – ANTHROPOLOGY OF PSYCHEDELICS

Sacramental use for 7,000+ years:

- Religious and medicinal
- Initiation rites
- Diverse cultures
- Widely used
- Influenced religion, philosophy, art



MARIA SABINA

"Heal yourself, with beautiful love, and always remember ... you are the medicine."

-Maria Sabina

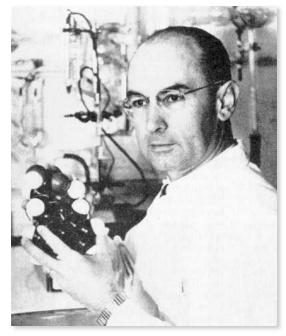


RECEIVING his mushrooms, Wasson takes his night's ration from the hand of *Cwandrva* Eva Mendez. In right background Guy Stresser-Péan, French anthropologist who accompanied Wasson, has begun to chew his own supply. EATING his mushrooms (below), Wasson takes them from cup holding his night's quota as the curowdera prays at the household altar. He chewed them slowly, as is the custom, and his six pair took about a half hour to eat.

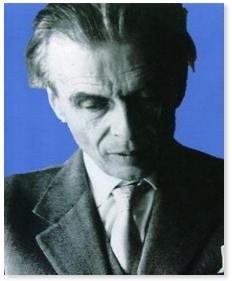
Wasson, Gordon. "Seeking the Magic Mushroom." Life Magazine. 13th May 1957. Pg 100.

WESTERN PSYCHEDELIC PIONEERS: 1940S-1960S

Dr. Albert Hofmann



Aldous Huxley



740 North Kings Road Los Angeles 46 Cal

March 30th 1956

Dear Humphry,

Thank you for your letter, which I shall enswer only briefly, since I look forward to taking to you at length in maxiMixikummaxx. New York before very long. About themacmargemaxes a name for these drugs --- what a x problem. I have looked into Liddell and Scott and find that there is a verb phanercein, to make visible or manifest; and an adjective phanerce, a make visible or manifest; and an adjective phanerce, a make visible or manifest; and an adjective phanerce, a make visible or manifest; and an adjective phanerce, a make visible or manifest; and an adjective phanerce, a make visible or manifest; and an adjective phanerce, a make visible or manifest; and an adjective phanerce, a make visible or manifest; and an adjective phanerce, a make the state of the set of the s

Institutetxpenxhearaxaan

I expect to be flying east on the tenth, or eleventh, and will let you know before than where we shall be staying ---possibly not in a hotel at all, but in a borrowed apartment.

Yours. AWWS Phanenothymy - subtantine Phanenothismic - aspective To make this trivial word sublime, Take half a framme of phanerothym To pumb the depths on soar angelic, Just take a prich of psychodelic

Aldous Huxley to Humphrey Osmond, March 1956

DOX 1056 Weyburn iny dear Aldon To fation Hell OR go angelic take a prich of . PSYCHEDELIC (Delos te manifest like phoneno mymes, I suggest we discuss which to push for before the engagement. I have booked at the Buckingham, I trust successfully of should see you on the night of Wednesday 11th. I shall call you pravided 1 don't get in too late. We might decide to lama muy whole address into Rhyming couple to . It would be arresting. I hope to get anothere coffen of cloceon stut the one we bought togethere was a great success. Yeary

Humphry Osmond's reply to Aldous Huxley's letter of 30 March 1956, featuring his revised "psychedelic" ditty, April 1956.

Humphrey Osmond to Aldous Huxley, April 1956

Bisbee, Cynthia Carson, et al., eds. Psychedelic Prophets: The Letters of Aldous Huxley and Humphry Osmond. Vol. 48. McGill-Queen's Press-MQUP, 2018,

NOMENCLATURE

Psychedelic: Mind manifesting

(Aldous Huxley, Humphrey Osmond)

Entheogen: Accessing the divine within

- (Huston Smith)
- Hallucinogen: Mind journeying
 - (ancient Latin "Allucinari")

NOMENCLATURE

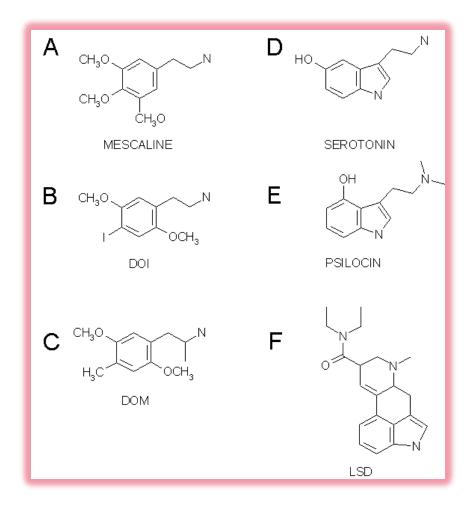
Alternative Terms:

"Deliriants", "Delusionegens", "Eidetics", "Misperceptinogens", "Mysticomimetics", "Phanerothymes", "Phantasticants",
"Psychodysletpics", "Psychogens",
"Psychointegrators",
"Psychosomimetics", "Psychotaraxics",
"Psychoticants", "Psychotogens",
"Psychotomimetics", "Schizogens"

Handbook of MEDICAL HALLUCINOGENS edited by **Charles S. Grob Jim Grigsby**

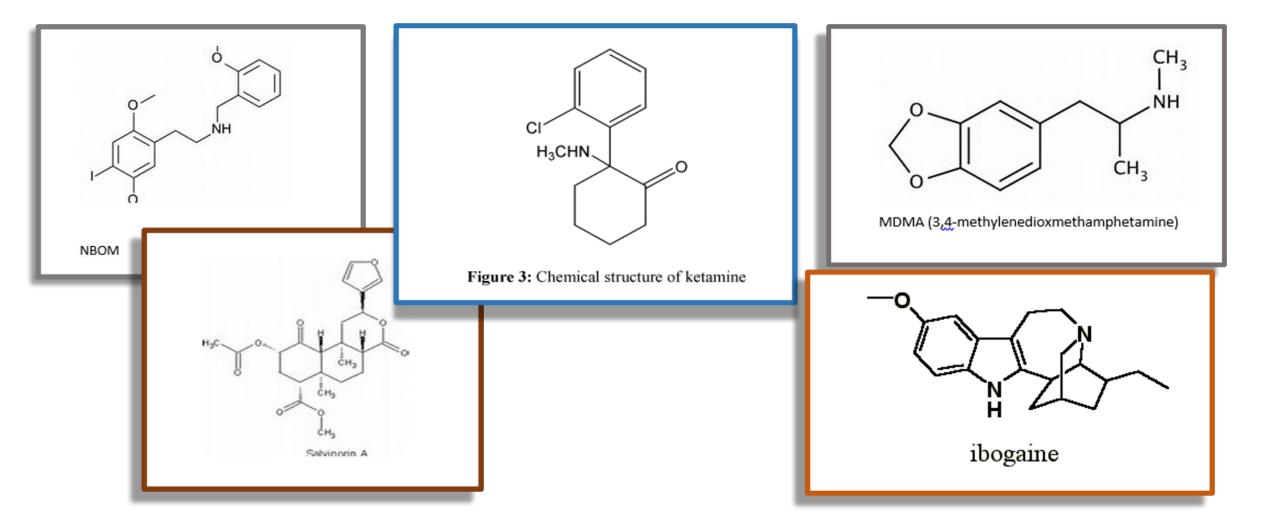
Guilford Press, 2021

PHARMACOLOGY OF CLASSICAL HALLUCINOGENS



- Role in discovery of serotonin neurotransmitter system (Freedman, 1961)
- 5-HT2A receptor agonists
- Blocked by 5-HT2A antagonist ketanserin (Vollenweider et al, 1998)
- Repeated administration leads to rapid development of tolerance and downregulation of 5-HT2A receptor (Nichols, 2016)

PHARMACOLOGY OF NON-CLASSICAL HALLUCINOGENS



ETHNOBOTANY OF HALLUCINOGENS



Psilocybe cubensis



Lophophora williamsii



Claviceps purpurea

ETHNOBOTANY OF HALLUCINOGENS



Psychotria viridis





Banisteriopsis caapi

Ayahuasca

SUBJECTIVE EFFECTS OF PSYCHEDELICS

This state is marked by:

- Stimulation of affect
- Enhanced ability for introspection
- Similar to dream and hypnogogic states
- Perceptual changes (e.g., illusions, synaesthesias, affective activation and alterations of thought and time)

SUBJECTIVE EFFECTS OF PSYCHEDELICS

- Characteristics Of The Psychedelic Peak Experience¹
 - Sense of awesomeness and reverence
 - Deeply felt positive mood
 - Transcendence of time and space
 - Sense of unity or oneness
 - Transiency
 - Paradoxicality
 - Ineffability
 - Meaningfulness of psychological and/or philosophical insight

EXTRAPHARMACOLOGICAL VARIABLES: SET & SETTING

Set:

- Personality structure
- Current thoughts
- Current mood
- Expectations
- Intention

Setting:

- Physical, social and cultural environment
- Safety parameters
- Embedding of therapeutic context
- Guiding and oversight of psychedelic experience by trained therapist(s)

PARADIGM SHIFT

Conventional Psychopharmacology:

- Drug administered on daily basis for weeks/months/years
- Ameliorate a presumed pathological brain state
- Relief not dependent on patient's attitude or insight



PARADIGM SHIFT

Psychedelic Psychopharmacology:

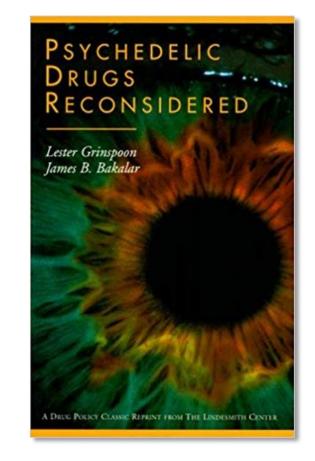
- Drug administered once or several times
- Loosens defenses
- Facilitates insight
- May induce a mystical experience
- Carefully monitored
- Supportive psychotherapy



EARLY WESTERN RESEARCH: 1940S-1960S

"Over a thousand clinical papers were published in the professional literature discussing the experiences of 40,000 patients treated with hallucinogens."

- Grinspoon and Bakalar, 1979



EARLY WESTERN RESEARCH: 1940S-1960S

Treatment applications included:

- Alcoholism and drug addiction
- Psychosomatic disorders
- Chronic post-traumatic stress
- Obsessive-compulsive disorder
- Anti-social behavior
- Autism
- Existential anxiety in terminal cancer

CULTURAL TURMOIL LATE 1960S-1970S

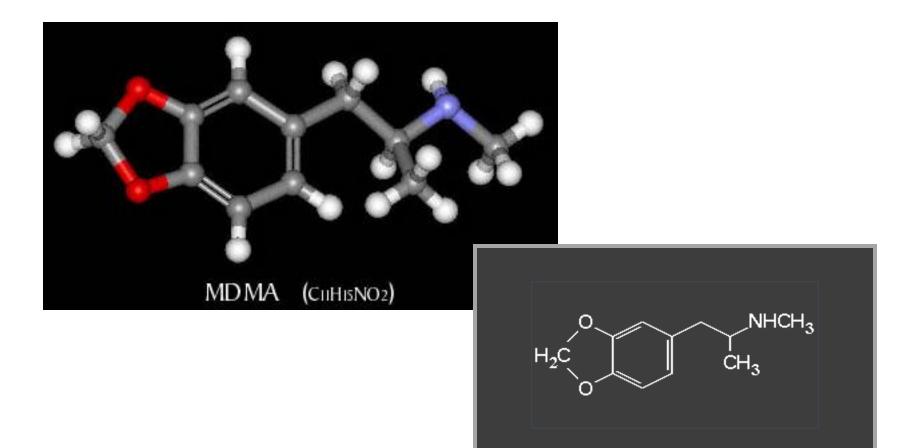
All Kinds of 'Kooks' Gather for 'Happening' Seattle Daily Times (Seattle, Washington), 15 January 1967, page 1



Maher, Stephen. "The Lost Counterculture." Jacobin. Feb 2015.

AP Photo/Steve Rees

MDMA: CHEMICAL STRUCTURE



MDMA: ANALOGS IN NATURE



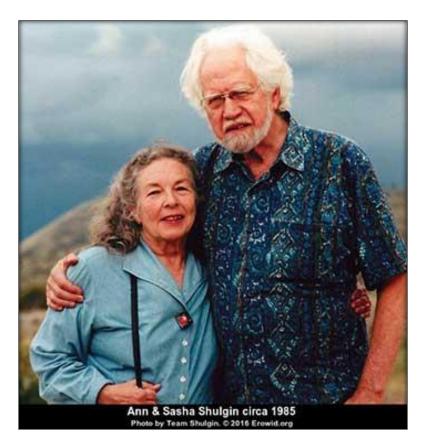
Myristica fragrans - Nutmeg



Sassafras albidum - Sassafras tree

3,4-METHYLENEDIOXYMETHAMPHETAMINE (MDMA)

- I912 Chemical Synthesis
- 1914 Patented by Merck Pharmaceutical Co.
- I953 U.S.Army sponsored toxicology studies-EA 1475
- 1976 Initial therapeutic explorations



MDMA 1980S-1990S

- 1981 Popularization outside of medical area
- I984 DEA scheduling hearings
- 1985 DEA Schedule I
- 1986 Initiation of animal studies
- I994 First Phase I Clinical Study

A Hallucin	ogenic Dru
WASHINGTON, May 31 (AP) — Fed- eral officials announced today that they were taking emergency action to ban a drug widely known as Ecstasy, saying that abuse of the drug that be- mergen and the second second second the second second second second transmission of the brug Enforcement Ad- ministration. Ecstasy, whose scientific name is 3,4-methylemedioxymethampheta- mine. will continue to undergo tests while the emergency ban remains in ef- fect for one year. Some psychothera- pists maintain that the drug creates a feeling of well-being in patients, mak- ing them more receptive to treatment. MDMA is deminative to treat the controled Substances Act. This is the most restrictive of the five catego- ries established by Federal drug law. Warning of Health Threat A drug agency said. Other substances on the list include heroin, cocaine and LSD. "All of the evidence D.E.A. has re- ceived shows that MDMA abuse thas be- come a national threat," Mr. Lawn said in a statement. "This emer- gency action is a stoggap measure to curb MDMA abuse until the adminis- trative process can be completed." Officials of the drug agency said their intention was to replace the emer-	I gency ban on MDMA with a permi ban within a year. Possession of a "trace" of a Sch i drug by a first-time offender ca sult in 15 years in prison and a Si fine. The drug agency was grantee emergency power to ban drugs u the Comprehensive Crime Contro (1984. It has been used once befor March when the Justice Depart agency banned "synthetic her methylentanyl. The drug agency acted against stasy after it received inform about partices being held in Texas i drug A. Officials and toda", sai drug agency's office of Diversion Co said that effective July I there woo no lawful use of the drug unless e tions were granted by the agency. He said hearings scheduled for summer in Los Angeles, Kansas i "In the literirin, D.E. A. is estat ing cheffer de priversion con schedule I" on a permanent besi is foud "determine the future stat is foud "determine the future stat is foud "determine the future stat is fut found in the bitric of Colu would "determine the future stat ing appelited registration proced be effects of MDMA con continuer terrupted," Mr. Haislip said. MDMA is found in tabet, ca and powder form and sells from Jab tra dosage unt, or 70 to \$100 gram, the agency said.
Mount St. Helens Lava Flow VANCOUVER, Wash., May 31 (UP1) — Mount St. Relens today continued a dow coring emption that a deded new lava to a huge dome that has formed in the steaming, cloud-shrouded crater of the \$3,35-foot-high volcano in southwest Washington.	young protessionals. He interest LSD, which proved attractive to n drug users in the 1960's. Officials of the drug agency said had no estimate of how many pe used the drug, but they said us MDNA seemed to be most widesp in California, Texas, south Florida New York and other Northeas states.

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Rave in Manchester, UK dubbed "Madchester" in 1989

New York Times, June 1, 1985

MDMA-ASSISTED TREATMENT

- Adjunct to psychotherapy
- Treatment paradigm shift
- Importance of set and setting

- Relatively mild
- Easily controlled

Short acting

MDMA-ASSISTED TREATMENT

- Empathogen/Entactogen
- Enhanced capacity for introspection
- Improved mood

FUTURE

- Optimize safety
- Strengthen ethical standards
- Prioritize public health
- Create opportunity for greater diversity
- Respond to changing legal status
- Mitigate risks of rapid commercialization



CENTRAL AMERICAN MUSHROOM STONES 1500 BCE

