

# Lysergic acid diethylamide (LSD)

*By Drug Science and  
Small Pharma*



Part 1 - History & Law

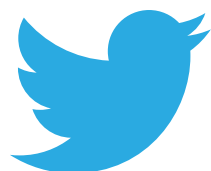


Drug Science was formed by a committee of scientists with a passionate belief that the pursuit of knowledge should remain free of all political and commercial interest.

Founded in 2010 by Professor David Nutt, following his removal from his post as Chair of the Advisory Council on the Misuse of Drugs, Drug Science is the only completely independent, science-led drugs charity, uniquely bringing together leading drugs experts from a wide range of specialisms to carry out ground-breaking research into drug harms and effects.

The Drug Science mission is to provide an evidence base free from political or commercial influence, creating the foundation for sensible and effective drug laws. Equipping the public, media and policy makers with the knowledge and resources to enact positive change.

Drug Science wants to see a world where drug control is rational and evidence-based; where drug use is better informed and drug users are understood; where drugs are used to heal not harm



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Led by an experienced team committed to making a difference for people suffering from mental health conditions, Small Pharma believes that together, as a community, we can help unlock cutting edge science and bring new therapies to treat mental health disorders.

Small Pharma is a virtual biopharmaceutical company on a mission to improve mental health by progressing psychedelic therapies to the clinic. At Small Pharma, they have identified the field of psychedelic medicine as an exciting and unexplored area of drug discovery, with the ability to completely transform our understanding and approach to mental health. As compounds neglected by risk averse traditional pharma, the Small Pharma team are passionate about becoming the R&D leaders of psychedelic drug discovery and development.

Small Pharma funds clinical trials of DMT and related psychedelic compounds as a tool to augment psychotherapy for the treatment of depression and other mental health conditions. Their current focus is to unlock the exciting potential of DMT therapy as a treatment for Major Depressive Disorder.



# The discovery of LSD



**1938**

Lysergic acid diethylamide (LSD) was first synthesised by Albert Hoffman at the Sandoz AG Pharmaceutical Company in Basel, Switzerland, during a discovery project for pharmacologically active derivatives of lysergic acid

Hoffman hoped LSD could act as an analeptic however, it caused unintended excitable behaviour in experimental animals and testing was halted



**1943**

**16th April**

Hoffman accidentally ingested a small amount and recorded his experiences as seeing “*extraordinary shapes with intense, kaleidoscopic play of colors*”

**19th April (Bicycle day)**

Hoffman took a larger dose, experiencing intense psychedelic effects whilst on his bicycle ride home





# Structural elucidation



**1947**

Dr Werner Stoll, a psychiatric researcher from the University of Zurich, published the first paper on the psychological effects of LSD following a pilot study on humans



**1949**

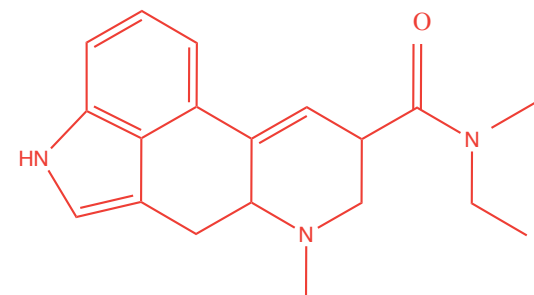
11 years after it's first synthesis, the entire chemical structure of LSD was resolved and confirmed



**1956**

Dr Edmund Kornfeld, along with his colleagues at Eli Lilly, published the first synthesis of Lysergic acid

Hoffman's documentation of it's powerful properties led to an increased interest by organic and medical chemists



[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES AND THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

## The Total Synthesis of Lysergic Acid

BY EDMUND C. KORNFIELD, E. J. FORNEFELD, G. BRUCE KLINE, MARJORIE J. MANN, DWIGHT E. MORRISON, REUBEN G. JONES AND R. B. WOODWARD<sup>1</sup>

RECEIVED DECEMBER 24, 1955

# Pharmaceutical LSD - rise & fall

**1943**

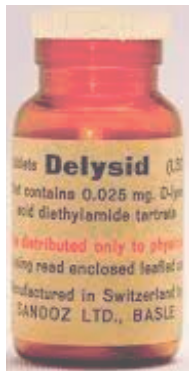
Shortly after it's first production, Sandoz pharmaceutical company filed for a patent on LSD as a therapeutic product

**1963**

Sandoz' patent expired enabling LSD to be used and developed by any pharmaceutical manufacturer or scientist

**1970**

The controlled substance act was passed in US congress, which classifying LSD (and psilocybin) as Schedule 1 compounds



**1948**

Sandoz were granted their patent, enabling them to own and restrict LSD manufacture and use for the medical and psychiatric community under the name **Delysid**

**1968**

LSD was made illegal in the US forcing research and clinical use to end



# LSD use in medicine

While the use of ergot alkaloids in folk medicine has been practiced for millennia, particularly for the treatment of migraine and to reduce bleeding from the uterus after childbirth, systematic investigations on their therapeutic potential began about 100 years ago

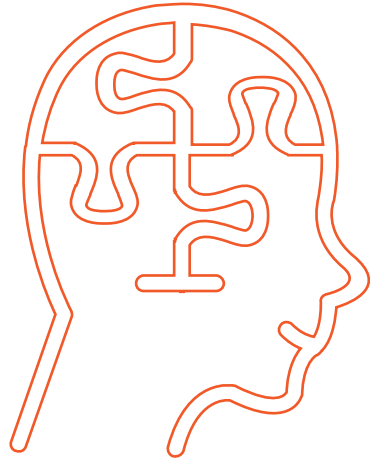
The discovery of LSD & its psychoactive effects gained worldwide attention in the 1950's, giving rise to its use within clinical and research settings

LSD assisted therapy was used to treat over 40,000 psychiatric patients and children with autism in the 50-70's

Many early LSD studies during this time were not robust due to a lack of clear endpoints, control group and unethical practices



# LSD insights into psychiatry



LSD has been termed a '**psychotomimetic**', a substance induced psychological state which mimics psychotic symptoms

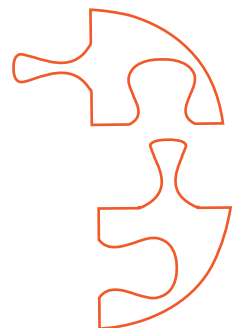
Scientists and clinicians anticipated that these psychoactive properties could help to understand psychiatric disorders

This led to personal experimentation with the objective to shed light on their patients' experience

Despite effort, ambitions to understand psychiatric pathology were not realised

Psychiatrist Humphrey Osmond believed that the altered sense of consciousness and awareness had therapeutic potential in the treatment of alcoholism and other mental health disorders, which he tested in the 1950's and 60's

He coined the term psychedelics, which means "***mind manifesting***" to describe LSD's psychological effects which led him to hypothesise a controversial theory at the time, that schizophrenia was a result of a chemical imbalance within the brain



# Therapeutic LSD

Osmond and others, inspired his colleague Colin Smith to postulate the utility of psychedelics as a ***“useful adjunct to psychotherapy”*** following a study treating 24 patients with LSD which was published in 1958

In 1955, British Psychiatrist Ronald Sandison opened the **first purpose-built LSD-therapy clinic** in a Worcestershire hospital. The treatment incorporated **psychotherapy, music, art** and patients had the opportunity to discuss their experiences in **daily group sessions**

Following LSD's ban in the 1970's, the past 30 years has seen a resurgence in psychedelic research

Today, there are over 17 clinical trials involving LSD listed on [clinicaltrials.gov](https://clinicaltrials.gov)

A combination of controlled clinical trials and modern technology has enabled a better understanding of their mechanism at the molecular level and structural level



# Types of LSD therapy

## Psychanalytic therapy



Evolved in Europe between the 1950s - 1970s, inspired by Sandison's work



Small to moderate doses of LSD (30–50 µg) used as an adjunct to psychoanalytical informed talk therapy, which can be administered over multiple sessions



The non-hallucinatory state produced is thought to help the patient access and process suppressed memories and emotions

## Psychedelic therapy



Inspired by Psychiatrics in the 1950's such as Osmond & his collaborator Abram Hoffer



Preparatory therapy sessions, followed one-several high doses of LSD (75-250 ug), followed by an integration therapy session after the drug effects have subsided



To create a so-called peak psychedelic experience which describes extreme changes in consciousness and sometimes mystical experiences. These acute changes can help to promote longer-term improvements in psychiatric and functional symptoms

# LSD in the cold war

## 1953 - 1973

The U.S government's Central Intelligence Agency (CIA) exploited LSD's psychoactive properties during the cold war in an illegal project named **'MK-Ultra'**, also referred to as the **'mind-control program'**

The project was directed by a CIA chemist, Sydney Gottlieb, who aimed to develop psychological warfare that could be used against the soviet bloc

LSD was tested on both volunteers and naïve U.S. and Canadian citizens to assess its potential as a mind-control, interrogation and psychological torture technique

Experiments took place in prisons, hospitals and universities



The UK's MI5 and MI6 were also reported to have used LSD as a method of interrogation during the time

# Operation midnight climax

Operation midnight was a series of activities conducted by the CIA as part of MK-Ultra whereby prostitutes were employed to lure men into government run '*Safe houses*' set up across San Francisco, California and New York City

Men were unknowingly dosed with LSD, watched and recorded by CIA agents

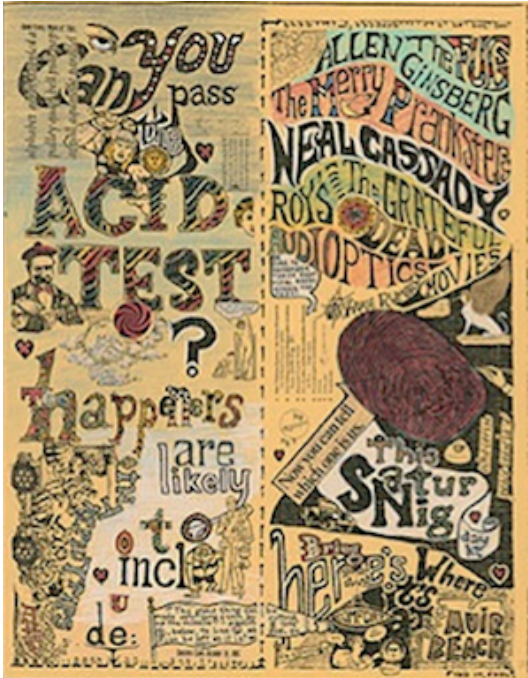
These activities were largely unregulated with some reports describing CIA agents creating a fun and party-like atmosphere



The MK-Ultra project ran for 20 years, ending in 1973. In 1975 its details were uncovered leading to a congressional investigation of the CIA's activities



# Ken Kelsey's 'acid tests'



Author of the novel 'One Flew over the Cuckoo's nest', Ken Kesey, was one of the MK-Ultra experiment volunteers who took LSD while he was a student at Stanford University

In late 1965, Kesey hosted his first of a series of parties called 'Acid tests'

Over the course of the next 3 years, multiple 'acid test' parties took place mostly in California, which centred around the taking of LSD and listening to music

Author Tom Wolfe based his 1968 non-fiction book, The Electric Kool-Aid Acid Test, on the experiences of Ken Kesey and the Merry Pranksters. The book chronicles the Acid Test parties and the growing 1960s hippie counterculture movement

# Early research

## 1960 - 1962

Psychology professor, **Timothy Leary**, and his colleague, **Richard Alpert**, documented their observations on changes to consciousness after giving LSD (as well as psilocybin and mescaline) to students in series of controversial studies conducted at Harvard University

Leary was interested in exploring the potential of psychedelic drugs to provide insight into mental illnesses

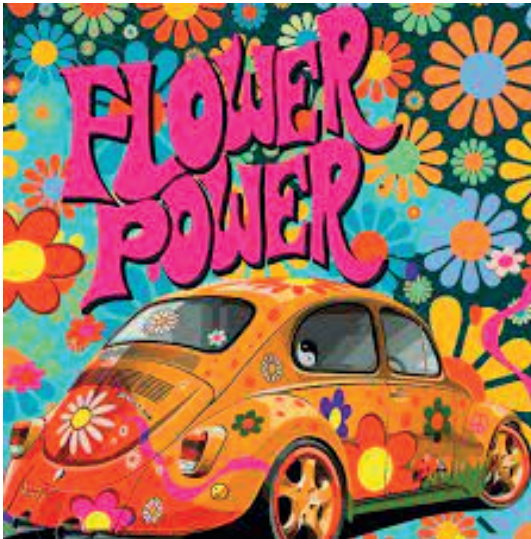
## 1963

Leary was fired from Harvard after the legitimacy and ethics of his research was questioned

Despite this, he and Alpert (now known as Ram Dass) continued to advocate LSD's use and became key figures in the psychedelic counterculture movement of the 1960's

# 1960's counterculture

During the 1960's there was a growing theme of anti-establishment and anti-war in the western world following widespread social tensions and events such as the Vietnam war and nuclear weapon proliferation



This era produced a revolutionary youth movement based on love, peace, creative exploration which often involved experimentation with LSD and other psychoactive drugs, used as an aid to help bring people together

# Nixon's war on drugs

In the late 1960's, the US government faced increasing public opposition and anti-war protests in relation to their involvement in the vietnam war

The white house associated this opposition with drug-taking and an anti-establishment youth culture which led President Nixon to launch his monumental **war on drugs** on 1969



This noteworthy public campaign declared drug abuse to be “public enemy number one” and the legislation declared strict law enforcement against illicit drug use. Measures included mandatory sentencing, no-knock warrants and a drug offense conviction could result in an american to lose their voting rights

Drug related crime provided a scapegoat to incarcerate opposers of the Nixon cabinet and black US citizens

# LSD influence on music

Music was heavily influenced by LSD and psychedelics over the past 60 years

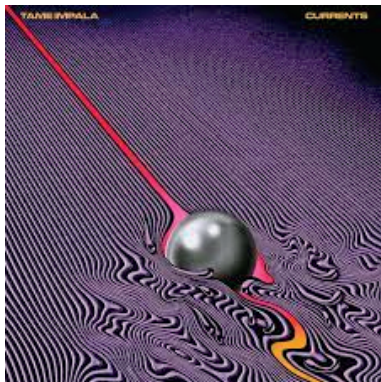


## Acid-rock

Originated during and drew inspiration from the psychedelic movement of the mid-60's, with the term '**acid**' specifically referring to LSD

It combined sounds of rock, blues, distorted sounds and psychedelic lyrics

Examples include: Pink Floyd, The Charlatans & Jimi-Hendrix



Other forms of so-called psychedelic music include the sub-genre of **Psychedelic folk** e.g., Tim Buckley, The incredible String band, T.Rex

Influences remain today with bands such as Stealing Sheep and Tame Impala



# LSD influence on western culture

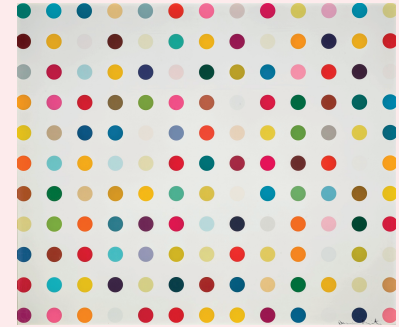
As well as music, LSD has also influenced art, literature, film and fashion over the years

## Art

LSD has influenced a lot of artwork, such as kaleidoscopic imagery, bright colours, swirling and morphing scenes and shapes

## Examples

**Mati Klarwein's** iconic psychedelic imagery including many album covers during the 60's and 70's



**Damien Hirst's** famous "Spots" collection of pharmaceutical paintings presented a series of uniquely coloured and precisely placed painted spots, one of which was titled 'LSD'

## Literature and film

The effects of LSD have been depicted in many films and books through the years, both visually and narratively

## Examples

***Fear and Loathing in Las Vegas*** and ***Easy rider*** are two stories of the 1960's counterculture which featured their characters taking LSD

# LSD - Law

**1970** - The controlled substance act was passed in US congress. The act served to consolidate various drug laws and implemented a system of categorising substances based on their medicinal value, harmfulness and abuse liability

**1971** - United Nations' Convention on Psychotropic Substance required all participating parties or nations to prohibit the use of LSD making it illegal

UK Misuse of Drugs Act was passed classifying regulated substances into classes A, B and C, **LSD was determined as a Class A drug**. Since 1971, this has not been formally reviewed

LSD was determined and remains a Schedule 1 compound. It describes LSD as having ***“little or no accepted medical use and a high potential for abuse”***

**1974** - NIMH declared that there were no medical benefits associated with LSD, halting all ongoing and future research

# References



Abramson A (1959) The Use of LSD in Psychotherapy. Josiah Macy, Jr. Foundation: New York

Busch AK, Johnson WC (1950). L.S.D. 25 as an aid in psychotherapy; preliminary report of a new drug. Dis Nerv Syst 11: 241–243

Cole JO, Katz MM (1964). The Psychotomimetic Drugs: An Overview. JAMA 187(10):758–761

Fuentes, J. J., Fonseca, F., Elices, M., Farré, M., & Torrens, M. (2020). Therapeutic Use of LSD in Psychiatry: A Systematic Review of Randomized-Controlled Clinical Trials. Frontiers in psychiatry, 10, 943

Grinspoon L, Bakalar JB (1979) Psychedelic Drugs Reconsidered. Basic Books: New York

Stoll W (1947). Lysergsäure-diäthyl-amid, ein Phantastikum aus der Mutterkorngruppe. Schweiz Arch Neur 60: 1–2

<https://www.bbc.com/culture/article/20181016-how-lsd-influenced-western-culture#:~:text=LSD%20is%20still%20most%20strongly,and%20Jimi%20Hendrix%20dropped%20acid.>

<https://www.history.com/topics/crime/history-of-lsd>