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# Lysergic Acid Diethylamide (LSD): Unveiling the Mysteries of a Mind-Altering Journey

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**ABSTRACT**

In this captivating review article, we delve into the extraordinary world of lysergic acid diethylamide (LSD), an infamous psychedelic compound that has intrigued generations. Our journey begins with the discovery and historical milestones of LSD, unraveling its enigmatic path through time. We explore its physicochemical properties, revealing the intriguing characteristics that contribute to its unique pharmacology. The absorption, distribution, metabolism, and excretion of LSD are unveiled, shedding light on its pharmacokinetic profile. The mechanism of action of LSD is a puzzle waiting to be solved, as we delve into the intricate interplay between this compound and the human mind. The methods of synthesis employed to create this compound are demystified, providing insights into its production and quality control. Moreover, we explore the medicinal uses of LSD, both past and present, and examine the potential therapeutic applications that continue to captivate researchers. But the journey doesn't end there. We confront the darker side of LSD, exploring its adverse effects and the management of overdose situations. The contraindications of LSD usage are outlined, cautioning against potential risks and interactions. Additionally, we shine a spotlight on the current controversies surrounding LSD, including its recreational use and potential long-term effects on mental health. IN this comprehensive review, we also discuss the conventional and novel marketed formulations of LSD, highlighting the evolution of its administration methods. Patents related to LSD are explored, shedding light on the innovative advancements in this field. As we conclude our exploration, we reflect on the current state of knowledge regarding LSD, emphasizing the need for further research and understanding. Prepare to embark on an enthralling journey through the captivating history, properties, mechanisms, controversies, and potential of LSD. Whether you are a scientist, clinician, or simply curious about the enigmatic realms of psychedelics, this review article promises to captivate and ignite your imagination.

## DISCOVERY

Lysergic acid diethylamide (LSD) was initially synthesized in 1938 and its psychoactive properties were discovered in 1943. It is commonly stated in the scientific literature that the discovery of LSD was a chance occurrence. However, a careful examination reveals that LSD was not a fortuitous finding, but rather the result of a complex process initiated by a well-defined concept and followed by deliberate experimentation. During this process, a serendipitous observation served as a catalyst for a planned investigation, ultimately leading to the actual discovery. This sequence of events often underlies what is commonly referred to as a chance discovery.[1] Albert Hofmann, PhD, the Director of Research at the Department of Natural Products, Sandoz Ltd., Basel, Switzerland, synthesized lysergic acid diethylamide for the first time in 1938 as part of a systematic chemical and pharmacological exploration of partially synthetic amides derived from Lysergic acid. These investigations were conducted at the Sandoz pharmaceutical-chemical research laboratories in Basle, under the leadership of Professor Arthur Stoll. Lysergic acid, which forms the core structure of ergot alkaloids, can be obtained through alkaline hydrolysis of these alkaloids. By employing a newly developed technique, it was demonstrated that lysergic acid could be combined with amines through peptide linkage. This enabled the production of ergometrine, the specific oxytocic component of ergot, also known as ergonovine. This marked the first partial synthesis of a natural ergot alkaloid. By modifying the alkanolamine side chain of ergometrine, a novel synthetic derivative was obtained and named Methergine. Methergine demonstrated superior pharmacological properties compared to the natural alkaloid and is now used worldwide in obstetrics to control hemorrhage. While the primary focus of these investigations was on the oxytocic and hemostatic activities, the newly developed synthesis method was also employed to produce amides of lysergic acid that were expected to possess distinct pharmacological properties based on their chemical structure. As part of this endeavor, the diethylamide of lysergic acid was synthesized with the aim of developing an analeptic compound. The structural relationship between this compound and the well-known circulatory stimulant nikethamide suggested that it might possess analeptic properties. In 1947, the similarity between the subjective psychotomimetic effects of LSD and symptoms of schizophrenia was noted, leading to the experimental use of LSD as a model for psychosis. From 1949 to 1966, LSD (Delysid, LSD 25) was made available to psychiatrists and researchers for gaining insights into the mental state of patients and to facilitate psychotherapy. During the 1950s and 1960s, LSD and LSD-assisted psychotherapy were investigated in relation to anxiety associated with terminal cancer, alcoholism, opioid use disorder, and depression. The scientific literature contains over 1000 published reports on LSD, indicating its extensive study as a pharmacological substance. LSD has been a valuable tool in neuroscience research and drug development and has had a significant impact on the arts and society as a whole.[2]


Fig.1 Lysergic Acid Diethylamide "(6aR,9R)-N,N-diethyl-7-methyl-4,6,6a,7,8,9-hexahydroindolo[4,3-fg]quinoline-9-carboxamide."

**Chemical Formula;** $C_{20}H_{25}N_3O$

## PHYSICOCHEMICAL PROPERTIES

1. **Molecular Weight:** LSD, scientifically known as lysergic acid diethylamide, possesses a molecular weight of 323.4 g/mol. This compound is a sizable molecule comprised of carbon, hydrogen, nitrogen, and oxygen atoms.
2. **Taste**: LSD is universally recognized as tasteless, exhibiting no discernible flavor profile. This attribute poses challenges in detecting LSD in diverse settings, especially when it is mixed with other substances or consumed in minute doses.
3. **Odor**: LSD is characterized by its odorless nature, lacking any distinctive aroma. This attribute enhances its inconspicuousness, making it arduous to detect solely based on olfactory cues.
4. **Color**: LSD exhibits complete colorlessness, devoid of any noticeable hues. This achromatic appearance further contributes to its inconspicuous nature.
5. **Solubility**: LSD exhibits distinctive solubility characteristics. It demonstrates moderate solubility in pyridine, an organic solvent commonly employed in laboratory settings. However, LSD displays slight solubility in water and neutral organic solvents. In contrast, it exhibits high solubility in both alkaline and acidic solutions. In aqueous environments, LSD exhibits a solubility of approximately 67.02 mg/L at 25 °C. These solubility properties significantly influence its bioavailability and distribution within the human body upon ingestion.[1]
6. **pKa**: The acid-base behavior of LSD is elucidated by its dissociation constant, represented by pKa. LSD possesses a pKa value of 7.8, indicating its capability to donate or accept protons under suitable conditions.
7. **UV**: LSD exhibits distinctive absorption characteristics in the ultraviolet (UV) range. In ethanol, it manifests a maximum absorption peak at 311 nm, accompanied by an epsilon value of 257, 1%, 1cm. This specific UV absorption pattern facilitates the identification and quantification of LSD in laboratory settings, particularly when employing spectroscopic techniques.
8. **Crystal Formation**: LSD undergoes crystallization, resulting in the formation of prismatic crystals derived from benzene. The crystal structure of LSD significantly influences its stability and various physical properties.
9. **Melting Point**: LSD possesses a melting point range of 176 to 185 °F (80 to 85 °C). This temperature range represents the phase transition from the solid state to the liquid state, highlighting the compound's thermal sensitivity. The precise melting point may slightly vary depending on the purity and specific form of LSD.
10. **Thermal Instability**: LSD is recognized for its thermal instability, with decomposition occurring at higher temperatures, typically around 240 °C. During the decomposition process, LSD releases toxic fumes containing nitrogen oxides. It is crucial to handle and store LSD appropriately to prevent thermal degradation, as it may lead to the loss of its pharmacological activity and the formation of potentially harmful byproducts.
11. **Optical Rotation**: LSD exhibits a specific optical rotation of 17 degrees at 20 °C/C when a concentration of 0.5 g is dissolved in 100 mL of pyridine.
12. **Stability**: LSD is recognized to exhibit relatively limited stability under various conditions. It is notably sensitive to light, heat, and oxygen exposure, thereby leading to potential degradation.
13. **Partition Coefficient (LogP):** The partition coefficient, often expressed as LogP, delineates the distribution of a compound between two immiscible phases, typically octanol and water. LSD possesses a LogP value of approximately 2.9, signifying its preference for the lipid-rich phase, such as cellular membranes.

14. **Acidity**: LSD exhibits weak acidic properties due to the presence of a carboxylic acid functional group. Under appropriate pH conditions, LSD can undergo ionization, contributing to its interactions with receptors and other molecular targets.

15. **Basicity**: LSD also displays weak basic properties owing to the presence of a nitrogen atom within its structure. Under suitable conditions, it can accept protons and form positively charged species.

16. **Lipophilicity**: LSD is classified as a lipophilic compound, exhibiting an affinity for lipid-rich environments. This attribute allows LSD to readily traverse cell membranes, including the blood-brain barrier, thereby contributing to its psychoactive effects. The lipophilic nature of LSD is influenced by its molecular structure and LogP value.

17. **Hydrolysis**: LSD can undergo hydrolysis, particularly under basic conditions. The cleavage of the ester bond within LSD results in the formation of lysergic acid, which serves as a metabolite of LSD and possesses distinct pharmacological properties. Hydrolysis plays a pivotal role in the metabolism and elimination of LSD from the body.[3]

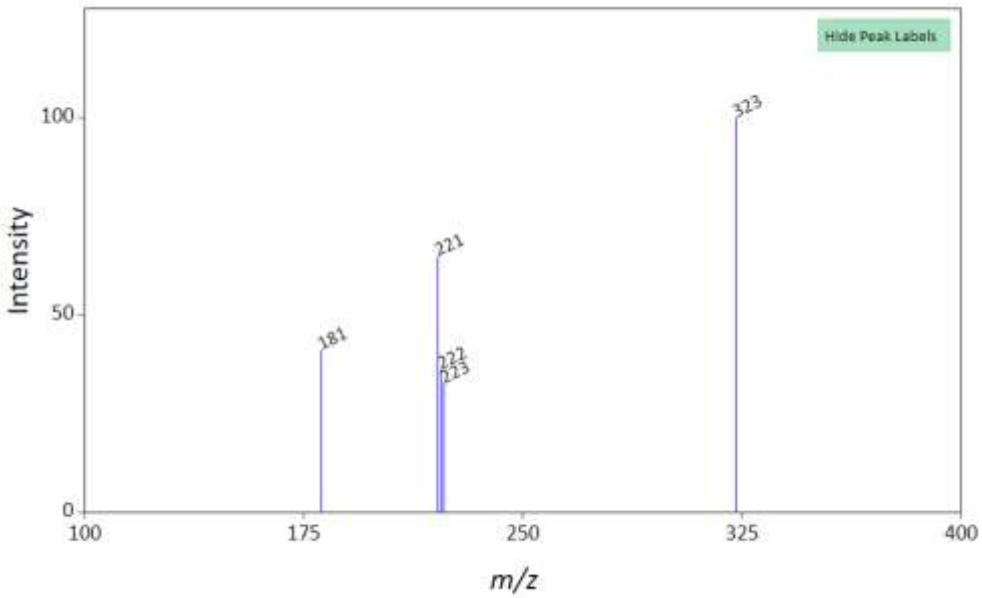



Fig.2. Mass Spectrometry (Top 5 Peaks323 99.99, 221 64.90, 181 41.10, 222 36.20, 223 32.60)

**(Source - https://spectrabase.com/spectrum/6i7IzVplfKQ)**

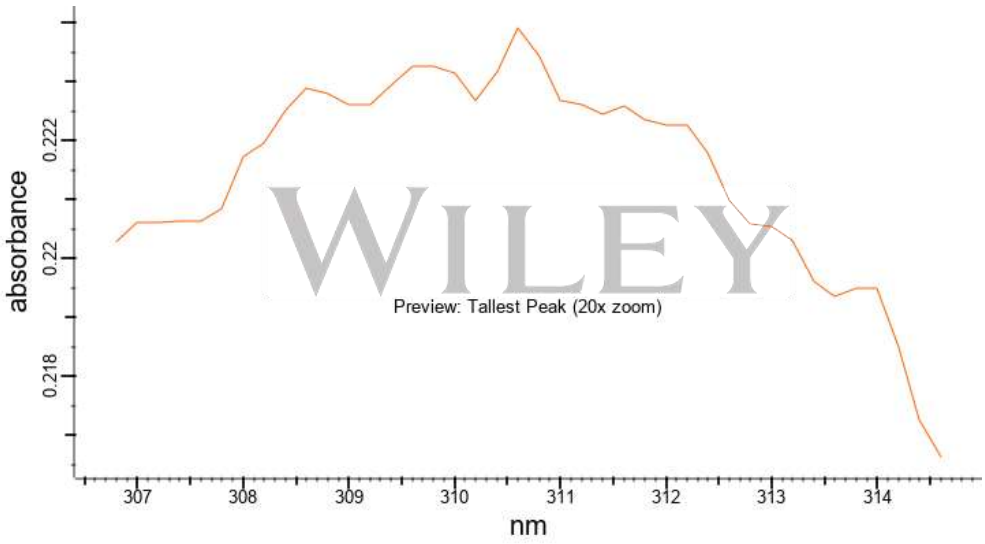



Fig.3.UV-VIS Spectra of LSD

**(Source - https://spectrabase.com/spectrum/6i7IzVplfKQ)**

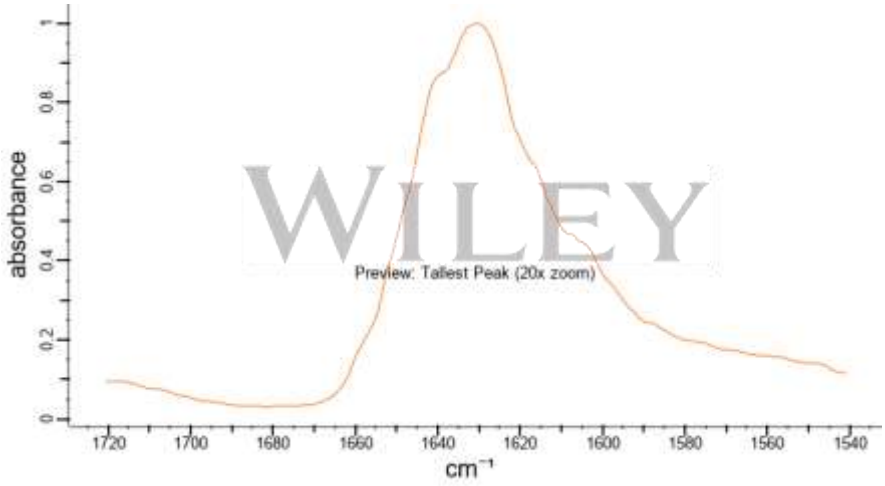



Fig.4. FTIR Spectra of LSD

**(Source - https://spectrabase.com/spectrum/6i7IzVplfKQ)**

## PHARMACOKINETIC PROPERTIES:

| | |
|---|---|
| BCS Classification: | Lysergic acid diethylamide (LSD) falls under Class I of the Biopharmaceutics Classification System (BCS), which categorizes drugs as high solubility and high permeability compounds. |
| Route of Administration: | Oral, IV |
| **ORAL** | **PHARMACOKINETIC PARAMETERS** |
| Cmax | Mean maximal concentration of approximately 4.5 ng/mL at a median of 1.5 hours (range: 0.5-4 hours) post-administration. |
| Tmax | Median time of 1.5 hours (range: 0.5-4 hours) to reach peak concentration. |
| Half-Life | Terminal half-life of 8.9±5.9 hours. |
| ADME | LSD is well-absorbed orally and undergoes metabolism to inactive metabolites, including O-H-LSD. Only 1% of the administered drug is excreted unchanged in urine, while 13% is eliminated as O-H-LSD within 24 hours. |
| **INTRAVENOUS** | **PHARMACOKINETIC PARAMETERS** |
| Cmax | The maximum plasma concentration of LSD after oral administration was reported to be maximal at 1.5 hours (median) for a dose of 200 µg |
| Tmax | 2.8 ± 0.8 h (range 1.2–4.6 h) |
| Half-Life | The mean plasma elimination half-life of LSD after IV administration (2 µg/kg) was reported to be 175 minutes |

Lysergic acid diethylamide (LSD), a renowned serotonergic psychedelic, has gained significant popularity as a recreational substance. It is characterized by its potent effects on the mind and perception, leading to altered states of consciousness. In recent years, there has been a growing interest in exploring the potential therapeutic applications of LSD for various disorders, such as depression, anxiety, substance use disorders, and cluster headaches. When administered orally, LSD is efficiently absorbed into the bloodstream, reaching peak concentrations approximately 1.5 to 2 hours after ingestion. The duration of LSD's effects typically ranges from 6 to 12 hours, depending on factors such as dosage, individual tolerance, and age. A study by Aghajanian and Bing in 1964 reported a relatively short elimination half-life of 175 minutes (around 3 hours) for LSD. However, more recent research by Papac and Foltz in 1990 utilized improved techniques and found that a single oral dose of 1 µg/kg of LSD had an apparent plasma half-life of 5.1 hours. The peak plasma concentration of LSD, measured at 3 hours post-dose, was reported as 5 ng/mL in this study. The comprehensive understanding of LSD's pharmacokinetics took time to develop and was not properly determined until 2015, primarily due to the drug's extremely low potency, typically in the microgram range. In a study involving 16 healthy subjects, a moderate dose of 200 µg of LSD administered orally resulted in mean maximal concentrations of 4.5 ng/mL at a median time of 1.5 hours (ranging from 0.5 to 4 hours) after administration. This rapid absorption contributes to the relatively quick onset of its psychedelic effects. Concentrations of LSD in circulation decreased following first-order kinetics, with a half-life of 3.6±0.9 hours and a terminal half-life of 8.9±5.9 hours. The effects observed from the given dose of LSD persisted for up to 12 hours and were closely correlated with the concentrations of LSD detected in the bloodstream over time. Notably, no acute tolerance to the effects of LSD was observed. Metabolically, LSD undergoes transformation into its primary inactive metabolite, O-H-LSD, which is subsequently eliminated from the body through renal excretion. The plasma half-life of LSD is relatively short, ranging from 3 to 4 hours. The oral bioavailability of LSD was approximately estimated as 71% using previous

data from intravenous administration. The study sample consisted of an equal distribution of male and female subjects, with no significant differences observed in the pharmacokinetics of LSD between sexes. Researchers have begun investigating the potential of LSD in the treatment of mental health disorders. Studies have shown promising results in using LSD-assisted therapy for conditions like depression and anxiety, with the compound's unique pharmacological effects believed to facilitate introspection and emotional processing. Moreover, LSD has shown potential in addressing substance use disorders, offering a novel approach to addiction treatment. Additionally, the use of LSD has been explored as a potential therapy for cluster headaches, a debilitating condition that often proves challenging to manage. IN recent years, the practice of "microdosing" LSD has gained traction. Microdosing involves taking sub-threshold doses of LSD on a regular basis, with the intention of experiencing subtle cognitive and mood enhancements without the full psychedelic effects. Advocates claim that microdosing LSD may enhance creativity, focus, and overall well-being, although rigorous scientific evidence supporting these claims is still limited. It is important to note that the recreational use of LSD poses risks, including the potential for adverse psychological reactions and unpredictable experiences. Furthermore, LSD is classified as a controlled substance in many countries, and its use outside of approved medical contexts is illegal. IN conclusion, LSD, a serotonergic psychedelic compound, has captivated both recreational users and researchers alike. Its potent effects on consciousness, coupled with ongoing investigations into its therapeutic potential, have sparked a renewed interest in understanding the intricate mechanisms underlying its actions. However, it is crucial to approach LSD use with caution, ensuring responsible and evidence-based practices to maximize its benefits while minimizing potential risks.[4]

## MECHANISM OF WORKING:

The mechanism of action underlying the effects of LSD primarily involves the activation of serotonin receptors, specifically the 5-HT2A receptors (5-hydroxytryptamine 2A receptors). LSD may also modulate the activity of 5-HT2C and 5-HT1A receptors. However, the precise interactions between receptor activation and the resulting cognitive impairment and hallucinations are still not fully understood. Studies suggest that LSD-induced activation of 5-HT2A receptors may disrupt inhibitory processes in the hippocampal prefrontal cortex, leading to alterations in brain activity. Specifically, LSD has been shown to reduce activity in regions such as the right middle temporal gyrus, superior/middle/inferior frontal gyrus, anterior cingulate cortex, left superior frontal and postcentral gyrus, and cerebellum. Furthermore, LSD has been found to activate the right hemisphere, affect thalamic functioning, and increase activity in the paralimbic structures and frontal cortex, ultimately resulting in the formation of induced visual images. In the context of substance abuse, it is well-established that anxiety and stress contribute to relapse. It is hypothesized that the downregulation of 5-HT2A receptors by hallucinogens like LSD may potentially mitigate stress-induced relapses. Additionally, LSD has been found to influence the expression of brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF). Both BDNF and GDNF play crucial roles in neurogenesis, synaptic plasticity, learning, and memory. There is emerging evidence suggesting that LSD can induce neuroplastic changes, providing a potential basis for persistent behavioral alterations. LSD has also been shown to induce remodeling of dendrites in pyramidal cells. [5,6,7]

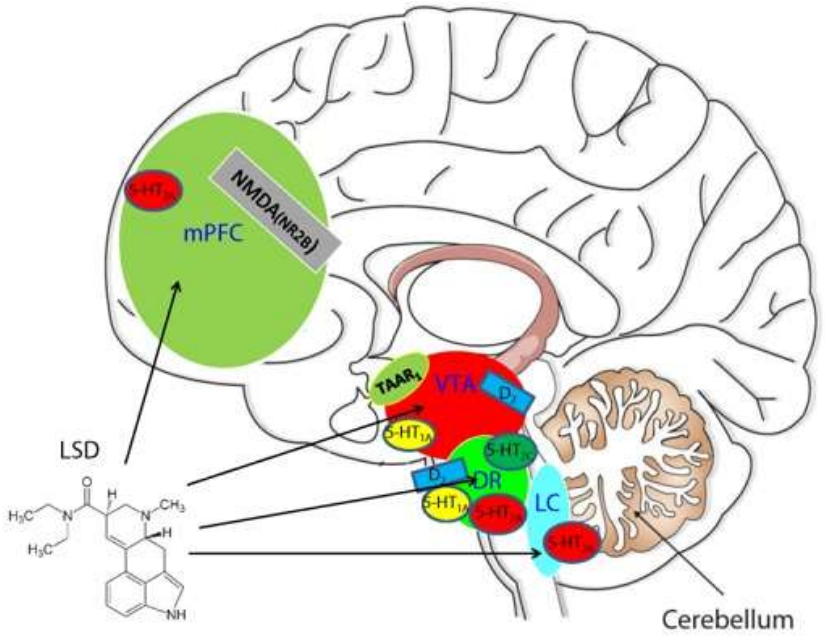


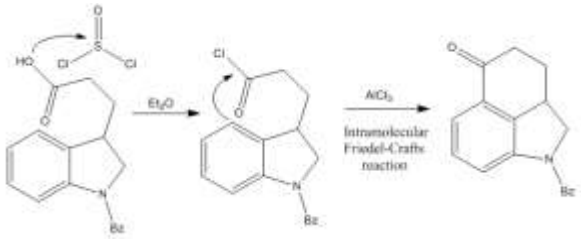

Fig.5 LSD, also known as d-Lysergic Acid Diethylamide, has a multifaceted mechanism of action in various regions of the brain. It affects serotonin receptors 5-HT1A, 5-HT2A, and 5-HT2C, as well as dopamine receptors D2 in the Dorsal Raphe (DR). In the Ventral Tegmental area (VTA), LSD interacts with dopamine D2 receptors and Trace Amine Associate Receptor 1 (TAAR1). Additionally, it influences serotonin 5-HT2A receptors in the Locus Coeruleus (LC). These three nuclei project to the prefrontal cortex (PFC), where they modulate the release of neurotransmitters, resulting in the regulation of psychotic-like effects and cognitive changes. The medial prefrontal cortex (mPFC) and the N-methyl-d-aspartate (NMDA) receptor subunit NR2B are also involved in these processes.

## METHOD OF SYNTHESIS:

The psychedelic substance lysergic acid diethylamide, also referred to as LSD, was initially synthesized on November 16, 1938, by a scientist by the name of Albert Hofmann. Hofmann's synthetic route for LSD is simple, using ergotamine as a starting material. The drug's structure is like compounds extracted from the ergot fungus, with most structural work done by nature. Arthur Stoll played a significant role in studying ergot fungus compounds, including ergotamine and ergonovine.[8]

A. The First Step: Ring C Formation

Thionyl chloride was used to transform the original chemical into the corresponding acid chloride. This increases the carbonyl group's electrophilicity significantly. Aluminium chloride is then added, and the molecule then goes through an intramolecular Friedel-Crafts acylation reaction, putting together the ketone depicted in the top image.




B. Elaboration of the New Ring

The production of the compound's ring D proved to be the most challenging step in the synthetic process. In order to add a substituent to the ketone carbonyl's -carbon, a harsh molecular bromination was carried out in acidic media. Although the required brominated product was produced in a relatively high yield, the initial attempts to carry on with the synthesis were unsuccessful. Alkyl bromide substitution processes were frequently unsuccessful. It was discovered, however, that treating the brominated intermediate with methylamino acetate ethylene ketal in a non-polar solvent gave the desired alkylated intermediate in an excellent yield, which could then be hydrolysed using HCl to deprotect the acetal (releasing the ketone) after many unsuccessful attempts (and some successful but in rather poor yields). The benzoyl group that shields the dihydroindole is also taken out at the same time.

C. Finishing The Tetracyclic Core for the LSD Synthesis

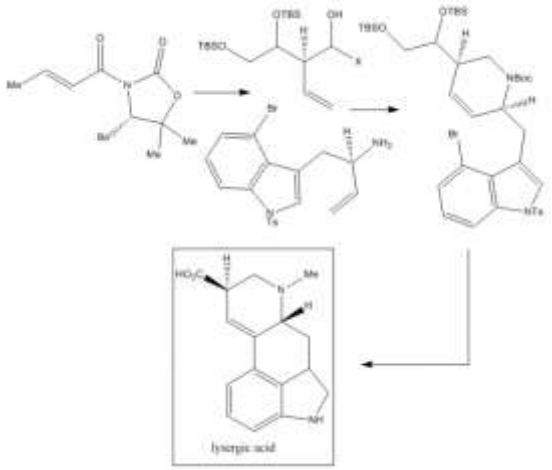
The final ketone intermediate was successfully treated with sodium methoxide in methanol to generate the heterocyclic ring D, which is the following step.This step's process basically entails the kinetic enolation of the most accessible methyl ketone, followed by the nucleophilic addition of that enolate to the other ketone to complete the molecule's third and final ring. An elimination reaction that produces the matching -unsaturated ketone follows right after this. The ketone group in this chemical is then converted to alcohol and the nitrogen of the dihydroindole is protected by treatment with sodium borohydride and sodium anhydride. The newly introduced alcohol was then replaced with a chloride. The required intermediate was discovered to be produced with good yields after the alcohol was treated with thionyl chloride in sulfur dioxide (liquid). As a result, the next reaction, which involved treating the compound with an excess of sodium cyanide in anhydrous liquid hydrogen cyanide (pretty scary thing!), had to be carried out quickly and under special conditions. The obtained chlorinated intermediate was discovered to be very susceptible to hydrolysis to yield once again the alcohol. However, the reaction was successfully carried out by Woodward's team, and the resultant intermediate was then treated with acidic methanol to yield the matching methyl ester. Additionally, under the acidic conditions, the nitrogen's acetyl protective group was lost.The product was then hydrolysed to produce the appropriate carboxylic acid. The selective oxidation of the dihydroindole to indole was the sole step left to complete in order to obtain lysergic acid. Based on the application of Ni Raney and sodium arseante, several extremely enigmatic reaction conditions were used. The necessary indole (which is already lysergic acid) was produced as a result, leaving the remaining molecular functions unaffected.

D. Final Amination of Lysergic Acid to Give LSD

This does not, however, finish the synthesis of LSD. The creation of an amide using diethylamine is the final step. Shulgin utilized the following reaction conditions to produce LSD from lysergic acid:

E. Modern LSD amination Route

Tohru Fukuyama et al. from the Graduate School of Pharmaceutical Sciences, University of Tokyo, published a very recent technique for the entire synthesis of LSD in 2013. The Evans aldol reaction, which enables the stereoselective construction of the required chiral center, is the foundation for this LSD synthesis. This reaction is then followed by a series of steps, including a metathesis reaction to produce the ring-closure and a Heck reaction to complete the construction of the two rings.[9]




## PHARMACOLOGICAL ACTION

At moderate doses (75–150 g orally), lysergic acid diethylamide (LSD) causes noticeable changes in consciousness. Enhancement of introspection, euphoria, and shifts in psychological functioning toward fundamental processes or hypnagogic dreams-like experiences are the characteristics of these modifications. Illusions, false hallucinations, synesthesia, and changes in thought and time perception are a few famous examples of perceptual shifts. Changes in ego function and body image are frequently noted as well.

Depending on the dosage used, the acute psychological effects of LSD often last 6 to 10 hours. The "optimum" dosage for a normal LSD experience is thought to be in the range of 100-200 g, while the minimum recognized dose in humans is approximately 25 g orally.

It is crucial to remember that traumatic events, also known as "bad trips," can leave LSD users with enduring repercussions such as mood swings and occasional flashbacks. However, these negative outcomes frequently take place under uncontrolled circumstances. Contrarily, it has been shown that the LSD experience, when carried out under safe and encouraging circumstances, may have long-lasting favorable impacts on attitudes and personality.

**Acute Neurocognitive Effects**

Clinical doses of LSD (100 g or more) are used in acute cognitive testing, but a drawback is that the strong perceptual and bodily alterations brought on by the drug frequently cause people to become too impaired to participate. It's possible that lower doses don't properly capture LSD's cognitive effects. Nevertheless, several tests have been carried out, and pertinent papers have been mentioned.

LSD has been shown to often impair psychomotor abilities, such as timing and coordination. Additionally, it makes people perform worse on tests of concentration and attention. Studies have indicated that dosages of LSD between 75 and 150 g have no effect on learning processes, but levels of 100 g impair the ability to recognize and recall stimuli.

100 mg of LSD, but not 50 mg, dramatically lowers performance on computational tasks. LSD also has an impact on memory, both general and visual. Higher LSD doses can affect thought processes, and while under its effect, people frequently overestimate the length of time periods. Intelligence tests have shown that LSD impairs intellectual functioning, and some tests even suggest a regression to a younger developmental stage.[10]

## MEDICINAL USES

LSD, which is a Schedule I drug under the Controlled Substances Act because of its great potential for misuse and lack of medical applications, is outlawed in many nations. Despite lack of study, historical and modern studies have looked into its therapeutic uses, such as psychedelic-assisted therapy for mental health issues, cluster headache treatment, substance use disorder treatment, and end-of-life anxiety. However, due to moral and legal restrictions, LSD is not a recognized treatment for many ailments.

1. **ANXIETY**: In a medically supervised, secure setting, a study indicated that LSD-assisted psychotherapy decreased anxiety in 12 patients with advanced-stage cancer. There were two LSD-assisted sessions and two drug-free sessions included in the therapy, and there were no negative side effects or grave adverse occurrences. However, it is challenging to draw firm conclusions because of the study's small sample size and methodological issues. Large-scale studies are still needed to corroborate previous findings that LSD may help cancer patients sleep better and with less pain.

2. **EMOTIONAL EMPATHY, SOCIALITY, AND SUGGESTIBILITY**: According to a study, healthy volunteers who received intravenous LSD (40–80 g) had considerably higher scores on the Creative Imagination Scale (CIS), which could influence psychotherapy. According to the study, LSD makes people more susceptible to the influence of suggestions, with those who have high trait conscientiousness being especially affected. Previous research has demonstrated that LSD can enhance positive emotions such as joy, trust, closeness, and emotional empathy. However, there have been few recent studies on sociality, empathy, and suggestibility; more need to be done in current clinical trials.
3. **ALCOHOL AND DRUG ADDICTION**: Due to their substantial hazards and scant clinical evidence, hallucinogens like LSD for addiction are debatable. The use of hallucinogens and high-dose LSD for addiction treatment deserves more research, according to a meta-analysis. Large-scale controlled experiments are, however, lacking. LSD may help drug addicts rehabilitate, according to a 2012 study, but this notion is still unverified.
4. **CLUSTER HEADACHES:** Patients with cluster headaches are using hallucinogens more frequently to stop cluster periods, however there are no adequate clinical trials for this practice. In a study of 53 individuals, it was discovered that 7 out of 8 LSD users reported ending their cluster phase, while 4 out of 5 had no symptoms expanding.
5. **MOOD DISORDERS AND DEPRESSION:** Clinical research is limited, but recent behavioral and neuroimaging findings suggest psychedelics like LSD may modify brain circuits in mood disorders, potentially alleviating symptoms. Serotonin in the brain is impacted by LSD.[11]
6. Moreover, LSD's therapeutic potential was employed in the 1950s and 1970s to treat advanced cancer patients' pain, anxiety, and sadness as well as to cause behavioral and personality changes and to relieve psychiatric symptoms associated with a variety of illnesses. Studies on schizophrenia patients, however, revealed a lesser response and worse clinical outcomes, with negative impacts on their mental and physical health. LSD users ended cluster periods in 78% of cases, while 22% ceased attacks and 18% prolonged the remission time, according to a study on people with cluster headaches who used psilocybin or LSD. Understanding how psilocybin and LSD affect cluster headaches requires more study. [12]

## SIDE EFFECTS:

Characteristic sensory and psychological consequences of an LSD dose of 100 to 200 mg orally-

- Reexperiencing Significant Biographical Memories
- Hypermnesia
- Age-Regression
- Mystical-Type Experiences
- Sensory Changes (Auditory, Visual, Gustatory, Olfactory, And Kinaesthetic)
- Illusion
- Pseudo-Hallucination
- Enhanced Recognition Of Color
- Changes That Resemble Metamorphosis In Things And Faces
- Intense Visual Imagery With Changing Content (Kaleidoscopic Or Scenic) Changes In Affectivity
- Increased Emotional Intensity, Including Euphoria, Dysphoria, Anxiety, And Mood Swings
- Transformations In Thinking
- Thought That Is More Creative And Less Abstract
- Reduction In Attention Span
- Alteration On How You Perceive Your Body
- Body Image Alteration
- Bizarre Inner View Of Physical Functions
- Alteration Of Bodily Characteristics Through Metamorphosis
- Memory Alters
- Crucial Biographical Thoughts Being Relived.

- Hypermnesia
- Age-Regression
- Spiritual Experiences

Other short-term effects include-

- Increased blood pressure and heart rate.
- Elevated body temperature.
- Insomnia.
- Dizziness.
- Loss of appetite.
- Dry mouth.
- Excessive sweating.
- Tremors.

## ADVERSE EFFECTS:

- LSD effects: LSD can have highly variable and unpredictable effects. Positive effects include hallucinations, visuals, sensations, expanded awareness, and euphoria, known as a "good trip." Negative effects can include anxiety, fear, panic, depression, despair, and disappointment, known as a "bad trip." Users may experience both positive and negative effects at different times.
- Flashbacks: Flashbacks are unsettling effects of LSD. They can occur suddenly, even without current LSD use, and may be triggered by stress, exhaustion, or the use of other substances. Flashbacks can be a recurrence of a previous "bad trip."
- Tolerance and withdrawal: With repeated use, tolerance to LSD develops. A period of abstinence allows the individual to quickly return to baseline emotionally, physically, and mentally. LSD withdrawal does not typically result in physical cravings but rather psychological dependence.
- Chronic daily abuse: Chronic daily LSD abuse is challenging due to the intense positive effects ("good trip") experienced with regular intake. The reliance on LSD is primarily psychological rather than driven by physical side effects or cravings. [13]

**Other Adverse Effects Includes:**

1. Panic reaction: LSD can induce a state of panic, particularly if the user is exposed to unexpected and stressful situations.
2. Amplification of unconscious fears: Under the influence of LSD, individuals may experience heightened awareness of their fears and anxieties, potentially leading to feelings of distress or unease.
3. Self-aggression: In some cases, LSD can contribute to self-destructive behaviors or aggressive tendencies towards oneself, which can pose a risk to personal safety.
4. Suicidal or homicidal ideation: Rarely, LSD use may result in thoughts or contemplation of self-harm or harm towards others, indicating the need for immediate professional intervention.
5. Fear of going insane or inability to return to normal: LSD's profound alteration of perception and thought processes can cause individuals to develop intense fears of losing touch with reality or being permanently trapped in a distorted state of consciousness.
6. Perception of rapid aging of self or others: LSD can distort one's perception of time, leading to the subjective experience of accelerated aging or perceiving others as rapidly aging, which can be distressing.
7. Profound depression: LSD use may trigger or exacerbate feelings of profound sadness or depression, potentially leading to a depressive episode.

**TOXICITY:**

The LD50 (lethal dose for 50% of the test population) of LSD varies among species. In rabbits, the most sensitive species, the LD50 is 0.3 mg/kg when administered intravenously. Rats have a higher LD50 of 16.5 mg/kg intravenously, while mice can tolerate doses of 46-60 mg/kg intravenously. Monkeys, specifically Macaca mulatta, have been injected with doses as high as 1 mg/kg intravenously without any lasting somatic effects.

There have been no documented human deaths resulting from an LSD overdose. In cases where individuals accidentally consumed very high doses intranasally (mistaking it for cocaine), plasma levels of 1000-7000 μg per 100 mL blood plasma were observed. These individuals experienced comatose

states, hyperthermia, vomiting, light gastric bleeding, and respiratory problems. However, with hospital treatment, all individuals survived without residual effects.

A report in 1967 suggested LSD-induced chromosomal damage, but subsequent studies discredited this claim. Empirical studies conducted later found no evidence of teratogenic (causing malformations in fetuses) or mutagenic (causing genetic mutations) effects in humans who use LSD. Teratogenic effects were observed in animals (mice, rats, and hamsters), but only with extraordinarily high doses (up to 500 μg/kg subcutaneously), and the most vulnerable period for mice was the first 7 days of pregnancy. LSD has no known carcinogenic (cancer-causing) potential. [14]

Somatic symptoms of LSD toxicity, which are usually due to sympathomimetic effects, include the following:

- Mydriasis
- Hypertension
- Tachycardia
- Flushing
- Sweating
- Loss of appetite
- Nausea
- Diarrhea
- Dry mouth
- Drowsiness
- Sleeplessness
- Weakness
- Paresthesias
- Tremors
- Hyperactive reflexes
- Piloerection
- Mild pyrexia
- Seizures - Rare; typically, with doses above 10 mcg/kg

Massive overdoses can lead to the following

- Respiratory arrest
- Intracranial hemorrhage
- Cardiac arrhythmias
- Coma - Very rare
- Emesis
- Hyperthermia
- Autonomic instability
- Coagulopathies
- Rhabdomyolysis
- Seizures

## TREATMENT OF OVERDOSE

**General precautions:**

1. Scene safety assessment: Before initiating patient management, the healthcare team must assess the situation for any potential violence or threat, ensuring the safety of both the patient and the healthcare team.

2. Approach and guidelines: If there is a potential threat, the team should approach the patient quickly while minimizing harm to themselves. Developing and practicing guidelines for managing such situations helps ensure a calm and safe approach.
3. Supportive reassurance: For patients who have ingested hallucinogens like LSD, the primary approach is supportive reassurance in a calm and stress-free environment, commonly referred to as "talking down."
4. Sedation and physical restraint: Sedation or physical restraint is rarely necessary in LSD intoxication. Benzodiazepines can be administered safely to treat agitation, while neuroleptic medications like haloperidol are not recommended due to potential adverse psychomimetic effects.
5. Avoid excessive physical restraint: Excessive physical restraint should be avoided due to the potential complications of LSD intoxication, such as hyperthermia and rhabdomyolysis.
6. Substance abuse treatment guidelines: Substance abuse treatment guidelines, including those specific to LSD and hallucinogens, have been established by organizations like the Substance Abuse and Mental Health Services Administration (SAMHSA).
7. Gastrointestinal decontamination: Gastrointestinal decontamination, such as activated charcoal administration, is rarely required in LSD intoxication unless the patient has ingested a large amount within a short period before presentation.
8. Enhanced elimination measures: Enhanced elimination measures are generally not recommended and may be counterproductive in the management of LSD intoxication.[15]

**Supportive care:**

Supportive care is the mainstay of treatment for massive ingestions of LSD. It involves providing necessary respiratory support, and if required, endotracheal intubation to ensure proper breathing. Symptomatic treatment is essential for managing hypertension, tachycardia, and hyperthermia. Hypotension is initially managed with fluid administration and, if necessary, with the use of pressor medications.

**Ergotism Therapy:**

In cases of ergotism, the primary approach is discontinuing any drugs that may have triggered the condition, followed by supportive care. Intravenous administration of anticoagulants, vasodilators, and sympatholytics may be beneficial. In severe cases, percutaneous transluminal angioplasty with a balloon may be considered as a treatment option.

**Treatment programs:**

1. 12-Step programs: Group settings that utilize peer discussion to reinforce a substance-free lifestyle, providing social support and encouragement.
2. Behavioral therapy: Various therapies are employed to engage individuals in treatment, provide incentives for abstinence, and teach skills to maintain sobriety.
3. Cognitive behavioral therapy (CBT): Focuses on improving self-control, teaching new skills, and developing coping strategies to prevent relapse.
4. Contingency management: Offers tangible rewards or incentives as positive reinforcement for achieving and maintaining abstinence.
5. Rational emotive behavioral therapy: A form of CBT that concentrates on regulating thoughts, feelings, and behavioral disturbances.
6. Dialectical behavioral therapy (DBT): A form of CBT that teaches acceptance of uncomfortable emotions, behaviors, and thoughts while also providing skills for managing them.
7. Motivational interviewing: A technique used to quickly motivate individuals to engage in treatment and commit to abstinence.
8. Eye movement desensitization and reprocessing (EMDR): Primarily used to treat post-traumatic stress disorder (PTSD) by reducing emotional distress associated with traumatic memories.
9. Family- and community-based treatment: Focuses on addressing substance use as well as co-occurring issues like family conflict, mental illness, childhood mistreatment, and unemployment.
10. Community reinforcement approach: Utilizes a variety of reinforcers or rewards from different areas of an individual's life (family, monetary, social) to make abstinence more rewarding than substance use.[16]

**Medications**:

**Benzodiazepines**: While benzodiazepines help calm agitated individuals' behavior and autonomic symptoms, they do not lower seizure thresholds like antipsychotics do. In circumstances of extreme LSD poisoning, this is useful. To produce the intended effects, doctors must carefully adjust the dosage of sedative.

1. Diazepam- Contribute to the symptomatic alleviation of acute agitation, tremor, imminent or acute delirium tremens, and hallucinations.

Brand name- Valium, Diastat AcuDial, Valtoco

Dose- 10 mg PO q6-8hr during first 24hr; reduce to 5 mg PO q6-8hr PRN OR

10 mg IV/IM, initially may give additional doses of 5-10 mg IV q6-8hr as needed

2. Lorazepam- lorazepam, depresses the central nervous system (CNS) by raising the activity of the inhibitory neurotransmitter GABA. Patients with severe LSD poisoning are treated with it.

Brand name- Ativan, Loreev XR

Dose- Usual 4 mg/dose slow IV at 2 mg/min

If seizure persists after 5-10 min, administer 4 mg IV again

**Antihypertensives**: Some LSD poisoning signs and symptoms have been demonstrated to be alleviated by the antihypertensive medication clonidine.

1. Clonidine- It has been discovered that clonidine can lessen the severity of flashbacks and HPPD while also reducing the sympathetic hyperactivity brought on by LSD usage.

Brand name- Catapres, Catapres-TTS, Duraclon, Jenloga, Kapvay, Nexiclon XR

Dose- PO administration: 0.4-1.4 mg/day in divided doses.

## CONTRAINDICATION

LSD can be harmful in non-clinical situations even though it is a classic hallucinogen and does not often cause compulsive drug-seeking behaviour like most other substances do. In a few rare instances, non-medical use can trigger protracted mental problems. Absolute contraindications include medical illnesses which comprises cardiovascular disease, pregnancy, epilepsy, paranoid personality disorder, overt psychosis, and organic-toxic brain pathology that have pronounced excitatory states. LSD has teratogenic effects that have been shown by some researchers but not supported by others.

***INTERACTIONS:***

| **Substance** | **Interaction** | **Effect** |
|---|---|---|
| 1-(2-Phenylethyl)-4-phenyl-4-acetoxypiperidine | Metabolism of LSD | Decreased metabolism |
| 2,5-Dimethoxy-4-ethylamphetamine | Risk/severity of serotonin syndrome | Increased risk/severity |
| 4-Bromo-2,5-dimethoxyamphetamine | Risk/severity of CNS depression | Increased risk/severity |
| 4-Bromo-2,5-dimethoxyphenethylamine | Hypertensive and vasoconstricting activities | Increased activities |
| 4-Methoxyamphetamine | Hypertensive and vasoconstricting activities | Increased activities |
| 5-methoxy-N,N-dimethyltryptamine | Vasoconstricting activities | Increased activities |
| Alfentanil | Risk/severity of CNS depression | Increased risk/severity |
| Alphacetylmethadol | Risk/severity of CNS depression | Increased risk/severity |
| Alphaprodine | Risk/severity of CNS depression | Increased risk/severity |
| Alprazolam | Risk/severity of CNS depression | Increased risk/severity |
| Amineptine | Risk/severity of CNS depression | Increased risk/severity |
| Amobarbital | Risk/severity of CNS depression | Increased risk/severity |
| Amphetamine | Risk/severity of serotonin syndrome | Increased risk/severity |
| Aprobarbital | Risk/severity of CNS depression | Increased risk/severity |
| Barbital | Risk/severity of CNS depression | Increased risk/severity |
| Benzphetamine | Hypertensive and vasoconstricting activities | Increased activities |
| Bezitramide | Risk/severity of serotonin syndrome | Increased risk/severity |
| Bromazepam | Risk/severity of CNS depression | Increased risk/severity |
| Butyrfentanyl | Metabolism of Butyrfentanyl | Decreased metabolism |
| Camazepam | Risk/severity of CNS depression | Increased risk/severity |
| Carfentanil | Risk/severity of CNS depression | Increased risk/severity |
| Cathinone | Risk/severity of CNS depression | Increased risk/severity |
| Chloral hydrate | Risk/severity of CNS depression | Increased risk/severity |
| Chlordiazepoxide | Risk/severity of CNS depression | Increased risk/severity |
| Chlorhexadol | Risk/severity of CNS depression | Increased risk/severity |

| | | |
|---|---|---|
| Chlorphentermine | Risk/severity of serotonin syndrome | Increased risk/severity |
| Clobazam | Serum concentration of LSD | Increased concentration |
| Clonazepam | Risk/severity of CNS depression | Increased risk/severity |
| Clorazepic acid | Risk/severity of CNS depression | Increased risk/severity |
| Clotiazepam | Risk/severity of CNS depression | Increased risk/severity |
| Cocaine | Metabolism of LSD | Decreased metabolism |
| Codeine | Risk/severity of CNS depression | Increased risk/severity |
| Delorazepam | Risk/severity of CNS depression | Increased risk/severity |
| Desomorphine | Risk/severity of CNS depression | Increased risk/severity |
| Dexfenfluramine | Risk/severity of serotonin syndrome | Increased risk/severity |
| Diethylpropion | Risk/severity of CNS depression | Increased risk/severity |
| Difenoxin | Risk/severity of CNS depression | Increased risk/severity |
| Dihydrocodeine | Risk/severity of CNS depression | Increased risk/severity |
| Dihydroetorphine | Risk/severity of CNS depression | Increased risk/severity |
| Dihydromorphine | Risk/severity of CNS depression | Increased risk/severity |
| Dimethyltryptamine | Risk/severity of CNS depression | Increased risk/severity |
| Diphenoxylate | Risk/severity of CNS depression | Increased risk/severity |
| Dronabinol | CNS depressant activities | Increased activities |
| Drotebanol | Risk/severity of CNS depression | Increased risk/severity |
| Estazolam | Risk/severity of CNS depression | Increased risk/severity |
| Ethchlorvynol | Risk/severity of CNS depression | Increased risk/severity |
| Ethyl loflazepate | Risk/severity of CNS depression | Increased risk/severity |
| Ethylmorphine | Risk/severity of CNS depression | Increased risk/severity |
| Etorphine | Risk/severity of CNS depression | Increased risk/severity |
| Fencamfamin | Risk/severity of CNS depression | Increased risk/severity |
| Fenfluramine | Risk/severity of serotonin syndrome | Increased risk/severity |
| Fentanyl | Risk/severity of CNS depression | Increased risk/severity |
| Fludiazepam | Risk/severity of CNS depression | Increased risk/severity |
| Flunitrazepam | Risk/severity of CNS depression | Increased risk/severity |
| Flurazepam | Risk/severity of CNS depression | Increased risk/severity |
| Fospropofol | Risk/severity of CNS depression | Increased risk/severity |
| gamma-Hydroxybutyric acid | Risk/severity of CNS depression | Increased risk/severity |
| Glutethimide | Risk/severity of CNS depression | Increased risk/severity |
| Halazepam | Risk/severity of CNS depression | Increased risk/severity |
| Hydrocodone | CNS depressant activities | Increased activities |
| Hydromorphone | Risk/severity of CNS depression | Increased risk/severity |
| Lofentanil | Risk/severity of CNS depression | Increased risk/severity |
| Midazolam | Risk/severity of sedation and CNS depression | Increased risk/severity |
| Midomafetamine | Risk/severity of CNS depression | Increased risk/severity |
| MMDA | Risk/severity of CNS depression | Increased risk/severity |
| Normethadone | Risk/severity of CNS depression | Increased risk/severity |
| Opium | Risk/severity of CNS depression | Increased risk/severity |
| Oxycodone | Risk/severity of CNS depression | Increased risk/severity |
| Phencyclidine | Risk/severity of CNS depression | Increased risk/severity |
| Phendimetrazine | Hypertensive and vasoconstricting activities | Increased activities |
| Phenmetrazine | Risk/severity of hypertension | Increased risk/severity |
| Phentermine | Risk/severity of serotonin syndrome | Increased risk/severity |
| Prazepam | Risk/severity of CNS depression | Increased risk/severity |
| Quazepam | Risk/severity of CNS depression | Increased risk/severity |
| Sibutramine | Risk/severity of adverse effects | Increased risk/severity |
| Talbutal | Risk/severity of CNS depression | Increased risk/severity |
| Tenamfetamine | Risk/severity of CNS depression | Increased risk/severity |
| Zaleplon | Risk/severity of CNS depression | Increased risk/severity |
| Adrafinil | Adrafinil may increase hypertensive and vasoconstricting activities of LSD | Increased activities |
| Alclofenac | Risk/severity of hypertension increased | Increased risk/severity |
| Alosetron | Risk/severity of CNS depression increased | Increased risk/severity |

| | | |
|---|---|---|
| Alprenolol | Alprenolol may increase vasoconstricting activities of LSD | Increased activities |
| Bepridil | Metabolism of LSD decreased when combined with Bepridil | Decreased metabolism |
| Bezitramide | Risk/severity of serotonin syndrome increased | Increased risk/severity |
| Bitolterol | LSD may increase hypertensive and vasoconstricting activities of Bitolterol | Increased activities |
| Boceprevir | Risk/severity of adverse effects increased | Increased risk/severity |
| Bromocriptine | LSD may increase hypertensive and vasoconstricting activities of Bromocriptine | Increased activities |
| Brotizolam | Risk/severity of CNS depression increased | Increased risk/severity |
| Butriptyline | Risk/severity of CNS depression increased | Increased risk/severity |
| Candicidin | Serum concentration of LSD increased when combined with Candicidin | Increased concentration |
| Caroxazone | Risk/severity of CNS depression increased | Increased risk/severity |
| Carprofen | Risk/severity of hypertension increased | Increased risk/severity |
| Cerivastatin | Metabolism of LSD decreased when combined with Cerivastatin | Decreased metabolism |
| Levacetylmethadol | Risk/severity of CNS depression increased | Increased risk/severity |
| Lorcaserin | Risk/severity of adverse effects increased | Increased risk/severity |
| Mebanazine | Risk/severity of CNS depression increased | Increased risk/severity |
| Mephenytoin | Risk/severity of CNS depression increased | Increased risk/severity |
| Metamfetamine | LSD may increase hypertensive and vasoconstricting activities of Metamfetamine | Increased activities |
| Metamizole | Risk/severity of hypertension increased | Increased risk/severity |
| Methapyrilene | Risk/severity of CNS depression increased | Increased risk/severity |
| Methaqualone | Risk/severity of CNS depression increased | Increased risk/severity |
| Metharbital | Risk/severity of CNS depression increased | Increased risk/severity |
| Methoxyflurane | Risk/severity of CNS depression increased | Increased risk/severity |
| Methyprylon | Risk/severity of CNS depression increased | Increased risk/severity |
| Metocurine iodide | Risk/severity of CNS depression increased | Increased risk/severity |
| Mibefradil | Metabolism of LSD decreased when combined with Mibefradil | Decreased metabolism |
| Moricizine | Risk/severity of CNS depression increased | Increased risk/severity |
| Muzolimine | LSD may decrease antihypertensive activities | Decreased activities |
| Nefazodone | Serum concentration of LSD increased when combined with Nefazodone | Increased concentration |
| Nialamide | Risk/severity of CNS depression increased | Increased risk/severity |
| Nimesulide | Risk/severity of hypertension increased | Increased risk/severity |
| Nomifensine | Risk/severity of CNS depression increased | Increased risk/severity |
| Octamoxin | Risk/severity of CNS depression increased | Increased risk/severity |
| Ondansetron | Risk/severity of CNS depression increased | Increased risk/severity |
| Oxyphenbutazone | Risk/severity of hypertension increased | Increased risk/severity |
| Pergolide | LSD may increase hypertensive and vasoconstricting activities of Pergolide | Increased activities |
| Phenacetin | Metabolism of LSD decreased when combined with Phenacetin | Decreased metabolism |
| Phenformin | Metabolism of LSD decreased when combined with Phenformin | Decreased metabolism |
| Pheniprazine | Risk/severity of CNS depression increased | Increased risk/severity |
| Phenoxypropazine | Risk/severity of CNS depression increased | Increased risk/severity |
| Phenylpropanolamine | LSD may increase hypertensive and vasoconstricting activities of Phenylpropanolamine | Increased activities |
| Pivhydrazine | Risk/severity of CNS depression increased | Increased risk/severity |
| Ranitidine | Metabolism of LSD decreased when combined with Ranitidine | Decreased metabolism |
| Rapacuronium | Risk/severity of CNS depression increased | Increased risk/severity |

| | | |
|---|---|---|
| Remoxipride | Risk/severity of CNS depression increased | Increased risk/severity |
| Reserpine | Risk/severity of CNS depression increased | Increased risk/severity |
| Rofecoxib | Risk/severity of hypertension increased | Increased risk/severity |
| Roxithromycin | LSD may increase vasoconstricting activities | Increased activities |
| Safrazine | Risk/severity of CNS depression increased | Increased risk/severity |
| Sertindole | Risk/severity of CNS depression increased | Increased risk/severity |
| Sibutramine | Risk/severity of adverse effects increased | Increased risk/severity |
| Sitaxentan | LSD may decrease antihypertensive activities | Decreased activities |
| Sparteine | Metabolism of LSD decreased when combined with Sparteine | Decreased metabolism |
| Tegaserod | Metabolism of LSD decreased when combined with Tegaserod | Decreased metabolism |

**Here are substances that interact with LSD:**

1. SSRIs and other antidepressants: Combining LSD with selective serotonin reuptake inhibitors (SSRIs) or other antidepressants can potentially increase the risk of serotonin syndrome, a serious condition that can cause agitation, rapid heartbeat, high body temperature, and other symptoms. LSD itself affects serotonin receptors in the brain, so combining it with drugs that also affect serotonin levels could lead to an excessive increase in serotonin activity.
2. MAOIs: Monoamine oxidase inhibitors (MAOIs) are another type of antidepressant. Combining LSD with MAOIs can be dangerous and may lead to serotonin syndrome, high blood pressure, or other severe reactions.
3. Stimulants: Combining LSD with stimulant drugs, such as amphetamines or cocaine, can potentially increase the risk of anxiety, agitation, or cardiovascular problems. The combined effects can put additional strain on the heart and increase the risk of adverse reactions.
4. Cannabis: Combining LSD with cannabis can intensify the psychoactive effects and potentially lead to increased anxiety, confusion, or paranoia. The combination may also amplify the hallucinogenic experience, potentially making it more challenging to manage.[17]

**Different type of interaction:**

1. Mild interactions: These interactions may cause minimal or manageable effects, and they generally do not pose significant risks. For example, combining LSD with caffeine or alcohol may lead to increased alertness or altered perceptions. While these interactions might not be inherently dangerous, they can enhance the effects of both substances, potentially intensifying the experience.
2. Moderate interactions: Moderate interactions have the potential to produce more pronounced effects or increase the risk of certain side effects. Combining LSD with substances such as marijuana (cannabis) or certain prescription medications like benzodiazepines (e.g., diazepam) may heighten the psychoactive effects, leading to increased anxiety, confusion, or sedation. These combinations can be challenging to predict, and caution is advised.
3. Severe interactions: Severe interactions are those that can result in significant risks to your health and well-being. For example, combining LSD with substances like monoamine oxidase inhibitors (MAOIs), which are antidepressant medications, can lead to potentially life-threatening serotonin syndrome. Combining LSD with other hallucinogens or stimulant drugs (e.g., amphetamines, cocaine) can put additional strain on the cardiovascular system, increasing the risk of adverse reactions such as high blood pressure, rapid heartbeat, or cardiac events.[18]

## DOSAGE FORMS:

25 to 75 micrograms (ug): A threshold/mild experience characterized by mild mood alterations and mild euphoria. Visual hallucinations are limited to color sensations, a mild "breathing" effect, and psychedelic color flashes, particularly when observing bright objects such as computer monitors or phones. The primary trip typically lasts four to six hours, but the comedown may extend to the standard duration.75 to 150 micrograms (ug): A substantial experience encompassing all phases of the LSD encounter described above. At the lower end of the range, hallucinations are limited to a breathing effect, vivid psychedelic colors, and mild visual distortions (e.g., distorted objects). At the higher end of the range, full hallucinations occur, including the perception of non-existent objects, substantial distortion of real objects, strong swaying of objects like trees, and cartoon-like images. The sense of self remains intact, and standard logic still applies, although self-judgment and fear/anxiety are significantly reduced.

150 to 200 micrograms (ug): The presence of beautiful colors throughout the experience, accompanied by stronger overall visual hallucinations. Closed eye visuals become prominent, and the individual may undergo life-changing spiritual experiences or realizations. Anxiety may arise during this dose range.200 to 300 micrograms (ug): The peak of this trip can be highly intense or even frightening. However, like any LSD trip, a state of contentment may follow once the peak effects subside. The sense of self remains intact, but irrational thoughts and obsessive thought patterns may emerge, including "thought loops" or repetitive thinking. Panic regarding personal safety or the safety of loved ones may occur. Closed-eye visuals are particularly intense at this dose.300 to 400 micrograms (ug): Strong visuals are experienced, accompanied by a loss of the sense of self and ego dissolution. Standard logic may not apply consistently during this range. The visuals are intense, and engaging in normal day-to-day activities, including walking and understanding them, may become challenging.400 to 500 micrograms (ug): Time distortions intensify, including the sensation of time stopping. The sense of self often

disappears, leading to complete ego dissolution. Body movement becomes difficult and disorienting. Rational thought processes diminish as individuals enter a temporary psychotic state (which is generally not unpleasant). Visual hallucinations are highly intense, and closed-eye hallucinations may feel overwhelming, with some individuals desiring to escape the intensity of the trip.

500 to 700 micrograms (ug): Very strong hallucinations occur, with the perception of objects that do not exist and elaborate visual distortions. A profound loss of reality is experienced, often accompanied by complete ego dissolution. Strong religious or symbolic imagery may arise, and mystical experiences are frequently reported. The intensity of the trip can be overwhelming.700 to 1000 micrograms (ug): Full out-of-body experiences are common, and synesthesia (cross-sensory perception) becomes more likely. Religious imagery is often pronounced. Rationality is completely lost, and individuals may struggle to walk or engage in meaningful interactions.1000 to 1500 micrograms (ug): Perception of standard reality ceases, and the entire field of vision may be filled with hallucinations, including vivid fractal patterns. The sense of death or the sensation of ceasing to exist often occurs during this dose range.1500 micrograms (ug) and beyond: Experiences in this range may resemble those induced by DMT (dimethyltryptamine), but they are extended in duration. Basic bodily functions become challenging. Vision is dominated by hallucinations, and the sense of self is completely absent. Auditory hallucinations may be intense. Standard reality no longer applies, and merging with objects becomes likely. Rational thought processes cease entirely.[19]

| **Dosage Range** | **Experience Summary** |
|---|---|
| 25 ug - 75 ug | Threshold/mild experience. Mild mood alteration, mild euphoria. Limited visual hallucinations. |
| 75 ug - 150 ug | Substantial experience. Full range of LSD effects. Hallucinations progress from mild to substantial. |
| 150 ug - 200 ug | Strong visual hallucinations, potential for life-changing experiences or realizations. Anxiety may occur. |
| 200 ug - 300 ug | Intense peak effects, sense of self intact but irrational thoughts and panic may arise. |
| 300 ug - 400 ug | Strong visuals, ego dissolution begins, difficulty with normal activities. |
| 400 ug - 500 ug | Intense time distortions, full ego dissolution, difficulty with movement and rational thoughts. |
| 500 ug - 700 ug | Very strong hallucinations, elaborate and overwhelming experiences. Sense of reality lost. |
| 700 ug - 1000 ug | Out-of-body experiences, synesthesia, lack of rationality and ability to interact. |
| 1000 ug - 1500 ug | Perception of standard reality stops, strong hallucinations, sense of death or ceasing to exist. |
| 1500 ug+ | Similar to DMT but extended, basic body functions challenging, no sense of self or rational thought. |

| NAME [LEVOSULPRIDIE] | DOSE | COMPANY NAME | COST |
|---|---|---|---|
| Lesuride | CHEABLE TAB. 25MG SR 75 MG | Sun pharmaceutical industries Ltd. | 82 TO 238 |
| Levazeo | 25\50\75\100\150 MG SR 75 MG | Torrent pharmaceutical Ltd. | 54 TO 230 |
| levogastrol | 25 MG SR 75 MG | Alembic pharmaceutical Ltd. | 113 TO 236 |
| nexipride | 25\50\100 MG SR 150\100\200 MG | Sun pharmaceutical industries Ltd. | 70 TO 240 |
| Neopride | 50\25\75 MG | Intas pharmaceutical Ltd. | 64 TO 178 |
| Ulpride | 25MG SR 75 MG | Eris Lifescience Ltd | 88 TO 151 |
| volapride | 25MG | Mankind Pharma. Ltd | 13 TO 59 |
| Levogut | 25\50 MG | Mission Research Laboratories Pvt. Ltd | 70 TO 90 |
| Lefit | 25\50 MG | Tas Med India Pvt Ltd | 79 TO 90 |
| levipride | 25\50\100 MG | Intas pharmaceutical Ltd. | 90 TO 244 |

## PATENTS

1. Patent Title: Improved method for the production of lysergic acid diethylamide (LSD) and novel derivatives thereof Patent Number: Not provided Application Date: July 7, 2021 Status: Patent application filed Inventor: Matthias Grill Assignee: Compass Pathfinder Limited Summary: This patent describes an improved method for producing lysergic acid diethylamide (LSD) in compliance with Good Manufacturing Practice (GMP) regulations. The goal is to provide a process that meets GMP objectives and introduces novel LSD derivatives denoted by formula I. These derivatives have been shown to exhibit affinity for the 5-HT2A receptor, suggesting potential therapeutic applications in fields such as depression and drug addiction.

2. Patent Title: Lysergic acid amides Patent Number: US2,997,470 Application Date: March 5, 1956 Status: Expired - Lifetime Inventor: Richard P. Pioch Assignee: Eli Lilly and Company Summary: This patent focuses on the unique amides produced from lysergic acid, represented by the chemical formula RCOR. The patent describes a wide range of amido radicals that can be used in the synthesis of these amides. It also explains the formation of acid addition salts of the amides and their potential use in separating and purifying reaction mixtures. Various acids, both mineral and organic, can be used to form the salts.

3. Patent Title: LSD salt crystal form Patent Number: Not provided Application Date: April 26, 2022 Status: Patent application filed Inventors: Daniel Emil Levy, Stephen E. Schneider Assignee: Mind Medicine, Inc. Summary: The invention pertains to the discovery of polymorphic forms of lysergic acid diethylamide (LSD) in crystalline salt forms. These polymorphic forms have prompted the development of pharmaceutical formulations that incorporate these forms along with suitable excipients. The patent highlights the significance of polymorph screening in optimizing drug performance, particularly for substances with inherent delivery barriers. The selection of the appropriate polymorphic form can impact factors such as stability, targeting, solubility, dissolution rate, and bioavailability.

4. Patent Title: Immediate release formulations of d-lysergic acid diethylamide for therapeutic applications Patent Number: US20230107398A1 Application Date: December 7, 2022 Status: Pending Inventors: Peter Mack, Dustin Melton, Bethany Amber Doty, Jon Schroeder, James Coghill, Daniel Emil Levy Assignee: Mind Medicine, Inc. Summary: This patent describes a solid oral immediate release formulation of d-lysergic acid diethylamide (LSD) in various dosage forms, including tablets, capsules, and orally disintegrating tablets. The formulation aims to achieve quick drug release upon administration. Different granulation procedures, such as dry granulation with moisture activation or dry blending, can be used to create the formulation. The patent also covers the method of treating patients by administering LSD in this solid oral formulation with immediate release.

5. Patent Title: D-lysergic acid - d-l-hydroxybutyl Patent Number: US2265207A Application Date: December 9, 1941 Status: Expired - Lifetime Inventor: Not provided Summary: This patent relates to the production of a novel lysergic acid amide with advantageous pharmacological characteristics. The patent describes the synthesis process involving the condensation of isolysergic acid azide with d-Z-aminobutanol-1, followed by transposition treatment of the resulting product. The amide produced, d-lysergic acid-d-l-hydroxybutylamide-2, exhibits superior physiological qualities compared to other known ergot alkaloids. The patent provides detailed steps for the synthesis and properties of the resulting amide, including its crystalline form, melting point, and optical rotation.[20,21,22,23]

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