A critical analysis of lysergic acid diethylamide in the present light!

Baskaran M, Meera Saravanan, Maheswari T, Muthulakshmi S and Dr. Jayasudha A

Abstract
Lysergic acid diethylamide (LSD) is a semisynthetic compound with solid psychoactive properties. Chemically related to serotonin, LSD was initially hypothesized to produce a psychosis-like state. Afterward, LSD was accounted for to have benefits in the treatment of addictions. However, far-reaching unpredictable use and reports of unfriendly impacts brought about the arrangement of LSD as an illegal medication with no acknowledged clinical use. This article audits LSD's celebrated history from its disclosure, to its utilization as an exploration instrument, trailed by it across the board relationship with the counterculture development of the 1960s, lastly to its resurrection as a medication with expected advantages in the treatment of addictions. LSD's pharmacology, phenomenology, impacts at synapse receptors, and consequences for examples of quality articulation are looked into. In view of a survey of the writing, it is reasoned that further examination into LSD's potential as a treatment for addictions is justified.

Keywords: LSD, Addiction, hallucinogen, lysergic acid, psychedelic drugs, psycholytic therapy

Introduction
LSD (lysergic acid diethylamide) is a synthetic (man-made) drug that has been abused for its hallucinogenic properties since the 1960s. If consumed in a sufficiently large dose, LSD produces delusions and visual hallucinations that distort the user’s sense of time and identity.

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Lysergic Acid Diethylamide
Since its discovery in 1938 by Swiss chemist Albert Hofmann, lysergic acid diethylamide (lysergide, LSD) has maintained an unstable relationship with psychiatry. Hofmann synthesized LSD in an effort to develop ergot derivatives with the goal of reducing postpartum hemorrhage. Even the US Army and CIA experimented with this substance as a truth serum, and LSD was further investigated by the US Army as a potential incapacitating agent, however without success. LSD is one of the most potent, mood-changing, semi-synthetic psychedelic agents, colloquially measured in 'hits' or 'tabs'. Numerous synthetic methods in clandestine laboratories have been used successfully or unsuccessfully to produce this drug. The interesting uses of this drug in psychiatry, such as an antianxiety agent, a creativity enhancer, a suggestibility enhancer, a performance enhancer, and also its other successful uses like in drug and alcohol dependence.

LSD, Different Forms!
LSD typically is sold as a liquid (often packaged in small bottles designed to hold breath freshening drops) or applied to blotter paper, sugar cubes, gelatin squares, and tablets. LSD generally is taken by mouth. The drug is colorless and odorless but has a slightly bitter taste.

- Blotter paper (LSD soaked onto sheets of absorbent paper with colorful designs; cut into small, individual dosage units)—the most common form
- Thin squares of gelatin (commonly referred to as window panes)
- Tablet form (usually small tablets known as Microdots) or capsules
- Liquid on sugar cubes
- Pure liquid form (may be extremely potent)

LSD, a Classical Hallucinogen!
LSD is part of the pharmacological group known as “classical hallucinogens” or “psychedelics” (term coined by Osmond in 1957), sharing its chemical structure with psilocybin and dimethyltryptamine (DMT) as a variant of indolamine (chemical structure similar to the neurotransmitter serotonin). From an anthropological perspective, as an “entheogen”, which implies that users experience (mainly in a religious, shamanic or spiritual context) an altered state of consciousness: “as if the eyes had been cleansed and the person could see the world as new in all respects” [3]

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<th>Table 1: Lysergic Acid Diethylamide</th>
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LSD is one of the most potent classical hallucinogens available, with active doses between 0.5 and 2 mcg/kg (100-150 mcg per dose). Its half-life is approximately 3 hours, varying between 2 and 5 hours, and its psychoactive effects are prolonged over time (up to 12 hours depending on the dose, tolerance, weight and age of the subject). Recently LSD has been used in micro doses as low as 10 mcg to enhance performance. Effects typically include altered thoughts, feelings and awareness of one’s surroundings. The usual mental effects of LSD are distortion of sense of time and identity, alteration in depth and time perception, visual hallucinations, sense of euphoria or certainty, distorted perception of the size and shape of objects, movements, color, sounds, touch and body image and delusions. Its frequent or long-term use can lead to tolerance, and after a single dose, emotional, physical and mental stability is quickly recovered [3]. Recent studies with LSD regarding changes in neural networks have been carried out. Modularity and integration networks (as observed in resting-state functional connectivity) have been shown to decrease due to effects of LSD. Patterns compared to normal waking consciousness have been demonstrated with LSD, and a correlation between subjective reports of “ego dissolution” during LSD and an increment of the overall connectivity and global integration of the brain was found. These changes at the cerebral level during the acute effects of hallucinogens have been associated with the aforementioned subjective effects “ego dissolution” and “mystical-type”, and could be related to the wide therapeutic value of these substances. The LSD user’s reactions are extremely subjective, variable, and unpredictable. Thus one trip may be filled with brilliant hallucinogenic sights and sensations, mind expansion, as well as euphoric feelings of oneness with the universe; while, another trip may bring anxiety, panic, fear, and depression, despair, and solitude of disappointment [4].

LSD, an Update!
The National Survey on Drug Use and Health in 2018 estimated that 5.6 million people aged 12 or older were past year users of hallucinogens (which includes LSD, PCP, peyote, mescaline, psilocybin mushrooms, Ecstasy, ketamine, DMT/AMT/“Foxy,” and Salvia divinorum), corresponding to 2% of the population. The percentage of people aged 12 or older in 2018 who were past year hallucinogen users was higher than the percentages in 2015 and 2016, but it was similar to the percentage in 2017 [5]. Individuals of all ages use LSD. Data reported in the National Household Survey on Drug Abuse indicate that an estimated 20.2 million U.S. residents aged 12 and older used LSD at least once in their lifetime. The survey also revealed that many teenagers and young adults use LSD 742,000 individuals aged 12 to 17 and 4.5 million individuals aged 18 to 25 used the drug at least once [6]. Rates of LSD use remain low among youth in the U.S. In 2018, it was estimated that 376,000 adolescents aged 12 to 17 were past year users of hallucinogens, which corresponds to about 1.5% of adolescents. The percentage of adolescents in 2018 who were past year hallucinogen users was lower than the percentages in 2015 and 2017, but it was similar to the percentage in 2016 [7]. In 2019, based on data from NIDA’s Monitoring the Future 2019 Survey Results: Overall Findings, past year illicit drug
use for LSD among surveyed 12th graders was 3.6%, far below illicit drug use for marijuana, which stood at 35.7%. Between the years 2015 to 2016, trends in annual prevalence of use of LSD for Grades 8, 10, and 12 combined were 1.9% (2015) and 2.0% (2016), a +0.1 percentage points increase. The Monitoring the Future National Survey Results on Drug Use: 2016 Overview. Key Findings on Adolescent Drug Use found that "generational forgetting" - students stating that they are not familiar with the drug - has resulted in a decline in perceived risk of LSD among younger groups, which may put them at higher risk of use in future years.

LSD use among high school students is a particular concern. More than 8 percent of high school seniors in the United States used the drug at least once in their lifetime, and nearly 4 percent used the drug in the past year, according to the University of Michigan’s Monitoring the Future Survey. The effects associated with LSD use are unpredictable and depend upon the amount taken, the surroundings in which the drug is used, and the user’s personality, mood, and expectations. Some LSD users experience a feeling of despair, while others report terrifying fears of losing control, going insane, or dying. Some users have suffered fatal accidents while under the influence of LSD. LSD users often have flashbacks, during which certain aspects of their LSD experience recur even though they have stopped taking the drug. In addition, LSD users may develop long-lasting psychoses, such as schizophrenia or severe depression. LSD is not considered an addictive drug - that is, it does not produce compulsive drug-seeking behavior as cocaine, heroin, and methamphetamine do. However, LSD users may develop tolerance to the drug, meaning that they must consume progressively larger doses of the drug in order to continue to experience the hallucinogenic effects that they seek.

LSD, a Retrospect!
Scenario 1: A Case History during March 2019
N Karthik Anand aged 27 is Karthik is a BA visual communication graduate from a private college in Coimbatore. He works with a TV channel in Chennai, translating Hindi serials into Tamil. He himself was an addict. He was not making enough money through his job to buy his own drugs. So, he started a trade by the side, selling drugs to students. He attracted customers through his connections. He had built a customer base. He was earning just Rs 16,000 from the television channel and Rs 70,000 profit from drug dealing. He got the drugs from a foreigner in Goa. The foreigner, as per preliminary probe, brings drugs to Goa once a month from European countries. The drugs include LSD (psychedelic drug-Lysergic Acid Diethylamide), Cocaine, MDMA (Methylenedioxymethamphetamine) and Ketamine. All these are banned in the country [8].

Many others like Karthik used to buy in bulk from the foreigner who has not yet been identified. Few dealers caught over the last five years were employees of IT firms, managers of private companies and engineers. They had quit their job to become a dealer. Reason: drugs pay much more than their job. D Purushothaman DSP of NIB CID started watching Karthik’s house, posing as a customer and arrested the culprit. Sleuths have seized 30 LSD stamps weighing 830 mg and 45 MDMA tablets weighing 13.190 grams from him, total worth of which is around Rs 3 lakh.

Dr. S. Bruno Bharathi, Psychiatrist brought to light the trend of synthetic drugs might have greater social disturbance in the longer run. The behaviour of consumers drastically change where people will do anything for the sake of the high they get.

Scenario 2: Youngsters Discover LSD
The psychedelic drug seems to have become the poison of choice at high-end pubs and rave parties in the city, worrying police officers. Youngsters are wearing the habit on their sleeve: The 2cm x 2cm like LSD stamps that are making their way into the city double up as temporary tattoos. They take a dose, stick stamp on triceps, and think you’re cool. Never mind that using acid can give a person a very bad trip, severely impair judgment, put the individual and others at risk, result in acute adverse reactions such as acute anxiety and, ultimately, cause psychoses such as schizophrenia. The LSD stamps (blotter paper soaked in the drug), brought to the city from Mumbai, Goa and Delhi, and were becoming increasingly popular on the city’s party circuit, especially over the past six months. It has become popular among party-goers and that’s a worrying development. Some party organizers are bringing it to Chennai and the rave gatherings happen on the outskirts of the city [9].

The drug is also expensive, with one stamp costing at least Rs 1,000. Students from affluent backgrounds, techies and others with large incomes are the main users of LSD in Chennai. Youngsters are with 10 to 15 LSD stamps on strips in their pockets at parties. The stamps, which a user places on the tongue or inside the cheek, are brightly coloured and have pictorial representations of animals or cartoon characters and can pass off for temporary tattoos.

LSD, Brain Physiology

LSD, a banned narcotic, is tasteless, colourless and odourless, and has hallucinogenic properties. Its effect, scientists believe, is similar to serotonin, a neurotransmitter in the brain responsible for regulating moods, appetite, muscle control, sexuality, sleep and sensory perception. It interferes with the way the brain's serotonin receptors work, inhibiting neurotransmission, stimulating it, or both [4].

Though the use of LSD is on the increase and police have caught quite a few youngsters in possession of the drug, they are yet to make arrests. They have so far let off users with a stern warning because if they book a case it will adversely affect their careers. They are monitoring the supply chain and hope to soon trace and arrest those smuggling and selling the drug.
Scenario 3: A Thought to Parents
Rajhansa said we are keeping an eye on each and every party in the city, starting from Christmas Eve. Parents can identify drug addiction through their children’s behaviour. Parents have to watch out for a change in sleeping pattern and changes in their facial expressions. The pupils too appear dilated or too small. They will refrain from making eye-contact while talking. Diet pattern also changes as most youngsters lose appetite. Parents can try to smell their hands and fingers which will smell like vomit. Parents should seek help if any of these alarming signs are found.

LSD, its Risks!
The effects associated with LSD use are unpredictable and depend upon the amount taken, the surroundings in which the drug is used, and the user’s personality, mood, and expectations. Some LSD users experience a feeling of despair, while others report terrifying fears-of losing control, going insane, or dying. Some users have suffered fatal accidents while under the influence of LSD. LSD users often have flashbacks, during which certain aspects of their LSD experience recur even though they have stopped taking the drug. In addition, LSD users may develop long lasting psychoses, such as schizophrenia or severe depression. LSD is not considered an addictive drug-that is, it does not produce compulsive drug-seeking behavior as cocaine, heroin, and methamphetamine do. However, LSD users may develop tolerance to the drug, meaning that they must continue to experience the hallucinogenic effects that they seek [6].

LSD, a Challenging Experience!
An individual’s body image may be distorted; the sensations can turn to a ‘bad trip’ and eventually culminate in frank psychosis. The drug moves quickly to the brain and throughout the body and acts on both the central and autonomic nervous systems. All traces of the drug disappear from the brain rapidly in about 20 minutes, although the effects may last many more hours.

LSD, its Side Effects!
LSD’s effects typically last around 8-10 hours, with peak effects occurring 4-6 hours after ingestion. Common side effects include:

Table 2: shows the Physiological Side effects and Psychological Side effects

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<th>Physiological Side effects</th>
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<td>Sensory enhancement</td>
<td>Delusions</td>
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<td>Sweating</td>
<td>Alienation</td>
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<td>Dry mouth</td>
<td>Visual hallucinations</td>
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<td>Tremors</td>
<td>Synesthesia (i.e. “hearing” colors, “seeing” sounds)</td>
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<td>Increased heart rate</td>
<td>Dissociation</td>
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<td>High blood pressure</td>
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<td>Dilated pupils</td>
<td>Distorted visual perceptions</td>
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<td>Depression</td>
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LSD, a Treatment!
The indications of LSD-assisted psychotherapy may be courageously listed as psychoneurotic disorders, conversion phobic depressive disorders, neurotic depressive reaction, reactive depression, other (mixed psychoneurosis, pan-neurosis, pseudo neurotic schizophrenia, borderline or latent schizophrenia) personality disorders, cyclothymic (obsessional) and passive-aggressive (obsessional) compulsive sexual deviation addiction, transient situational personality disorders, and manic-depressive reaction in remission [2].

Three different major approaches to LSD use as a treatment were then applied to clinical research: “psycholytic therapy”, “psychedelic-chemotherapy” and “psychedelic-peak therapy”. In psycholytic therapy, mainly practiced in Europe, low-moderate doses 25-200 mcg of this drug were used in more than one therapeutic session of psychodynamic orientation. In psychedelic-chemotherapy, drug use itself was emphasized at relatively high doses (200 mcg or more), with a very limited or absent psychotherapeutic approach. As for psychedelic-peak therapy or psychedelic therapy, it involves administering a single and relatively high dose with the aim of triggering a mystical type experience, peak experience or ego dissolution. This approach should include the proper prior preparation of the patient and a comfortable environment during the session, as well as a discussion on it during subsequent follow up sessions with the subject, after-care related to LSD session.

Finally, one of the authors highlighted that male patients showed a clear improvement in Global Adjustment with as full dose 350 mcg of LSD at six months post ingestion, while in females, a greater improvement was observed with low doses of 50 mcg. The results of few reviews could conclude that alcohol use disorder patients may benefit from LSD treatment.

LSD Use, its Treatment!
Once a decision is made to obtain treatment, there are several steps to take.
- Speak to a healthcare provider to help direct you to reliable sources of help and monitor your progress.
- Talk therapy (behavioral counseling) and group counseling may be an option to help you understand your behaviors and why you continue to use LSD.
- Keep your appointments and follow your provider’s treatment plan. Consider including trusted family or friends in your treatment plan.
- Take care of yourself: exercise, eat healthfully, and control your stress level.
- Surround yourself with supportive people.
- Added medical therapy may be needed to treat symptoms due to drug use, such as anxiety, depression, or schizophrenia.
- Work to find new hobbies and interests that will take your mind off of drug use. Consider a volunteer opportunity.
- Each day make an effort to stay away from people who abuse drugs, even if they are former friends.

LSD, Nursing Implications
Nurse’s insight into the health hazards of LSD helps to challenge them to take care of patients with multiple substance use when they encounter in a psychiatric setting.

LSD, an Illegal
Yes, LSD is illegal. LSD is a Schedule-I substance under the Controlled Substances Act. Schedule I drugs, which
include heroin and MDMA, have a high potential for abuse and serve no legitimate medical purpose.

**Conclusion**

LSD is known for its profound changes in consciousness and perception. LSD is revealed as a potential therapeutic agent in psychiatry; the evidence to date is strongest for the use of LSD in the treatment of alcoholism. Despite the difficulty of designing double-blind clinical trials with this substance, new studies performed under modern standards are necessary in order to strengthen our knowledge, help erase the stigma that still prevails around these substances and open new doors in the future.

**References**