

LSD – Lysergide

A scientific overview of LSD-25

TOXNET

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LSD - Lysergide

CASRN: 50-37-3

Human Health Effects:

Human Toxicity Excerpts:

IN MAN, ORAL DOSES OF **LSD** AS LOW AS 20 TO 25 UG PRODUCE CNS EFFECTS IN SUSCEPTIBLE INDIVIDUALS. ... **LSD** PRODUCES SOMATIC EFFECTS LARGELY SYMPATHOMIMETIC IN NATURE, SUCH AS PUPILLARY DILATATION, INCR IN BLOOD PRESSURE, TACHYCARDIA, HYPERREFLEXIA, TREMOR, NAUSEA, PILOERECTION, MUSCULAR WEAKNESS, AND INCR BODY TEMP.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 554]**PEER REVIEWED**

Following oral doses of 0.5 to 2 ug/kg, the somatic symptoms are usually perceived within a few min. These include dizziness, weakness, drowsiness, nausea, and paresthesias. They may be followed by a feeling of inner tension relieved by laughing or crying. Several feelings may seem to coexist at the same time, although euphoric effects tend to predominate. In the second or third hr, visual illusions, wavelike recurrences of perceptual changes (eg, micropsia, macropsia), and affective symptoms may occur. Afterimages are prolonged, and the overlapping of present and preceding perceptions occurs. Some subjects recognized these confluences, whereas others elaborate them into hallucinations. In contrast to naturally occurring psychoses, auditory hallucinations are rare. Synesthesias, the overflow from one sensory modality to another, may occur. Colors are heard and sounds may be seen. Subjective time is also seriously altered, so that clock time seems to pass extremely slowly. The loss of boundaries and the fear of fragmentation create a need for a structuring or supporting environment and experience companions. During the trip, thoughts and memories can vividly emerge under self-guidance or unexpectedly to the user's distress. Mood may be labile, shifting from depression to gaiety, from elation to fear. Tension and anxiety may mount and reach panic proportions. After about 4 to 5 hr, if a major panic episode does not occur, there may be a sense of detachment and the conviction that one is magically in control. Between the dose ranges of 1 to 16 ug/kg, the intensity of the psychophysiological effects of **LSD** is proportional to the dose. The entire syndrome, including the pupillary dilation, begins to clear after about 12 hr.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 554]**PEER REVIEWED**

A CASE OF SEVERE LIMB ISCHEMIA PREDOMINATING IN THE LEGS IN A YOUNG FEMALE DRUG ADDICT IS REPORTED. THE CAUSATIVE ROLE OF **LSD** WAS SUGGESTED BY THE HISTORY OF GREATLY INCR INTAKE IN THE PERIOD BEFORE THE ONSET OF SYMPTOMS. ANALYSIS OF A SAMPLE DOSE TAKEN BY THE PT SHOWED A VERY LARGE QUANTITY OF **LSD** AND OF LYSERGIC ACID AND A VERY SMALL AMT OF OTHER ERGOT ALKALOIDS KNOWN FOR THEIR PERIPHERAL VASOCONSTRICTOR EFFECTS.

[JUILLET Y ET AL; ARCH MAL COEUR 73 (11): 1359-63 (1980)]**PEER REVIEWED**

123 PERSONS WITH A HISTORY OF **LSD** USE WERE STUDIED FOR THE PRESENCE OF THE **LSD** FLASHBACK PHENOMENON AND COMPARED WITH 40 CONTROL SUBJECTS. A SYNDROME EMERGED THAT INCL 10 DISTANCE VISUAL DISTURBANCES. IT HAD LASTED FOR 5 YR IN HALF THE POPULATION AND WAS PRECIPITATED BY 19 DIFFERENT STIMULI, MOST COMMONLY EMERGENCE INTO A DARK ENVIRONMENT.

[ABRAHAM HD; ARCH GEN PSYCHIATRY 40 (8): 884-9 (1983)]**PEER REVIEWED**

FORTY-SIX USERS OF **LSD** WERE COMPARED WITH 31 CONTROLS ON A TEST OF COLOR DISCRIMINATION AN AVG OF 2 YR AFTER THEIR LAST EXPOSURE TO THE DRUG. THIS STUDY SUGGESTS THAT SOME USERS OF **LSD** MAY HAVE A SUSTAINED OR IRREVERSIBLE IMPAIRMENT IN COLOR DISCRIMINATION.

[ABRAHAM HD; BR J PSYCHIATRY 140: 518-20 (1982)]**PEER REVIEWED**

THE AUTHORS REPORT A PATIENT WHO SUFFERED A FULL-BLOWN MANIC ATTACK AFTER INGESTING **LSD** OR AN **LSD** ANALOG. THE PATIENT EXPERIENCED ACUTE SYMPTOMS OF **LSD** INTOXICATION, WHICH RESOLVED BUT WERE FOLLOWED IN ABOUT 3 WK BY A TYPICAL MANIC EPISODE OF PSYCHOTIC MAGNITUDE. THE MANIA CLEARED WITH LITHIUM THERAPY.

[LAKE CR ET AL; AM J PSYCHIATRY 138 (11): 1508-9 (1981)]**PEER REVIEWED**

LSD IS LONGER ACTING AND MORE THAN 100 TIMES AS POTENT AS PSILOCYBIN AND PSILOCIN, THE ACTIVE ALKALOIDS IN THE MEXICAN "MAGIC MUSHROOM"; IT IS 4000 TIMES AS POTENT AS MESCALINE IN PRODUCING ALTERED STATES OF CONSCIOUSNESS.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 556]**PEER REVIEWED**

A high degree of tolerance to the behavioral effects of **LSD** develops after three or four daily doses; sensitivity returns after a comparable drug-free interval. ... Tolerance to the cardiovascular effects is less pronounced. ... These drugs /including **LSD**/ do not give rise to patterns of repetitive use over prolonged periods. The most common psychedelic-use pattern is the occasional trip, separated by intervals of weeks or months during which marihuana is used with variable frequency. ... In man, deaths attributable to direct effects of **LSD** are unknown, although fatal accidents and suicides have occurred during states of **LSD** intoxication.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 556]**PEER REVIEWED**

The incidence of spontaneous abortion and fetal abnormalities appears to be higher among women who use illicit **LSD**, but the effects of pure **LSD** on pregnancy and the fetus remain uncertain.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 556]**PEER REVIEWED**

The evidence for significant psychological hazards in the use of psychedelic agents is unambiguous. The most common adverse effect is a temporary (24 hr) episode of panic, a bad trip. ... Such bad trips cannot be reliably prevented and have been experienced even by users who had previous good trips. Recurrences of drug effects without the drug flashbacks are a

puzzling phenomenon; they occur in more than 15% of users. Commonly precipitated by use of marijuana, anxiety, fatigue, or movement into a dark environment, flashbacks may persist intermittently for several years after the last exposure to **LSD**. They are exacerbated by the use of phenothiazines. In some individuals the use of psychedelics can precipitate serious behavior, or prolonged psychotic episodes. Whether such episodes would have occurred without the drug is not clear. Prolonged psychotic episodes following repeated use of **LSD** tend to resemble naturally occurring schizophreniform psychotic states, and the prognosis appears to be similar. It is possible that the repeated use of **LSD** can induce subtle deficits in the capacity for abstract thinking.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 556]**PEER REVIEWED**

Extremely potent drug capable of producing altered mental states at doses as low as 25 ug. ... Not physically addictive. ... Ability to perform complex mental and physical tasks is severely affected. ... Drug is known to sometimes cause bizarre behavior, which can lead to fatal accidents and suicide.

[DHHS/NIDA; Research Monograph Series 73: Urine Testing for Drugs of Abuse p.105 (1986) DHHS Pub No. (ADM)87-1481]**PEER REVIEWED**

/A study/ carried out ... of 121 pregnancies ... found no increase in defects but a possible increase in spontaneous abortions in the mothers who took **LSD** as compared to pregnancies where only the father took it.

[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986., p. 348]**PEER REVIEWED**

LSD flashbacks also are characteristic. ... Flashbacks refer to spontaneous recurrences of the somatic, perceptual, or psychic phases of an **LSD** experience that occur after cessation of drug use. They may occur under benign conditions or may be triggered by stress or other drug use (i.e., barbiturates or cannabis). Flashbacks have been reported to occur up to 10 times a day and up to 18 months after **LSD** use. They have been reported after a single **LSD** ingestion; however, the incidence of occurrences increases with increased **LSD** use.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 760]**PEER REVIEWED**

Eight people who "snorted" an unknown amount of **LSD** mistakenly instead of cocaine is reported. Within 5 min they developed anxiety, restlessness, generalized paresthesias, and vomiting. All had auditory and visual hallucinations. All had sinus tachycardia, widely dilated pupils, flushing, and sweating. Three had hypertension, and four became febrile (one to 41 deg C). Five became comatose. All eight had some degree of coagulopathy, and four had evidence of mild generalized bleeding. All patients recovered within 12 hr with supportive treatment.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 761]**PEER REVIEWED**

The first manifestations of drug effect are usually somatic. There is invariably mydriasis. Other somatic effects are not consistent findings and when present are usually inconsequential. These effects include increases in heart rate, blood pressure, and reflexes, paresthesias, twitches, incoordination, and cutaneous flushing. Increases in leukocyte count, glucose, and free fatty acids have been reported and are ascribed to stress-induced release of catecholamines.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 759]**PEER REVIEWED**

Intellectual function during **LSD** use shows variable objective impairment. Tests involving attention, concentration, and motivation demonstrate decreased performance. There is no improvement in creative tasks performed under the influence of **LSD**, nor is there objective evidence that past use improves overall intellectual or creative abilities.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 760]**PEER REVIEWED**

Perceptual distortions usually begin 30 to 60 min after oral ingestion. There is a magnified sense of color with increased vividness and contrast. Perception of distance and shape is altered, and objects appear to melt, vibrate, and flow. Sound becomes intensified, and users have difficulty locating the source of the sound. It is important to emphasize again that users do not fabricate sounds or images de novo but distort existing sensory clues. Two rather unique perceptual alterations are observed with **LSD** use. One is synesthesias, in which one sensory modality is translated into another, ie, smelling colors. The other is a failure to suppress a prior image, causing an overlay of images like a photographic double exposure.

[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982., p. 759]**PEER REVIEWED**

The psychic manifestations of a hallucinogenic experience consist of depersonalization, and loss of body image. Rarely, visual hallucination occur in this phase. Emotions can rapidly change from ecstasy to despair, often triggered by sensory clues. Thoughts and memories flow incessantly, often breaking the boundaries of repression. Four to six hr into a "trip" the user often turns inward to transcendental or contemplative thoughts. Users often perceive themselves as communicating in great philosophical depth, while in reality their conversations make no sense to the observer.

[Reynolds, J.E.F., Prasad, A.B. (eds.) Martindale-The Extra Pharmacopoeia. 28th ed. London: The Pharmaceutical Press, 1982., p. 760]**PEER REVIEWED**

The most commonly observed adverse effect is the panic attack. **LSD** interferes with the ability to filter and integrate sensory input. As the user is bombarded by stimuli, he may lose his control and reference points to reality and become overwhelmed with the fear of impending insanity. It is during a panic attack that a user can do the most harm to himself and others. **LSD** does not produce aggressive or violent behavior. In fact, there is no good correlation between **LSD** use and true homicidal or suicidal behavior. Instead, during a panic attack an individual may jump from a building in an attempt to fly or strike out in fear. Panic attacks usually last less than 24 hr, but they can degenerate into prolonged psychotic states.

LSD toxic psychosis can last from days to months. It is controversial but generally accepted that prolonged psychosis is not actually caused by the drug. Prolonged psychosis is felt instead to be a psychotic condition that is accelerated or exacerbated by the experience.

Symptoms of the psychotic state therefore depend on the patient's premorbid personality and may include thought disorders, hallucinations, depression, regression, or depersonalizations.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 760]**PEER REVIEWED**

In human beings, **lysergide** may produce acute intoxication resembling atropine poisoning, consisting of visual hallucinations, disorientation, elevated body temperature, increased heart rate, and dilated pupils, but most of these effects are sympathomimetic, rather than anticholinergic. In **lysergide** intoxication the skin characteristically shows "goose pimples."

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 569]**PEER REVIEWED**

Intraocular pressure in human volunteers given **LSD** 1 ug/kg orally rose less than 2 mm Hg.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 569]**PEER REVIEWED**

... A report, from a comparison of former users of **LSD** with controls, suggesting that some users may have irreversible impairment of color discrimination, but no published reports were found of blindness or of persistent alteration of the eyes or of vision in human beings after intoxication by **lysergide**, apart from effects of sun-gazing. Some actual persistent impairment of visual acuity, and persistent tiny central scotomas, have resulted from gazing at the sun while under the influence of **LSD**.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 569]**PEER REVIEWED**

A detailed pathological description of the muscle findings in a case of the neuroleptic malignant syndrome following ingestion of lysergic acid diethylamide (**LSD**) is given, including the first ultrastructural analysis. Focal necrosis, oedema, and hypercontraction of fibres with glycogen and lipid depletion, were identified, all of which had resolved completely a year later. The findings are compared with those in malignant hyperthermia. It is suggested that the results support the view that in neuroleptic malignant syndrome, the muscle rigidity is due to central mechanisms and, in both this disorder and malignant hyperthermia, it is responsible for the hyperpyrexia and its life-threatening complications.

[Behan WM et al; J Neurol Neurosurg Psychiatry 54 (8): 741-3 (1991)]**PEER REVIEWED**

Sperm chromosome studies were performed in seven males. One of them had a history of exposure to **LSD** although he was free of the drug for 1 yr before the study began. Sixteen ejaculates provided a total of 555 fully analyzable sperm cells. The overall frequency of hyperhaploid sperm cells was 2% and that of structural abnormality 3.6%. The most common structural abnormality was chromosome breaks followed by small chromosome fragments of unknown origin. Three chromosome breakpoints, 10q25, 2q21, and 9q21, were involved twice in different chromosome or chromatid type aberrations. Two of these, 10q25 and 2q21, correspond to chromosomal locations known as common fragile sites.

[Estop AM et al; Hum Genet 87 (4): 447-51 (1991)]**PEER REVIEWED**

Recreational drug (marijuana, **LSD**, speed, cocaine, and "other") exposures of women with primary infertility were compared with those of a matched control group of women with proven fertility. Women who reported smoking marijuana had a slightly elevated risk for infertility due to an ovulatory abnormality (RR = 1.7, 95% CI = 1.0 to 3.0). The risk was greatest among women who had used marijuana within one year of trying to become pregnant (RR = 2.1, 95% CI = 1.1 to 4.0). No consistent frequency or duration of use effects could be demonstrated, and the risk was confined to low-frequency users. Risks associated with the use of other drugs were not elevated. The risk of infertility from a tubal abnormality associated with cocaine use was greatly increased (RR = 11.1, 95% CI = 1.7 to 70.8). Our results are consistent with animal studies suggesting that smoking marijuana may cause a transient disruption of ovulatory function. The possibility that cocaine exposure influences the development of tubal infertility needs further investigation.

[Mueller BA et al; Epidemiology 1 (3): 195-200 (1990)]**PEER REVIEWED**

Emergency Medical Treatment:

Emergency Medical Treatment:

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The following Overview, *** **LSD** ***, is relevant for this HSDB record chemical.

Life Support:

- o This overview assumes that basic life support measures have been instituted.

Clinical Effects:

0.2.1 SUMMARY OF EXPOSURE

- A) Ingestion of **LSD** results in altered cognitive and perceptual states resulting in auditory and visual hallucinations, behavioral changes, paranoia, marked fluctuations in mood, and acute psychotic reactions.
- B) Dizziness, mydriasis, and diaphoresis may occur.
- C) TYPICAL CHRONOLOGY OF **LSD** INTOXICATION includes the following:

PHASE	TIME FROM INGESTION	SYMPTOMS
Somatic	0-60 mins	Tension, lightheadedness, mydriasis, twitching, flushing, tachycardia, hypertension, hyperreflexia
Perceptual	30-60 mins	Visual, auditory and sensory alterations; distortions of color, distance, shape, and time; synesthesias
Psychic	2-12 hrs	Euphoria, mood swings, Depressions, feelings of depersonalizati- on,

derealization,
loss of body
image

0.2.3 VITAL SIGNS

- A) Hypertension or hypotension, tachycardia, tachypnea, and hyperthermia may occur.

0.2.4 HEENT

- A) Mydriasis is frequently reported. Lacrimation may also occur.
- B) Impaired perception of color and other visual functions, persistent or recurrent visual illusions and halos around objects have been reported.

0.2.5 CARDIOVASCULAR

- A) Hypertension or hypotension along with tachycardia may occur.

0.2.6 RESPIRATORY

- A) Tachypnea and bronchoconstriction may occur at high doses.

0.2.7 NEUROLOGIC

- A) An acutely altered mental status characterized by restlessness, acute anxiety, behavioral changes, depersonalization, tremors and incoordination may occur.
- B) Sympathomimetic symptoms may predominate initially.
- C) Seizures, muscle weakness, and ataxia are rare adverse effects.

0.2.8 GASTROINTESTINAL

- A) Vomiting, diarrhea, salivation, and anorexia may occur.
- B) Retroperitoneal fibrosis has been associated with chronic **LSD** use.

0.2.10 GENITOURINARY

- A) Rhabdomyolysis and renal failure have been reported, but are probably result from seizures and coma. Uterine contractions may occur. **LSD** is not normally nephrotoxic but has been linked to retroperitoneal fibrosis.

0.2.13 HEMATOLOGIC

- A) Poor clot formation and retraction have been noted to occur early and to resolve spontaneously; leukocytosis is possible.

0.2.15 MUSCULOSKELETAL

- A) Muscle rigidity has been seen as a result of **LSD** associated neuroleptic malignant syndrome.

0.2.18 PSYCHIATRIC

- A) Hallucinations, acute psychotic reactions, paranoia, depersonalization, and altered cognitive and perceptual states are common. Hallucinations are usually visual and rarely auditory. Synesthesia is characteristic. "Flashbacks" and panic reactions occur unpredictably.

0.2.20 REPRODUCTIVE

- A) **LSD** has been implicated in teratogenicity, although the causative agent is not always clear and there is no consistency of findings.

Laboratory:

- A) Plasma and urine **LSD** levels are measurable and quantified by various techniques but are not clinically useful other than to establish diagnosis.

Treatment Overview:

0.4.2 ORAL/PARENTERAL EXPOSURE

- A) SUMMARY - Because of rapid absorption, the value of gastrointestinal decontamination is limited; decontamination is generally NOT necessary after

recreational ingestions. Do not induce emesis in patients who have a decreased level of consciousness, seizures, or respiratory difficulty. Consider activated charcoal after large ingestions.

- B) **ACTIVATED CHARCOAL:** Administer charcoal as a slurry (240 mL water/30 g charcoal). Usual dose: 25 to 100 g in adults/adolescents, 25 to 50 g in children (1 to 12 years), and 1 g/kg in infants less than 1 year old.
- C) Administer thiamine 100 milligrams IV and glucose 1 gram per kilogram IV if there is altered mental status and the cause is unknown. Naloxone 2 milligrams IV should also be administered.
- D) A dimly lit, quiet environment with minimal stimulation but with adequate observation should be provided during assessments.
- E) **ANXIETY/AGITATION:** ACUTE ANXIETY may be managed with IV or PO DIAZEPAM (Adult: up to 10 mg slowly: Child: 0.1 to 0.3 mg/kg slowly).
 - 1) AVOID CHLORPROMAZINE if possible since simultaneous ingestion of other drugs such as dimethyltryptamine may have also occurred resulting in marked hypotension following chlorpromazine administration. Chlorpromazine also lowers the seizure threshold.
 - 2) Alternative regimens for extreme agitation or hallucinosis include LORAZEPAM (1 to 2 mg in adults), CHLORDIAZEPOXIDE (50 to 100 mg in adults) and HALOPERIDOL (5 to 20 mg IM, IV, or orally in adults).
 - 3) PSYCHOLOGICAL ASSISTANCE may be helpful in talking down some patients who are undergoing a bad trip. Reassurance by a psychiatrist or a close friend may be helpful in ameliorating the acute anxiety state. A quiet, dimly lit room should be provided.
- F) **PSYCHOSIS** - Neuroleptics are recommended for persistent **LSD**-induced psychosis; some use only minor tranquilizers; others have used haloperidol, phenothiazine, lithium, and 1-5-hydroxytryptophan with carbidopa.
 - 1) There may be a possible role for serotonin-S2 receptor antagonists in the treatment of **LSD** induced psychoses.
- G) **NEUROLEPTIC MALIGNANT SYNDROME** - Treat neuroleptic malignant syndrome with dantrolene or bromocriptine along with conservative treatment.
- H) **RHABDOMYOLYSIS:** Administer sufficient 0.9% saline to maintain urine output of 2 to 3 mL/kg/hr. Monitor input and output, serum electrolytes, CK, and renal function. Diuretics may be necessary to maintain urine output. Urinary alkalinization is NOT routinely recommended.

Range of Toxicity:

- A) The minimal lethal or toxic dose of **LSD** in humans is unknown. The LD50 ranges from 0.3 to 50 mg/kg.
- B) A single 100 to 400 mcg dose of **LSD** can produce an altered state of consciousness. Illicit drug preparations may be contaminated with other drugs making it difficult to predict toxicity. Doses as low as 35 mcg can be hallucinogenic.

(Eds): TOMES(R) Information System Micromedex, Inc., Englewood, CO, 2005; CCIS Volume 125, edition expires Aug, 2005., p.]**PEER REVIEWED**

Antidote and Emergency Treatment:

LSD ingestions ... selflimited and require no intervention. The most common adverse effect is the acute panic reaction, which is best managed by "talking down" the patient in an unobtrusive, reassuring manner. The patient should be placed alone, oriented as necessary, and reminded that the experience is drug related and will eventually end. Efforts should be made to introduce pleasant thoughts, emphasize positive aspects, and divert the patient from frightening thoughts. The talkdown process should be devoid of condemnation, judgements, or sudden movements that might be misinterpreted as threatening. The patient should be allowed to move around, although suggestions to lie down and relax can be made.

Gastrointestinal decontamination and venipuncture may agitate and exacerbate the panic attack and should not be performed unless other drug ingestion is suspected. Acute panic reactions refractory to supportive care can be treated with benzodiazepines, preferably administered orally. Both diazepam (10 to 20 mg) and chloridiazepoxide (25 to 50 mg) have been used successfully. Acute psychotic reactions may need pharmacologic intervention; haloperidol (2 to 5 mg im) is the drug of choice for this treatment. Chlorpromazine should be avoided because there have been reports of cardiovascular collapse in patients who have taken drugs mixed with belladonnaaloids. Flashbacks are usually self-limited and thus can be treated with the same supportive care used in acute panic attacks. Recurrent episodes that are debilitating to the patient have been treated with psychotherapy, haloperidol, phenothiazines, and benzodiazepines with varying degrees of success. Patients should be cautioned that persistent drug use of any kind can stimulate flashbacks and should be avoided.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 761]**PEER REVIEWED**

Animal Toxicity Studies:

Non-Human Toxicity Excerpts:

DEATH DUE TO OVERDOSAGE IN ANIMALS RESULTS FROM RESP FAILURE, BUT IN RABBITS THERE IS A MARKED HYPERTHERMIA AS WELL.

[Gilman, A. G., L. S. Goodman, and A. Gilman. (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co., Inc. 1980., p. 566]**PEER REVIEWED**

IN FREE MOVING RATS TRAINED TO PRESS A BAR TO ESCAPE FROM RADIANT HEAT, LSD @ 8-16 UG PRODUCED A SIGNIFICANT AND DOSE-DEPENDENT INCR OF THE BAR-PRESSING RATE WHEN INJECTED IP. DURING THE INCR IN BAR-PRESSING RATE, THE RECTAL TEMP SHOWED AN INCR & BOTH THE TAIL-SKIN AND THE AMBIENT TEMP SELECTED DECR CONCOMITANTLY. THE RESULTS INDICATE THAT LSD-INDUCED HYPERTHERMIA IS MEDIATED THROUGH THE ACTION OF LSD ON THE EFFECTOR PATHWAYS IN THE RATS.

[MURAKAMI N ET AL; NEUROSCI LETT 20 (1): 105-8 (1980)]**PEER REVIEWED**

... Central nervous system abnormalities /were reported/ in day 11 mouse embryos after injecting 0.05 to 1.0 ug /of **LSD**/ on day 7. No dose response effect was seen ... Inbred mouse lines /were used/ ... /In another experiment/ in the hamster using 0.08 to 410 ug per kg /of **LSD**/ on the 8th day /of gestation/ ... a small increase in defects of the central nervous system

/was found/ in 12 day embryos.

[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986., p. 348]**PEER REVIEWED**

... Swiss-Webster mice /were injected/ on days 6, 7, 8 or 9 of pregnancy with 5 ug of **LSD-25** and ... a high incidence of histologic abnormalities of the lens /was found/.

[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986., p. 348]**PEER REVIEWED**

In the Wistar-O'Grady rat, ... fetal loss /was produced/ by administering **LSD** by mouth or sc (20 ug and 5 ug respectively) between the 1st and 4th day of gestation. No specific congenital defects were reported. ... /Another experiment/ could not produce defects in the hamster, but in one of two mouse strains (A-CUM) an increase in congenital defects was found when 30 ug was injected during organogenesis.

[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986., p. 348]**PEER REVIEWED**

... Rats /were injected/ with 5 to 100 ug on the 4th through the 7th day or the 7th through the 13th day /of gestation/ and ... no increase in fetal death or deformity /was found/. ... Swiss mice /were injected/ with 5 to 500 ug per kg between the 4th and the 14th day of gestation and ... no increased fetal mortality or defects /were found/. ... In hamsters ... injected /with/ 50 to 500 ug per kg during the 7th to 13th days ... no fetal changes /were found/.

[Shepard, T.H. Catalog of Teratogenic Agents. 5th ed. Baltimore, MD: The Johns Hopkins University Press, 1986., p. 349]**PEER REVIEWED**

Studies showed chromosomal breakage in leukocyte cultures.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 760]**PEER REVIEWED**

In cats, **lysergide** produced changes in the ERG or electric potential of the eye only when very large doses were administered, and these appeared to be nonspecific, such as might be induced by large amounts of barbiturates. In severely poisoned cats, spontaneous action potentials have appeared in the ERG, with exaggerated responses to stimulation by light. Simultaneously, large spikes appeared in recording from the occipital visual cortex and these spikes disappeared when the optic nerves were cut, suggesting that this spontaneous visual activity originated in the retina. The ERG of excised ... cat or monkey retina has not been affected by **lysergide**. Behavior suggesting blindness has been observed in cats, pigeons, and monkeys under the influence of **lysergide**. In monkeys this has been interpreted as "psychic blindness" and has been associated with loss of contact with the surroundings and impairment of skilled movements involving oculomotor control. In cats that acted blind after large doses of **lysergide**, electrical potentials have been picked up in the CNS, showing that although there might be effects on retina and optic nerve the changes were insufficient to cause blindness.

[Grant, W.M. Toxicology of the Eye. 3rd ed. Springfield, IL: Charles C. Thomas Publisher, 1986., p. 570]**PEER REVIEWED**

The behavioral response of guinea pigs to hallucinogenic agents was evaluated in order to characterize the response of this species to a variety of known hallucinogeni drugs. The systemic injection of **LSD** in the guinea pig elicited a "myoclonic-like" response the frequency of which was dose-dependent. This behavior exhibited rapid tolerance which was more prominent at higher doses. Subacute mescaline pretreatment reduced the myoclonic response to **LSD** suggesting cross-tolerance. Mescaline, DOM, TMA, DMA and 5 Me-

ODMT also elicited myoclonus in a dose-dependent manner and in potency ratios which approximate the human experience for hallucinogenic activity. Brom-**LSD** failed to induce myoclonus. Since the myoclonic response of the guinea pig shares a number of pharmacologic characteristics with the human hallucinogenic event, this species may be useful in the study of hallucinogenic compounds.

[Carvey P et al; Prog Neuropsychopharmacol Biol Psychiatry 13 (1-2): 199-210 (1989)]**PEER REVIEWED**

The effects of mescaline and **LSD** on the flash-evoked cortical potential were determined in unrestrained rats with chronically implanted electrodes. Systemic administration of mescaline or **LSD** significantly attenuated the primary component of the flash evoked cortical potential at three stimulus intensities with the greatest effect observed 60-90 minutes following drug administration. The magnitude and specificity of the effects of these agents on the primary response suggest that they produce deficits in conduction through the retino-geniculato-cortical system. The serotonin receptor antagonists, cyproheptadine and methysergide, antagonized the mescaline-induced depression of the flash evoked cortical potential in accordance with neurochemical and behavioral evidence that mescaline acts as a partial agonist on serotonin receptors. Topical or intraocular administration of atropine antagonized the actions of systemically administered mescaline. In addition, intraocular administration of mescaline or **LSD** attenuated the flash evoked cortical potential indicative of an action of these hallucinogens on visual processing in the retina which is modulated by muscarinic receptor activity.

[Eells JT, Wilkison DM; Pharmacol Biochem Behav 32 (1): 191-6 (1989)]**PEER REVIEWED**

Recurrent inhibition of the spinal monosynaptic reflex elicited by conditioning stimulation of the ventral root in anesthetized rats was weaker than both the recurrent inhibition of the disynaptic reflex and the inhibition of the monosynaptic reflex elicited by conditioning stimulation of the adjacent dorsal root. Among these inhibitions, the recurrent inhibition of the monosynaptic reflex was enhanced to a markedly greater extent by a preceding stimulation of the medullary raphe nucleus than were the other inhibitions. The magnitude of the enhancement of the recurrent inhibition of monosynaptic reflex also was much greater when the medullary stimulation was delivered 20 ms prior to the ventral root activation, as compared with a 30-ms interval. Recurrent inhibition of the monosynaptic reflex was enhanced by iv injection of **LSD**; however, the enhanced effect on recurrent inhibition elicited by stimulation of the raphe nucleus was not attenuated by the drug. These results suggest that there is a non-serotonergic, descending pathway which is capable of modulating motor output solely by means of recurrent inhibition of the monosynaptic reflex.

[Kaneko T et al; Brain Res 417 (2): 403-7 (1987)]**PEER REVIEWED**

Metabolism/Pharmacokinetics:

Metabolism/Metabolites:

IN RATS, **LSD** WAS METABOLIZED MAINLY BY AROMATIC HYDROXYLATION, MORE THAN ONE-HALF OF THE DOSE BEING ELIMINATED IN THE BILE AS CONJUGATES OF 13- AND 14-HYDROXY-**LSD** ... DE-ETHYLATION OF **LSD** OCCURRED MORE READILY IN GUINEA-PIGS THAN IN RATS, AS SHOWN BY A SIX-FOLD DIFFERENCE IN **LSD**-RELATED CARBON DIOXIDE IN THE EXPIRED AIR.

[The Royal Society of Chemistry. Foreign Compound Metabolism in Mammals.

Volume 6: A Review of the Literature Published during 1978 and 1979.
London: The Royal Society of Chemistry, 1981., p. 147]**PEER REVIEWED**

LSD IS CONVERTED, LARGELY IN THE LIVER, TO 2-OXY-LSD; THIS INACTIVE METABOLITE TOGETHER WITH GLUCURONIC ACID CONJUGATES IS EXCRETED PRIMARILY IN THE URINE.

[Osol, A. (ed.). Remington's Pharmaceutical Sciences. 16th ed. Easton, Pennsylvania: Mack Publishing Co., 1980., p. 1297]**PEER REVIEWED**

Absorption, Distribution & Excretion:

... AN IV DOSE OF (14)C-LYSERGIC ACID DIETHYLAMIDE (**LSD**) IN PREGNANT MICE ... READILY PASSED FROM THE BLOOD TO THE TISSUES. HIGH UPTAKE OF (14)C INTO BRAIN, LIVER, KIDNEYS, ADRENALS, THYMUS, LUNGS, AND SALIVARY GLANDS, AND IMMEDIATE EXCRETION INTO THE BILE, OCCURRED. IN EARLY PREGNANCY, ABOUT 2% OF THE (14)C CROSSED THE PLACENTA INTO THE FETUS WITHIN 5 MIN, MOSTLY AS UNCHANGED **LSD**. THE DISTRIBUTION OF **LSD** IN MOTHER AND FETUS WERE SIMILAR, BUT FETAL UPTAKE WAS LESSENED BY THE AFFINITY OF MATERNAL TISSUES FOR **LSD**.

[The Chemical Society. Foreign Compound Metabolism in Mammals. Volume 1: A Review of the Literature Published Between 1960 and 1969. London: The Chemical Society, 1970., p. 72]**PEER REVIEWED**

Biological Half-Life:

... THE HALF-LIFE OF THE DRUG IN MAN IS APPROX 3 HR.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 556]**PEER REVIEWED**

Mechanism of Action:

LSD CAN AFFECT PHYSIOLOGICAL OR BIOCHEMICAL PARAMETERS OF VARIOUS TRYPTAMINERGIC NEURONAL SYSTEMS BY INFLUENCING DIRECT RESPONSES TO 5-HYDROXYTRYPTAMINE OR ITS UPTAKE, SYNTHESIS, STORAGE, RELEASE, OR CATABOLISM.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 262]**PEER REVIEWED**

LSD ... REDUCES TURNOVER OF 5-HT IN THE BRAIN, AND IT INHIBITS THE FIRING OF RAPHE NEURONS.

[Gilman, A. G., L. S. Goodman, and A. Gilman. (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co., Inc. 1980., p. 252]**PEER REVIEWED**

IN IONTOPHORETIC TESTS, **LSD** AND 5-HYDROXYTRYPTAMINE ARE BOTH POTENT INHIBITORS OF THE FIRING OF RAPHE (5-HYDROXYTRYPTAMINE) NEURONS, BUT **LSD** AND OTHER HALLUCINOGENS ARE FAR LESS POTENT DEPRESSANTS THAN IS 5-HYDROXYTRYPTAMINE ON NEURONS THAT RECEIVE INNERVATION FROM THE RAPHE. THE INHIBITORY EFFECT OF **LSD** ON RAPHE NEURONS OFFERS A PALUSIBLE EXPLANATION OF THE DRUG'S HALLUCINOGENIC EFFECTS, NAMELY, THAT THEY RESULT FROM DEPRESSION

OF ACTIVITY IN A SYSTEM THAT TONICALLY INHIBITS VISUAL AND OTHER SENSORY INPUTS. HOWEVER, TYPICAL **LSD**-INDUCED BEHAVIOR IS STILL SEEN IN ANIMALS WITH RAPHE NUCLEI DESTROYED OR AFTER BLOCKADE OF THE SYNTHESIS OF 5-HYDROXYTRYPTAMINE BY P-CHLOROPHENYLALANINE.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 262]**PEER REVIEWED**

It became evident early that **LSD** acted in the 5-HT (serotonin) pathway, which was known to act as an inhibitor or modulator in the cortex, raphe, and limbic systems. It was initially postulated that hallucinogens worked by blocking the 5-HT system, thus decreasing the filtering of cognitive perceptions that resulted in sensory overload. This was supported by the observation that serotonin depletion potentiated the effects of **LSD**. It is now known that there are at least two 5-HT receptors. 5-HT1 receptors are presynaptic, and activation of these sites inhibits the release of serotonin. 5-HT2 receptors are postsynaptic and are excitatory when stimulated. There is possibly a third receptor, an autoreceptor on the raphe cell bodies, that when stimulated inhibits cell firing. There is excellent evidence that **LSD** acts primarily on the 5-HT2 receptor and not on the 5-HT1 receptor. Potentiation of the **LSD** effect by pretreatment with serotonin depleters is then explained, because presynaptic inhibition is decreased. Supporting the 5-HT2 receptor theory, piperperon (a specific 5-HT2 antagonist) blocks the ability of rats to distinguish **LSD** from saline. In addition, compounds that are the most behaviorally active in man possess the highest 5-HT receptor affinity. There also appears to be a decrease in 5-HT binding sites with repeated hallucinogen exposure, possibly explaining the rapid tolerance (4 to 5 days) that develops to these agents.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 761]**PEER REVIEWED**

LSD and related psychedelic drugs have actions at multiple sites in the CNS, from the cortex to the spinal cord. Some of the best studied of these involve agonistic actions at presynaptic receptors for 5-HT in the midbrain, where the firing rate of neurons in the dorsal raphe nuclei is sharply reduced after small doses of **LSD** are administered systemically. 5-HT itself is inhibitory when applied iontophoretically to 5-HT-containing neurons of the forebrain to which the dorsal raphe neurons project. There appear to be at least five subtypes of 5-HT receptors. As selective agonists and antagonists for these receptor subtypes have been developed, evidence has mounted that **LSD** and related agents act relatively selectively at the 5-HT2 receptor. However, whether it acts exclusively at 5-HT2 receptors is not yet settled. The actions of **LSD** and mescaline on the locus ceruleus (decreased spontaneous activity, but enhancement of activation by peripheral stimuli) are blocked by ritanserin, a selective 5-HT2 antagonist. Although **LSD** is more potent than 5-HT in stimulating phosphoinositide hydrolysis mediated by 5-HT2 receptors, the maximum response to **LSD** is only 25% of that to 5-HT, suggesting that it is a partial agonist. The administration of **LSD** causes a decreased capacity to bind 5-HT2 antagonists such as ketanserin in brain, an effect that can be detected within a few hr after single high doses. Thus, down regulation of receptors may account in part for the rapid development of tolerance to **LSD** and related agents.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 554]**PEER REVIEWED**

It has been shown that the hallucinogenic potencies of **LSD**, the phenylisopropylamines, such as 4-bromo-2,5-dimethoxyphenylisopropylamine and 4-iodo-2,5-dimethoxyphenylisopropylamine, and the indolealkylamines, such as dimethyltryptamine and 5-methoxy-dimethyltryptamine, strongly correlate with their in vitro 5-HT2 receptor binding

affinities in rat cortical homogenates. In order to ascertain if this correlation applies to human 5-HT₂ receptors as well, we examined the affinities of 13 psychoactive compounds at 3H-ketanserin-labelled 5-HT₂ receptors in human cortical samples. Both radioligand binding and autoradiographic procedures were used. As in rat brain, d-**LSD** was the most potent displacer of 3H-ketanserin specific binding with a K_i of 0.9 nM. The phenylisopropylamine, 4-iodo-2,5-dimethoxyphenylisopropylamine also displayed high affinity (K_i of 6 nM). Stereospecific interactions were found with 4-bromo-2,5-dimethoxyphenylisopropylamine; (-) 4-bromo-2,5-dimethoxyphenylisopropylamine had a K_i of 17 nM while (+) 4-bromo-2,5-dimethoxyphenylisopropylamine had a K_i of 55 nM. The behaviorally active compound 4-methyl-2,5-phenylisopropylamine had an affinity of 162 nM while its behaviorally less active congener iso-DOM had an affinity of 6299 nM. The indolealkylamines 5-methoxydimethyltryptamine and N,N-dimethyltryptamine competed with moderate affinities (207 and 462 nM, respectively). In general, Hill coefficients were significantly less than unity which is consistent with an agonist interaction with 5-HT₂ receptors. MDMA, a substituted amphetamine analog was inactive with a K_i of greater than 10 μM. A strong correlation was found for the hallucinogen affinities and human hallucinogenic potencies (r = 0.97). Also, human and rat brain 5-HT₂ receptor affinities were strongly correlated (r = 0.99). These results strongly support the hypothesis that the hallucinogenic effects of these drugs in humans are mediated in whole or in part via 5-HT₂ receptors. Furthermore, these studies imply that treatment with 5-HT₂ receptor antagonists may be effective in reversing the hallucinogenic effects caused by the ingestion of **LSD** and **LSD**-like drugs.

[Sadzot B et al; Psychopharmacology (Berl) 98 (4): 495-9 (1989)]**PEER REVIEWED**

Alterations in brain serotonergic function have been implicated in the mechanism of action of **LSD**, mescaline, and other similarly acting hallucinogenic drugs of abuse such as 2,5-dimethoxyphenylisopropylamine. In order to test the hypothesis that the mechanism of action of **LSD** and phenylisopropylamine hallucinogens is through stimulation of a specific brain serotonin receptor sub-type, the affinities of these compounds for radiolabelled 5-HT₂, 5-HT_{1A}, 5-HT_{1B}, and 5-HT_{1C} receptors have been determined using recently developed in vitro radioligand binding methodologies. The 5-HT₂ receptor was labelled with the agonist/hallucinogen radioligand 3H-4-bromo-2,5-dimethoxyphenylisopropylamine (4-bromo-2,5-dimethoxyphenylisopropylamine). The 5-HT_{1A}, 5-HT_{1B}, and 5-HT_{1C} receptors were labelled with 3H-OH-DPAT, 3H-5-HT, and 3H-mesulergine, respectively. In general, the phenylisopropylamines displayed 10-100 fold higher affinities for the 5-HT₂ receptor than for the 5-HT_{1C} receptor and 100-1000 fold higher affinities for the 5-HT₂ receptor than for the 5-HT_{1A} or 5-HT_{1B} receptor. There was a strong correlation between hallucinogenic potencies and 5-HT₂ receptor affinities of the phenylisopropylamines (r = 0.90); the correlation coefficients for the 5-HT_{1A}, 5-HT_{1B}, and 5-HT_{1C} were 0.73, 0.85, and 0.78, respectively. Because there is no evidence that 5-HT_{1A}-selective or 5-HT_{1B}-selective agonists are hallucinogenic and because the phenylisopropylamines are potent hallucinogens, a 5-HT₂ receptor interaction is implicated and supports our previous suggestions to this effect. A secondary role for 5-HT_{1C} receptors cannot be discounted at this time.

[Titeler M et al; Psychopharmacology (Berl) 94 (2): 213-6 (1988)]**PEER REVIEWED**

Interactions:

MOST OF THE PHARMACOLOGICAL ACTIONS OF **LSD ... ARE ANTAGONIZED BY CHLORPROMAZINE AND CYPROHEPTADINE ...**

[Gilman, A. G., L. S. Goodman, and A. Gilman. (eds.). Goodman and Gilman's

The Pharmacological Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co., Inc. 1980., p. 566]**PEER REVIEWED**

... GI ABSORPTION /OF **LSD**/ IS BOTH DELAYED AND REDUCED BY THE PRESENCE OF FOOD.

[The Chemical Society. Foreign Compound Metabolism in Mammals Volume 3. London: The Chemical Society, 1975., p. 138]**PEER REVIEWED**

MICROINJECTIONS OF **LSD** (0.05 UG), Mescaline (0.5 UG) AND SEROTONIN (10 UG) INTO THE MEDIAL RAPHE NUCLEUS OF RATS RESULTED IN A STRONG POTENTIATION OF APOMORPHINE (1 MG/KG IP)-INDUCED HYPERMOTILITY.

[FINK H, OELSSNER W; EUR J PHARMACOL 75 (4): 289-96 (1981)]**PEER REVIEWED**

Commonly precipitated by use of marijuana, anxiety, fatigue, or movement into a dark environment, "flashbacks" may persist intermittently for several years after the last exposure to **LSD**. They are exacerbated by the use of phenothiazines.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 556]**PEER REVIEWED**

Before the advent of neuroleptics, opioids such as morphine were used occasionally in the treatment of schizophrenia and other mental disorders. Recent interest in the possible therapeutic role of endogenous opioid peptides in various mental states has prompted a new look at the opioids. The present paper summarizes the research to date in the author's laboratory on opioid-hallucinogen interactions. A model behavioral state was induced in rat with N,N-dimethyltryptamine or lysergic acid diethylamide-25 (**LSD**). Several mu opioid agonists, antagonists, and synthetic enkephalin analogs interacted with N,N-dimethyltryptamine and **LSD**. Adult male Holtzman rats trained on a positive reinforcement fixed ratio four (FR4) behavioral schedule (ie, a reward of 0.01 ml sugar-sweetened milk was earned on every fourth bar press) were used in these studies. N,N-dimethyltryptamine (3.2 and 10.0 mg/kg) given with a 0.9% NaCl pretreatment ip, disrupted established food rewarded FR4 bar pressing behavior in a dose related fashion. Pre-determined behaviorally ineffective doses of mu opioid agonists showed selective biphasic effects against N,N-dimethyltryptamine and **LSD**. Low doses antagonized the effects of both hallucinogens, whereas larger doses enhanced their effects. In contrast to the antagonistic effects of low doses of mu opioid agonists, the mu-kappa opioid antagonist (-)-naloxone enhanced the effects of N,N-dimethyltryptamine and **LSD**. (-)-Naloxone enhanced the effects of N,N-dimethyltryptamine and **LSD**. Potentiation of N,N-dimethyltryptamine-induced behavioral disruption was attributed to a stereospecific opioid antagonist effect of (-)-naloxone in that the (+)-naloxone enantiomer failed to potentiate the effects of N,N-dimethyltryptamine. Further studies are indicated to determine hallucinogen-opioid interactions in various species, including man.

[Domino EF; Pharmacol Biochem Behav 24 (2): 401-5 (1986)]**PEER REVIEWED**

Yohimbine is a widely used pharmacological tool employed to produce a selective blockade of alpha 2-adrenergic receptors. In the present study operant behavior was used as a biobehavioral assay to determine the activity of yohimbine at serotonergic receptors, as indicated by its ability to antagonize the behavioral effects of a serotonergic agonist, **LSD**. Rats were trained to respond on a Fixed Ratio 15 schedule for food reinforcement. Yohimbine (0.5-5.0 mg/kg) or vehicle and **LSD** (50 ug/kg) were administered ip 30 min and immediately prior, respectively, to the 30 min operant session. In a separate study, the ability of yohimbine

(0.5-2.5 mg/kg) to antagonize a higher dose of **LSD** (100 ug/kg) was examined. Relatively low doses of yohimbine (0.5-1.0 mg/kg) were able to partially, but significantly antagonize the **LSD** induced suppression and typical hallucinogen induced disruption of schedule controlled responding. These results suggest that yohimbine, even at moderate doses, may act nonselectively as an antagonist at 5-HT receptors, in addition to its antagonist action at alpha 2-adrenergic receptors. This study demonstrates the utility of operant behavior as a biobehavioral assay to study the receptor mediated action of drugs.

[Dwoskin LP et al; Pharmacol Biochem Behav 31 (2): 321-6 (1988)]**PEER REVIEWED**

It has been shown that the caudally directed biting and scratching response to repeated intrathecal injections of substance P is decreased by the third injection of substance P and that this apparent desensitization to substance P is less pronounced in mice pretreated with Freund's adjuvant. This study was designed to study the mechanism of this desensitization to substance P and to examine the effect of lysergic acid diethylamide tartrate (**LSD**) on desensitization. Results indicate that while 25 ug of **LSD**/kg body wt ip in naive mice had no effect on the response to a single injection of substance P, **LSD** decreased the development of desensitization to substance P induced behaviors. In contrast, identical injections of **LSD** in adjuvant pretreated mice not only failed to prevent desensitization but enhanced the degree of apparent desensitization to substance P. Tolerance developed to the effects of **LSD** on desensitization to substance P induced behaviors in both adjuvant and saline pretreated mice. When injected intrathecal with substance P, **LSD** failed to alter the degree of desensitization to substance P induced behaviors, suggesting that the effect of **LSD** is not produced at the spinal cord level. Separation and quantification of substance P and its metabolites in the spinal cord using HPLC techniques indicated that either a single injection of **LSD** or pretreatment with Freund's adjuvant produced similar patterns of changes in the concn of substance P related peptides in mouse spinal cord.

[Larson AA et al; Pain 37 (3): 365-73 (1989)]**PEER REVIEWED**

Doses of **LSD**, quipazine, 8-OHDPAT and TFMPP were established that prominently disrupted FR-40 operant response pattern in two groups of rats. Subsequently, one group received daily ip injections of imipramine, 2.5 mg/kg, for 4 wk, then 10 mg/kg for 2 additional wk. The second group received 5 mg/kg/day, ip, of trazodone for the first 4 wk, then 20 mg/kg/day for the next two wk. For these periods and the 3 wk after discontinuing the chronic drug treatments (washout), test doses of the 4 agonists were evaluated twice weekly in random order for their effects to decrease FR-40 reinforcements and increase pauses. No consistent, systematic changes in sensitivity to the agonist effects on FR-40 behavior were observed during chronic drug treatments, although significant effects were at times observed. However, during the washout period in the imipramine group, both **LSD** and 8-OHDPAT effects on reinforcements were reversed to baseline levels. The effect of 5-OHDPAT on pauses during washout in this group was also attenuated. During washout in the trazodone group, the 8-OHDPAT-induced pausing and loss of reinforcements was reduced so as to be not significantly different from baseline values. Previous studies have demonstrated antagonism of **LSD**- and quipazine-induced disruption of FR-40 by pretreating with the 5-HT₂-selective antagonist pirenperone (28). Since chronic antidepressants down-regulate brain 5-HT₂ binding sites, the effects of **LSD** and quipazine were expected to be attenuated, which was not the case.

[Shukla R et al; Pharmacol Biochem Behav 34 (2): 275-81 (1989)]**PEER REVIEWED**

Pharmacology:

Therapeutic Uses:

Hallucinogens; Serotonin Agonists; Serotonin Antagonists

[National Library of Medicine's Medical Subject Headings online file (MeSH, 1999)]**QC REVIEWED**

EXPTL USE: HAS BEEN USED EXPERIMENTALLY AS ADJUNCT IN STUDY AND TREATMENT OF MENTAL DISORDERS

[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 886]**PEER REVIEWED**

LSD ONCE WAS PROPOSED AS AN AID IN PSYCHOTHERAPY, AS AN ADJUNCT TO THE TREATMENT OF ALCOHOLISM AND OPIOID ADDICTION. IN EACH SITUATION, THE USE HAS BEEN ABANDONED EITHER BECAUSE CONTROLLED STUDIES HAVE FAILED TO DEMONSTRATE THE VALUE OF LSD OR BECAUSE THE ELABORATE PRECAUTIONS REQUIRED TO MINIMIZE ADVERSE PSYCHOLOGICAL REACTIONS DAMPENED ENTHUSIASM AND RENDERED ITS THERAPEUTIC USE IMPRACTICAL. ... SERIOUS CONCERNS HAVE BEEN RAISED ABOUT THE POTENTIAL FOR NEUROTOXICITY.

[Gilman, A.G., T.W. Rall, A.S. Nies and P. Taylor (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 8th ed. New York, NY. Pergamon Press, 1990., p. 557]**PEER REVIEWED**

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[Dvoskin LP et al; Pharmacol Biochem Behav 31 (2): 321-6 (1988)]**PEER REVIEWED**

It has been shown that the caudally directed biting and scratching response to repeated intrathecal injections of substance P is decreased by the third injection of substance P and that this apparent desensitization to substance P is less pronounced in mice pretreated with Freund's adjuvant. This study was designed to study the mechanism of this desensitization to substance P and to examine the effect of lysergic acid diethylamide tartrate (**LSD**) on desensitization. Results indicate that while 25 ug of **LSD**/kg body wt ip in naive mice had no effect on the response to a single injection of substance P, **LSD** decreased the development of desensitization to substance P induced behaviors. In contrast, identical injections of **LSD** in adjuvant pretreated mice not only failed to prevent desensitization but enhanced the degree of apparent desensitization to substance P. Tolerance developed to the effects of **LSD** on desensitization to substance P induced behaviors in both adjuvant and saline pretreated mice. When injected intrathecal with substance P, **LSD** failed to alter the degree of desensitization to substance P induced behaviors, suggesting that the effect of **LSD** is not produced at the

spinal cord level. Separation and quantification of substance P and its metabolites in the spinal cord using HPLC techniques indicated that either a single injection of **LSD** or pretreatment with Freund's adjuvant produced similar patterns of changes in the concn of substance P related peptides in mouse spinal cord.

[Larson AA et al; Pain 37 (3): 365-73 (1989)]**PEER REVIEWED**

Doses of **LSD**, quipazine, 8-OHDPAT and TFMPP were established that prominently disrupted FR-40 operant response pattern in two groups of rats. Subsequently, one group received daily ip injections of imipramine, 2.5 mg/kg, for 4 wk, then 10 mg/kg for 2 additional wk. The second group received 5 mg/kg/day, ip, of trazodone for the first 4 wk, then 20 mg/kg/day for the next two wk. For these periods and the 3 wk after discontinuing the chronic drug treatments (washout), test doses of the 4 agonists were evaluated twice weekly in random order for their effects to decrease FR-40 reinforcements and increase pauses. No consistent, systematic changes in sensitivity to the agonist effects on FR-40 behavior were observed during chronic drug treatments, although significant effects were at times observed. However, during the washout period in the imipramine group, both **LSD** and 8-OHDPAT effects on reinforcements were reversed to baseline levels. The effect of 5-OHDPAT on pauses during washout in this group was also attenuated. During washout in the trazodone group, the 8-OHDPAT-induced pausing and loss of reinforcements was reduced so as to be not significantly different from baseline values. Previous studies have demonstrated antagonism of **LSD**- and quipazine-induced disruption of FR-40 by pretreating with the 5-HT₂-selective antagonist pirenperone (28). Since chronic antidepressants down-regulate brain 5-HT₂ binding sites, the effects of **LSD** and quipazine were expected to be attenuated, which was not the case.

[Shukla R et al; Pharmacol Biochem Behav 34 (2): 275-81 (1989)]**PEER REVIEWED**

Drug Tolerance:

Tolerance to the behavioral effects of **LSD** develops rapidly after three to four consecutive daily doses. Sensitivity returns to baseline after 3 to 4 days of abstinence. Interestingly, there is less tolerance to the aympathomimetic effects of **LSD**. There is cross tolerance between **LSD** and the hallucinogenic phenyl alkylamines and indole alkylamines, possibly due to a common site of action. Cross tolerance does not develop to phencyclidine, cannabis, or amphetamines.

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 759]**PEER REVIEWED**

Environmental Fate & Exposure:

Environmental Standards & Regulations:

FDA Requirements:

Manufacturers, packers, and distributors of drug and drug products for human use are responsible for complying with the labeling, certification, and usage requirements as prescribed by the Federal Food, Drug, and Cosmetic Act, as amended (secs 201-902, 52 Stat. 1040 et seq., as amended; 21 U.S.C. 321-392).

[21 CFR 200-299, 300-499, 820, and 860 (4/1/91)]**PEER REVIEWED**

Schedules of controlled substances are established by section 202 of the Controlled Substances Act (21 U.S.C. 812). Schedule I includes lysergic acid diethylamide DEA Code #7315; Drug class: Hallucinogen.

[21 CFR 1308.11(d) (4/1/91)]**PEER REVIEWED**

Chemical/Physical Properties:

Molecular Formula:

C20-H25-N3-O

PEER REVIEWED

Molecular Weight:

323.42

[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 887]**PEER REVIEWED**

Color/Form:

POINTED PRISMS FROM BENZENE

[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 887]**PEER REVIEWED**

Colorless

[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987., p. 716]**PEER REVIEWED**

Odor:

Odorless

[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987., p. 716]**PEER REVIEWED**

Taste:

Tasteless

[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987., p. 716]**PEER REVIEWED**

Melting Point:

80-85 DEG C

[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 887]**PEER REVIEWED**

Solubilities:

Water sol

[Haddad, L.M., Clinical Management of Poisoning and Drug Overdose. 2nd ed. Philadelphia, PA: W.B. Saunders Co., 1990., p. 759]**PEER REVIEWED**

Spectral Properties:

SPECIFIC OPTICAL ROTATION: 17 DEG @ 20 DEG C/D (CONCENTRATION BY VOLUME= 0.5 G IN 100 ML PYRIDINE) MAX ABSORPTION (ETHANOL): 311 NM (E= 257, 1%, 1CM)

[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 886]**PEER REVIEWED**

Intense mass spectral peaks: 181 m/z, 221 m/z, 323 m/z

[Pfleger, K., H. Maurer and A. Weber. Mass Spectral and GC Data of Drugs, Poisons and their Metabolites. Parts I and II. Mass Spectra Indexes. Weinheim, Federal Republic of Germany. 1985., p. 567]**PEER REVIEWED**

Other Chemical/Physical Properties:

SOLVATED, ELONGATED PRISMS FROM METHANOL; SOL IN WATER; MP: 198-200 DEG C; SPECIFIC OPTICAL ROTATION: 30 DEG @ 20 DEG C/D /LYSERGIDE D-TARTRATE/

[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 886]**PEER REVIEWED**

Sensitivity to both light and heat.

[DHHS/NIDA; Research Monograph Series 73: Urine Testing for Drugs of Abuse p.105 (1986) DHHS Pub No. (ADM) 87-1481]**PEER REVIEWED**

Chemical Safety & Handling:

Storage Conditions:

Two studies have shown that **LSD** is stable in urine for more than a month when stored at or below room temperature and protected from direct sunlight or other sources of ultraviolet radiation.

[DHHS/NIDA; Research Monograph Series 73: Urine Testing for Drugs of Abuse p.106 (1986) DHHS Pub No. (ADM) 87-1481]**PEER REVIEWED**

Occupational Exposure Standards:

Manufacturing/Use Information:

Major Uses:

IN BIOCHEMICAL RESEARCH AS ANTAGONIST TO SEROTONIN.

[Budavari, S. (ed.). The Merck Index - Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989., p. 886]**QC REVIEWED**

MEDICATION

QC REVIEWED

General Manufacturing Information:

THE BURDENSOME REGULATIONS AND THE RECOGNITION THAT **LSD** DOES NOT PRODUCE A "MODEL PSYCHOSIS" HAVE MARKEDLY DIMINISHED ITS USE IN SCIENTIFIC INVESTIGATIONS.

[Gilman, A. G., L. S. Goodman, and A. Gilman. (eds.). Goodman and Gilman's The Pharmacological Basis of Therapeutics. 6th ed. New York: Macmillan Publishing Co., Inc. 1980., p. 564]**PEER REVIEWED**

Synthetic derivative of lysergic acid. Only the D-form is active.

[Sax, N.I. and R.J. Lewis, Sr. (eds.). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987., p. 716]**PEER REVIEWED**

Laboratory Methods:

Clinical Laboratory Methods:

A radioimmunoassay (RIA) with a cutoff of 0.5 mg/ml for **LSD**-reactive substances gave a positive test for the urine collected from two volunteers who received **LSD** 1 ug/kg of body weight/ for up to 30 hours after administration. Two metabolites of **LSD** could be detected by a highly sensitive GC/MS assay in the urine specimens collected for up to 72 hr

[DHHS/NIDA; Research Monograph Series 73: Urine Testing for Drugs of Abuse p.105 (1986) DHHS Pub No. (ADM) 87-1481]**PEER REVIEWED**

High performance liquid chromatography combined with fluorescence detection has been used to detect **LSD** at urinary concentrations as low as 0.5 mg/ml. ... Capillary column gas chromatography and electron ionization mass spectrometry ... is also capable of measuring **LSD** concentrations as low as 0.5 mg/ml. However, neither of these assays is useful for detection of **LSD** in urine for more than about 12 hr after ingestion.

[DHHS/NIDA; Research Monographs Series 73: Urine Testing for Drugs of Abuse p.105 (1986) DHHS Pub No. (ADM) 87-1481]**PEER REVIEWED**

A gas chromatography/mass spectrometry assay for the N-dimethyl and 13-hydroxy metabolites of **LSD** in urine has been ... shown to permit detection of **LSD** use for more than 2 days after ingestion.

[DHHS/NIDA; Research Monograph Series 73: Urine Testing for Drugs of Abuse p.105 (1986) DHHS Pub No. (ADM) 87-1481]**PEER REVIEWED**

Analytical techniques that have been evaluated for detection of **LSD** in urine include the combination of liquid chromatography and mass spectrometry and tandem analyzer mass spectrometry.

[DHHS/NIDA; Research Monograph Series 73: Urine Testing for Drugs of Abuse p.105 (1986) DHHS Pub No. (ADM) 87-1481]**PEER REVIEWED**

Serum and urine specimens of 31 patients with suspected **LSD** intoxication were analyzed for **LSD** by both RIA and HPLC. The RIA assay, using 0.1 ng/ml as the limit of detection instead of the manufacturer's recommendation of 0.5 ng/ml, was positive for **LSD** in 13 blood and urine specimens from 14 patients. Results were compared to HPLC analysis using methysergide instead of lysergol as the internal standard and a limit of detection of 0.5 ng/ml. HPLC detected **LSD** in 9 of 13 serum specimens and 11 of 13 urine specimens that had tested positive by RIA. Of 18 patients with a final clinical diagnosis of **LSD** intoxication, **LSD** was

detected by RIA in 14 patients and by HPLC in 11 patients. For 13 other cases in which the final diagnosis was a condition other than **LSD** intoxication, serum and urine assays for **LSD** were negative in all cases by both techniques. **LSD** assays have not been generally available in clinical laboratories. We conclude that the qualitative determination of **LSD** in either serum or urine by a commercially available radioimmunoassay has made it possible to provide reliable laboratory confirmation of **LSD** intoxication.

[McCarron MM et al; J Anal Toxicol 14 (3): 165-7 (1990)]**PEER REVIEWED**

Because **LSD** was known to occur in urine in low concentration it was required that the procedure estimate amounts as low as 1 ng/ml urine, that it utilize combined GC/MS and that it utilize GC/MS equipment available to the various US Naval Laboratories. Requisite procedures which have been developed are described.

[Wall ME; Govt Reports Announcements & Index (GRA&I), Issue 06, 1987]**PEER REVIEWED**

The Diagnostic Products Corp. Coat-A-Count RIA kit for **LSD** in urine was evaluated for use in forensic toxicology with a variety of sample types. The cut-offs (defined as the mean response of blank samples plus three standard deviations) for **LSD** in serum, hemolyzed whole blood, urine, and stomach contents were 0.06, 0.050-0.055, 0.18, and 0.18 ng/ml, respectively. Preliminary extraction of **LSD** from the samples is not usually necessary. The precision of the analysis and the recoveries from spiked samples were satisfactory. The cross-reactivities of 2-oxo-**LSD**, lysergic acid Me propylamide, lysergic acid monoethylamide, and nor-**LSD** were estimated to be 11, 6, 2, and 1%, respectively, relative to **LSD** (100%).

[Altunkaya D, Smith RN; Forensic Sci. Int 47 (2): 1990,113-21]**PEER REVIEWED**

An instrumental high-performance TLC technique for the detn of **LSD** in urine was developed. Before chromatographic separation, a single-step extraction with alkaline wash is performed. The procedure can detect <1 ug **LSD**/l urine. Results of high-performance TLC detn are compared with those from a RIA procedure.

[Blum LM et al; J Anal Toxicol 14 (5):285-7 (1990)]**PEER REVIEWED**

A procedure for the detn of **LSD** (lysergic acid diethylamide) in urine at concn as low as 0.5 ng/ml is presented. After addition of deuterium-labeled **LSD** as the internal standard, a rapid n-butyl chloride extraction of **LSD** from urine at pH 8 is followed by formation of the trimethylsilyl derivative by treatment with N,O-bis(trimethylsilyl)trifluoroacetamide. The trimethylsilyl derivative of **LSD** is identified and quantified by selected ion monitoring with a fused-silica capillary column and electron impact ionization. The procedure was used to monitor **LSD** concn in urine for 8 hr following oral administration of 70.5 ug of **LSD** to 2 human volunteers. Concn of **LSD** detected by the assay are compared with concn detd by 2 other methods of analysis, a RIA and a HPLC assay. Data concerning the stability of **LSD** in urine are also presented.

[Francom P et al; J Anal Toxicol 12 (1): 1-8 (1988)]**PEER REVIEWED**

Demethylation of lysergic acid diethylamide in the human was demonstrated, both in vitro and in vivo, and arom. hydroxylation at positions 13 and 14 was tentatively identified. A gas chromatography-resonance electron capture ionization mass spectrometry (GC/MS) assay for **LSD** and N-demethyl-**LSD** in urine was developed in which the drug and its metabolite are converted to their N-trifluoroacetyl derivatives prior to GC/MS analysis. Linear and reproducible calibration curves were obtained for **LSD** concn from 0.05 to 5.0 ng/ml, and for N-demethyl-**LSD** concn from 0.03 to 5.0 ng/ml. The assay was used to determine the urinary

concn of **LSD** and N-demethyl-**LSD** following administration of a single oral dose of the drug (1 ug/kg) to an adult volunteer. The rates of excretion of **LSD** and N-demethyl-**LSD** reached max. in urine collected at time intervals of 4-6 and 8-10 hr after administration, respectively. The elimination half-lives for **LSD** and N-demethyl-**LSD** were 3.6 and 10.0 hr, respectively. [Lim HK et al; Anal Chem 60 (14): 1988,1420-5 (1988)]**PEER REVIEWED**

Procedures for detection and quantitation of **LSD**, iso-**LSD**, and N-demethyl-**LSD** by capillary chromatography/tandem mass spectrometry are presented. Several methods for derivatization, sample introduction, and ionization, in combination with mass spectrometry/mass spectrometry, were evaluated for overall ionization efficiency and product-ion sensitivity and specificity. Fragmentation pathways derived from low-energy collision-induced dissociation spectra of protonated **LSD**, and the protonated trimethylsilyl derivatives of **LSD** and deuterium-labeled analogs of **LSD**, were proposed. Principal dissociations primary involve the amide and piperidine-ring moieties in which losses of Me radical, MeNH₂, MeNCH₂, diethylamine, diethylformamide, and N,N-diethylpropenamide from MH⁺ are observed. Pos-ion ammonia chem. ionization and subsequent MS/MS anal. of the protonated mols. (MH⁺) of the trimethylsilyl derivatives of **LSD**, iso-**LSD**, and N-demethyl-**LSD** provide a high degree of specificity for identification of these compd in urine or blood at low-pg/ml concn. Neg-ion chemical ionization and capillary chromatography/tandem mass spectrometry analysis of the molecular anion of the trifluoroacetyl derivative is well suited for trace-level identification of N-demethyl-**LSD**, a metabolite of **LSD**.

[Nelson CC, Foltz RL; Anal Chem 64 (14): 1578-85 (1992)]**PEER REVIEWED**

A previously reported procedure for quantification of **LSD** in urine was modified to permit measurement of the drug in plasma. After addn. of deuterium-labeled **LSD**, the plasma is extracted and the extract is treated with trifluoroacetylimidazole to convert the **LSD** to its N-trifluoroacetyl derivative. The derivatized **LSD** is analyzed by capillary column gas chromatography/neg-ion chem-ionization. Plasma fortified with known concn of **LSD** gave linear responses from 0.1 to 3.0 ng/ml with this assay. The method was used to determine pharmacokinetic parameters for **LSD** after oral administration (1 ug/kg) to a male volunteer. The apparent plasma half-life was detd to be 5.1 hr. The peak plasma concn of 1.9 ng/ml occurred 3 hr after administration.

[Papac DI, Foltz RL; J Anal Toxicol 14 (3): 189-91 (1990)]**PEER REVIEWED**

A sensitive method for the detection and quantitation of lysergic acid diethylamide (**LSD**) in urine was developed. After initial solvent extraction, the compd was further purified by liquid-liquid extraction or by solid-phase extraction. The trimethylsilyl derivative of **LSD** was detected by the title method with selected-ion monitoring. The presence of **LSD** was confirmed by comparing retention times and relative abundances of ions of unknowns with that of a standard. The recovery of this procedure was >89%. The intra-run and inter-run relative standard deviations were <5% and <7%, respectively. This procedure allows detection of **LSD** concn as low as 29 pg/ml. Quantitation of **LSD** was linear over the concn range 50-2000 pg/ml.

[Paul BD et al; J Chromatogr 529 (1): 103-12 (1990)]**PEER REVIEWED**

A RIA was developed for the direct detection of **LSD** in biological fluids. The radiotracer, (+)-2-((25)I)iodo-**LSD**, allows the use of gamma-counting rather than the liquid scintillation counting currently used for existing (3)H radioimmunoassays. The assay is specific for **LSD** and very closely related compd. It is inexpensive, sensitive, simple to use and small vols of sample (50 ul) can be assayed directly without the need for any time-consuming extraction procedures. The cut-off levels are 1.2 ng/ml in blood and 3.0 ng/ml in urine. The results

obtained using this (125)I assay compare favorably with those obtained using the 3(H) assay. The advantages of the assay make it a most appropriate method for the routine screening of **LSD** in biological samples of forensic interest.

[Stead AH et al; Forensic Sci Int 32 (1): 49-60 (1986)]**PEER REVIEWED**

Commercial RIA kits were used to screen for **LSD** in urines containing various drugs commonly found in specimens from addicted persons. The excretion of **LSD** in the urine of a volunteer after ingestion of 50 ug was such that the drug could still be detected after 3 days (0.1 ng/ml threshold of detection). The results of the immunoassay were confirmed by GC/MS, using a 0.125 mg sample on trimethylsilyl-**LSD** and an ion trap.

[Vu Due T et al; Schweiz Med Wochenschr 121 (50): 1887-90 (1991)]**PEER REVIEWED**

Because **LSD** was known to occur in urine in low concn., it was required that the procedure estimates as low as 1 ng/ml urine, that it utilizes GLC/MS, and that it utilizes GLC/MS equipment available to the various US Naval Labs.

[Wall ME; Report; ISS Order No. AD-A174867/2/GAR): 1986,78 pp.]**PEER REVIEWED**

Analytic Laboratory Methods:

DETERMINATION OF **LSD IN DRUG POWDERS BY PAPER CHROMATOGRAPHIC SPECTROPHOTOMETRY @ 400 TO 200 NM.**

[Association of Official Analytical Chemists. Official Methods of Analysis. 15th ed. and Supplements. Washington, DC: Association of Analytical Chemists, 1990, p. V1 621]**PEER REVIEWED**

ROOM-TEMPERATURE FLUORESCENCE & LOW-TEMP PHOSPHORESCENCE ANALYTICAL CURVES AND LIMITS OF DETECTION HAVE BEEN DETERMINED IN METHANOL-WATER SOLN FOR 9 HALLUCINOGENIC DRUGS INCL **LSD. DETECTION LIMITS ARE VERY LOW, BETWEEN 1 AND 23 PPB.**

[AARON JJ ET AL; CLINICA CHIMICA ACTA 45: 375-86 (1973)]**PEER REVIEWED**

THIN LAYER CHROMATOGRAPHY AND FLUOROMETRY WERE USED TO DETECT **LSD IN POLICE SEIZURE MATERIALS.**

[DAL CORTIVO LA ET AL; ANAL CHEM 38 (13): 1959-60 (1966)]**PEER REVIEWED**

THE SEPARATION OF **LSD FROM DRUG SAMPLES BY USE OF METHYL SILICONE FUSED SILICA CAPILLARY COLUMNS AND GAS CHROMATOGRAPHY.**

[STAFFORD DT ET AL; J FORENSIC SCI 29 (1): 291-8 (1984)]**PEER REVIEWED**

Analyses based upon gas chromatography require a well-deactivated capillary column in order to avoid severe adsorptive loss of the drug. Conversion of **LSD** to its N-trimethylsilyl or N-trifluoroacetyl deative results in improved gas chromatographic behavior and permits higher persitivities ot be achieved.

[DHHS/NIDA; Research Monograph Series 73: Urine Testing for Drugs of Abuse p.106 (1986) DHHS Pub No. (ADM) 87-1481]**PEER REVIEWED**

The identification of **LSD** has posed an analytical challenge for forensic science labs. In those cases in which a few doses are seized, only microgram quantities are available, often in forms which make isolation of the miniscule amt. of **LSD** difficult. A method is described which yields small crystals of pure **LSD** in a form well-suited for analysis using a microscope

sampling device with a FT/IR spectrometer. These crystals produce excellent spectra from samples containing <50 ug **LSD**. Distinguishing between **LSD**, iso-**LSD**, and lysergic acid N-methylpropylamide poses no problem with the spectra obtained. This scheme combines preparative TLC followed by wick evaporatin, an old but not well-known technique for seperating solution components from high-solid mixt without filtration.

[Harris HA, Kane T; J Forensic Sci 36 (4): 1186-91 (1991)]**PEER REVIEWED**

The separation of **LSD** from related ergot alkaloids, and its isomer lysergic acid N-methylpropylamide, were investigated using capillary GC and HPLC. Capillary GC using fused silica nonpolar bonded phase columns gave good discrimination, and retention indexes of 10 ergot alkaloids were measured. The applicability of this technique to the analysis of illicit **LSD** preparations was demonstrated by preparing extracts from **LSD** microdot tablets and card and paper squares. The HPLC systems examined in the present study were unable to achieve resolution of **LSD** and lysergic acid N-methylpropylamide, whereas GC gave excellent separation. The 2 methods complement each other.

[Japp M et al; J Forensic Sci 32 (4): 933-40 (1987)]**PEER REVIEWED**

The specificity, sensitivity, and linearity of N-trimethylsilyl derivs. of **LSD** were studied by GC-MS using ions 279, 293, and 395; the lowest detection limit was 5 pg/ml. Quantitative linearity, using (2)H **LSD** as the internal standard was also established for **LSD** down to 40 pg/ml. This is a method of choice for confirming pos **LSD** samples at pg/ml levels.

[Sun J; Am Clin Lab 8 (6): 24-7 (1989)]**PEER REVIEWED**

Special References:

Special Reports:

Anon; **LSD**: Toxicology and Metabolism. (Latest citations from the Life Sciences Collection Database).Govt Reports Announcements & Index (GRA&I), Issue 17, 1992. Citations concerning the metabolism and central nervous system effects of **LSD** (lysergic acid diethylamide) are included. The action of **LSD** in humans is discussed and case histories are reported. The citations also explore the action of **LSD** in animals, including psychological and physiological changes. (Contains a minimum of 60 citations and includes a subject term index and title list.)

Anon; Trends in Drug Abuse Related Hospital Emergency Room Episodes and Medical Examiner Cases for Selected Drugs, DAWN 1976-1985. Topical Data from the Drug Abuse Warning Network (DAWN). Govt Reports Announcements & Index (GRA&I), Issue 16, 1992. The report presents trends in drug abuse data collected through the Drug Abuse Warning Network (DAWN) for the ten-year period from 1976 through 1985. It is based on drug abuse-related cases reported by 564 hospital emergency rooms and 62 medical examiner facilities which participated consistently in DAWN throughout the entire period. Drugs mentioned in conjunction with emergency room episodes and medical examiner cases are the focal point of DAWN data. Frequently, more than one drug is mentioned in conjunction with a single case or episode.

Carroll ME; PCP and Hallucinogens. Adv Alcohol Subst Abuse 9 (1-2): 167-90 (1990). In this review phencyclidine and related arylcyclohexylamines and hallucinogens, using **LSD** as the prototype, are considered as two distinct classes of abused drugs. Within these classes drugs that are found on the street are discussed, and a current epidemiological summary is provided. The abuse liability and dependence potential of these drugs are evaluated by

considering four major determinants of their abuse. First, is the ability of a drug to function as a positive reinforcer and increase the probability of operant behavior leading to its delivery. Animal data describing the reinforcing effects of PCP are reviewed with respect to the influence of variables controlling drug-reinforced behavior; however, there are no animal models of hallucinogen-reinforced behavior. Several methods of quantifying reinforcing efficacy are discussed. A second determinant is the subjective effects of the respective drugs. These effects are described and compared across drugs based on clinical reports in humans and drug discrimination studies in animals. A third determinant is the behavioral and physiological toxicity that results from acute and chronic use of these drugs. Clinical reports and results of sensitive tests that have been developed for laboratory animals are reviewed. A fourth determinant is the dependence potential that exists with these drugs, measured by tolerance development and the extent to which behavioral and physiological disturbances occur when drug use is terminated.

Kulberg A; Substance Abuse: Clinical Identification and Management.; *Pediatr Clin North Am* 33 (2): 325-61 (1986). Substance abuse is a significant health problem in the adolescent population. Prevention is a formidable challenge, but attempts at discouraging experimentation in early adolescence and the promotion of healthy adult role models may be effective strategies. Questions that may elicit a history suggestive of abuse should be a routine part of the adolescent medical history. Pediatricians should be familiar with the important clinical findings resulting from intoxication with the various substances of abuse and should be able to recognize the telltale signs of abuse. Effective management is based on attention to the basics of life support, careful attention to the physical findings, and judicious use of specific therapeutic agents. Above all, a compassionate attitude should prevail if acute-phase recovery and long-term rehabilitation are to be successful.

Kulig K; **LSD**.; *Emerg Med Clin North Am* 8 (3): 551-8 (1990). **LSD** is still readily available in the United States as a street drug of abuse. Emergency physicians may be called on to diagnose acute **LSD** intoxication in cases in which the history is unavailable. The typical **LSD** intoxication syndrome causes marked illusions of color and sound, along with a feeling of cosmic awareness. True hallucinations only occasionally occur; the pupils invariably are massively dilated. The diagnosis may be very difficult to establish when other drugs, particularly those causing coma, are present. The toxicology laboratory can now easily detect **LSD** by radioimmunoassay.

Leikin JB et al; Clinical Features and Management of Intoxication Due to Hallucinogenic Drugs. *Med Toxicol Adverse Drug Exp* 4 (5): 324-50 (1989). Hallucinogenic drugs are unique in that they produce the desired hallucinogenic effects at what are considered non-toxic doses. The hallucinogenic drugs can be categorised into 4 basic groups: indole alkaloid derivatives, piperidine derivatives, phenylethylamines and the cannabinoids. The drugs reviewed include **LSD**, phencyclidine, cocaine, amphetamines, opiates, marijuana, psilocybin, mescaline, and designer drugs. Particularly noteworthy is that each hallucinogen produces characteristic behavioural effects which are related to its serotonergic, dopaminergic or adrenergic activity. Cocaine produces simple hallucinations, PCP can produce complex hallucinations analogous to a paranoid psychosis, while **LSD** produces a combination of hallucinations, pseudohallucinations and illusions. Dose relationships with changes in the quality of the hallucinatory experience have been described with amphetamines and, to some extent, **LSD**. Flashbacks have been described with **LSD** and alcohol. Management of the intoxicated patient is dependent on the specific behavioural manifestation elicited by the drug. The principles involve differentiating the patient's symptoms from organic (medical or

toxicological) and psychiatric aetiologies and identifying the symptom complex associated with the particular drug. Panic reactions may require treatment with a benzodiazepine or haloperidol. Patients with **LSD** psychosis may require an antipsychotic. Patients exhibiting prolonged drug-induced psychosis may require a variety of treatments including ECT, lithium and l-5-hydroxytryptophan.

Scaros LP et al; *Illegal Use of Drugs: Current Review*; US Pharm 15 (May): 17-18, 23-24, 26, 28-30, 32-3615 (1990). An overview of widely used drugs of abuse and consequences of their use is presented. Cocaine, heroin (diacetylmorphine), marijuana (cannabis), lysergic acid diethylamide (**LSD**), amphetamines, phencyclidine and related drugs are discussed. The effects of the body manner of use, any medical uses, abuse patterns, adulterants and toxic effects on organ systems are described.

Grahame-Smith DG et al; *Human Platelet 5-Hydroxytryptamine Receptors: Binding of (3)H-Lysergic Acid Diethylamide (LSD)*. Effects of chronic neuroleptic and antidepressant drug administration; *Experientia* 44 (2): 142-5 (1988). A review with 25 references. Review serotonin receptor platelet **LSD** binding Neuroleptic platelet serotonin receptor review Antidepressant platelet serotonin receptor review

Nelson CC, Foltz RL; *Chromatographic and Mass Spectrometric Methods for Determination of Lysergic Acid Diethylamide (LSD) and Metabolites in Body Fluids*. *J Chromatogr* 580 (1-2): 97-109 (1992). A review with 41 refs. Continued illicit use of the potent psychedelic drug lysergic acid diethylamide (**LSD**) has stimulated efforts to develop effective analytical methods for detection of the drug and its metabolites in body fluids from suspected **LSD** users. Recently reported methods based on gas and liquid chromatography, combined with single- and multiple-stage spectral analysis, now permit accurate detection and quantitation of **LSD** at sub ng/ml concn.

Synonyms and Identifiers:

Synonyms:

ACID

PEER REVIEWED

CUBES

PEER REVIEWED

DELYSID

PEER REVIEWED

9,10-DIDEHYDRO-N,N-DIETHYL-6-METHYL-ERGOLINE-8-BETA-CARBOXAMIDE

PEER REVIEWED

N,N-DIETHYLLYSERGAMIDE

PEER REVIEWED

N,N-DIETHYL-D-LYSERGAMIDE

PEER REVIEWED

ERGOLINE-8-BETA-CARBOXAMIDE, 9,10-DIDEHYDRO-N,N-DIETHYL-6-METHYL-
PEER REVIEWED

ERGOLINE-8-CARBOXAMIDE, 9,10-DIDEHYDRO-N,N-DIETHYL-6-METHYL-,
(8BETA)-
PEER REVIEWED

ERGOLINE-8BETA-CARBOXAMIDE, 9,10-DIDEHYDRO-N,N-DIETHYL-6-METHYL-
PEER REVIEWED

HEAVENLY BLUE
PEER REVIEWED

D-LSD
PEER REVIEWED

LSD-25
PEER REVIEWED

LSD [ALKALOID]
PEER REVIEWED

LYSERGAMID
PEER REVIEWED

LYSERGAMIDE, N,N-DIETHYL-
PEER REVIEWED

LYSERGIC ACID DIETHYLAMIDE
PEER REVIEWED

D-LYSERGIC ACID DIETHYLAMIDE
PEER REVIEWED

LYSERGIC ACID DIETHYLAMIDE-25
PEER REVIEWED

LYSERGIDE
PEER REVIEWED

LYSERGSAEUREDIAETHYLAMID
PEER REVIEWED

LYSERGSAURE DIETHYLAMID
PEER REVIEWED

PEARLY GATES
PEER REVIEWED

ROYAL BLUE
PEER REVIEWED

WEDDING BELLS

****PEER REVIEWED****

Administrative Information:

Hazardous Substances Databank Number: 3920

Last Revision Date: 20020114

Last Review Date: Reviewed by SRP 3/11/1993

Source: TOXNET

<http://toxnet.nlm.nih.gov/>