From the Bureau of Drug Abuse Control

FDA

...MICRO-GRAM..

Volume I, No. 4 January 1968

Police Chemists School

BDAC's next school for those involved in forensic analytical work will be held February 5 - 9, 1968.

We plan to hold other sessions this fiscal year for April 8 - 12 and June 17 - 21. All sessions will be held in Washington, D.C.

Applications for the April and June sessions are now being accepted. An application form is attached to this issue of Micro-Gram. Please indicate session preference on this form.

"SMASH"

We have reports that narcotic peddlers are selling a new concoction called "SMASH".

Reportedly marijuana is cooked with acetone to obtain oil of cannabis. The oil is then added to hashish to form a tar-like material. This is then rolled into small pellets and smoked.

Supposedly "SMASH" is being made in Mexico.

Book Bargain

Public Health Service Publication No. 1589, January 1967: Psychotropic Drugs and Related Compounds, Usdin, Earl, Ph.D., and Efron, Daniel H., Ph.D.

Tabulation of psychotropic compounds with chemical names and structures, generic names (when possible), synonyms and trade names, manufacturers or distributors, LD_{50} values, psychotropic action, human dose and references, indexed.

Order from Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402. Price: $2.75.

FDA held two seminars on psychotropic drugs in 1967. The talks have been compiled and are reprinted on the following 34 pages.

CAUTION: Use of this publication should be restricted to forensic analysts or others having a legitimate need for this material.

FDA FOOD AND DRUG ADMINISTRATION—U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE—WASHINGTON, D.C. 20204

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N,N-DIETHYL LYSERGAMIDE (LSD) AND LSD-LIKE COMPOUNDS.
I. BACKGROUND INFORMATION

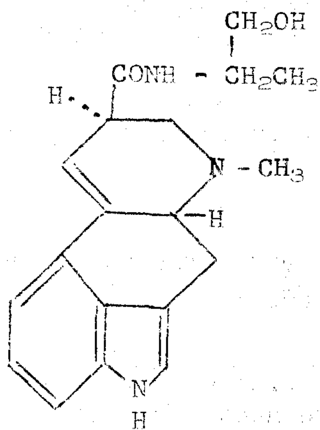
By Ted M. Hopes, San Francisco District

Ergot is a fungus (Claviceps purpurea) which grows on rye. It contains a number of pharmacologically active agents: ergosterol, tyramine, histamine, acetylcholine, and ergot alkaloids (1, 2).

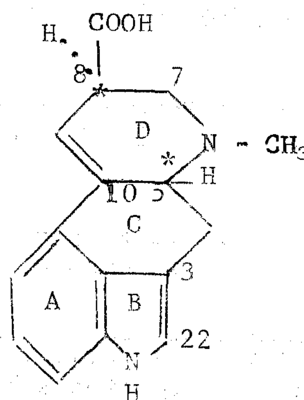
The identification of the ergot alkaloids as derivatives of lysergic acid, mostly polypeptide substituted amides, has been largely the work of Stoll in Switzerland. Each ergot alkaloid occurs as an isomeric pair; the levorotatory form, derived from lysergic acid, is pharmacologically active while the dextrorotatory form, derived from isolysergic acid, is inactive. These alkaloids have been classified into three groups: the ergotamine group, the ergotoxine group, and the ergonovine (ergometrine) group. The ergonovine group consists of the ergot alkaloids which are closest to LSD in structure since the N-substituent is a relatively simple one. The dextrorotatory form of ergonovine (N-[1-(hydroxymethyl) ethyl]-d-lysergamide), derived from isolysergamide, is called ergonovinine (ergometrinine); see structure below. The ergot alkaloids are not noted for having any hallucinogenic effects.

N,N-Diethyl lysergamide (LSD) has not been found in nature. Dr. Albert Hofmann first prepared LSD at the Sandoz Research Laboratories, Basle, Switzerland, in 1938. He noticed its hallucinogenic effect in 1943 when he accidently inhaled vapors of the free base LSD.

Stoll et al. (3) reported the structure of lysergic acid in 1949; see below. There are two asymmetric carbon atoms, indicated by asterisks. Only one configuration of C-5 is found in naturally occuring derivatives of lysergic acid. The lysergic acid molecule having that configuration at C-5 is dextrorotatory; $[\alpha]_D^{20} = +40$ (c=0.5, py) (4).



Ergonovine (Ergometrine)



Lysergic acid

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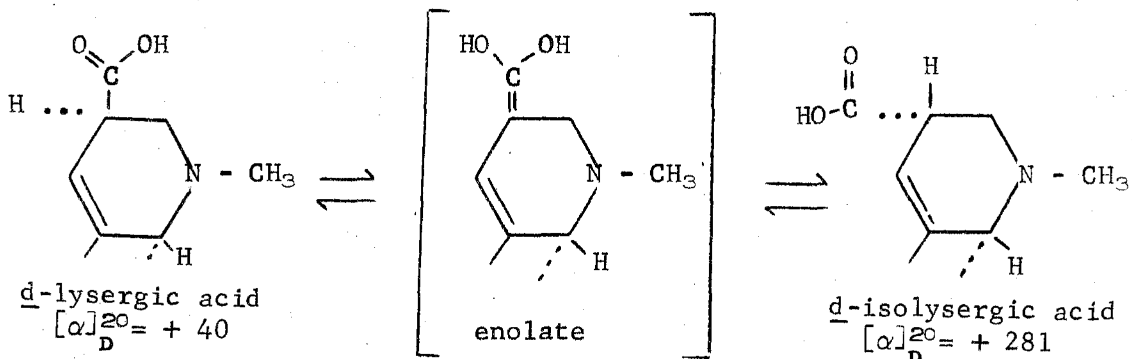
The configuration of C-8 is subject to easy interconversion through an intermediate acid enolate (5):



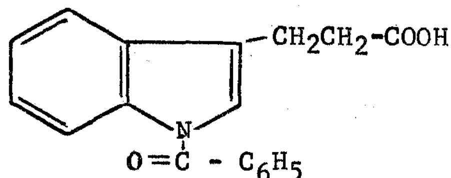
There has been some controversy regarding the stereochemistry of lysergic acid (6). Stenlake has argued that the semi-chair configuration is the most stable for ring D and that, on the basis of pK_a values and the comparable rates of esterification, lysergic acid is the form with an equatorial carboxylic acid group (6, 7). In isolysergic acid the carboxylic acid group is axial and thus nearer to the ring nitrogen. Stoll et al. concurred with this on the basis of additional information (8).

Derivatives of the isolysergic acids and of l-lysergic acid are practically inert physiologically. A thorough review of the ergot alkaloids, and proof of the structures of lysergic acid and isolysergic acid has been presented by Stoll (9).

Stoll et al. (10) also prepared a large number of lysergic acid amides and reported their physical constants.

Experiments with mice have shown that LSD rapidly disappears from the blood. The main detoxification product is reported to be 2-hydroxy LSD, which itself has been found to have no LSD-like activity (11).

Kornfeld et al. (12) synthesized lysergic acid with N-benzoyl-3-(β-carboxyethyl)-dihydroindole as the starting compound; their final product was dl-lysergic acid with a melting point of 242-243° (dec.) and an overall yield of less than 1%. This synthesis involved the preparation and characterization of about 130 compounds.



Stoll and Hofmann's method for the synthesis of LSD is described in a patent assigned to Sandoz Ltd. (13). The synthesis begins with the hydrazide of d-lysergic acid and proceeds as follows:

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COOR

N - CH_3

H_2NNH_2 →

hydrazide

$NaNO_2$ / HCl 0° →

azide

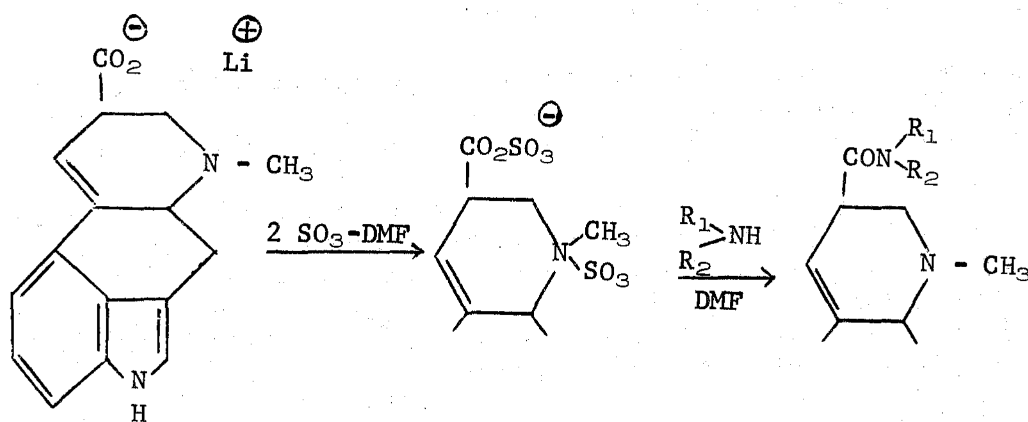
1. Neutralize with $NaHCO_3$
2. Extract into ether
3. Dry ether soln with K_2CO_3

$(C_2H_5)_2NH$ / dark, 24 hr →

LSD ← alumina chromatography

LSD + iso-LSD

Garbrecht (14) reviewed methods for the preparation of these amides and reported one relatively simple method in detail. Lithium lysergate is prepared and treated with sulfur trioxide-dimethylformamide complex; the product is treated with dialkyl amine. The method requires little time and has yields above 65%:



Some of the decomposition products of substituted lysergamide and isolysergamide are shown below (5):

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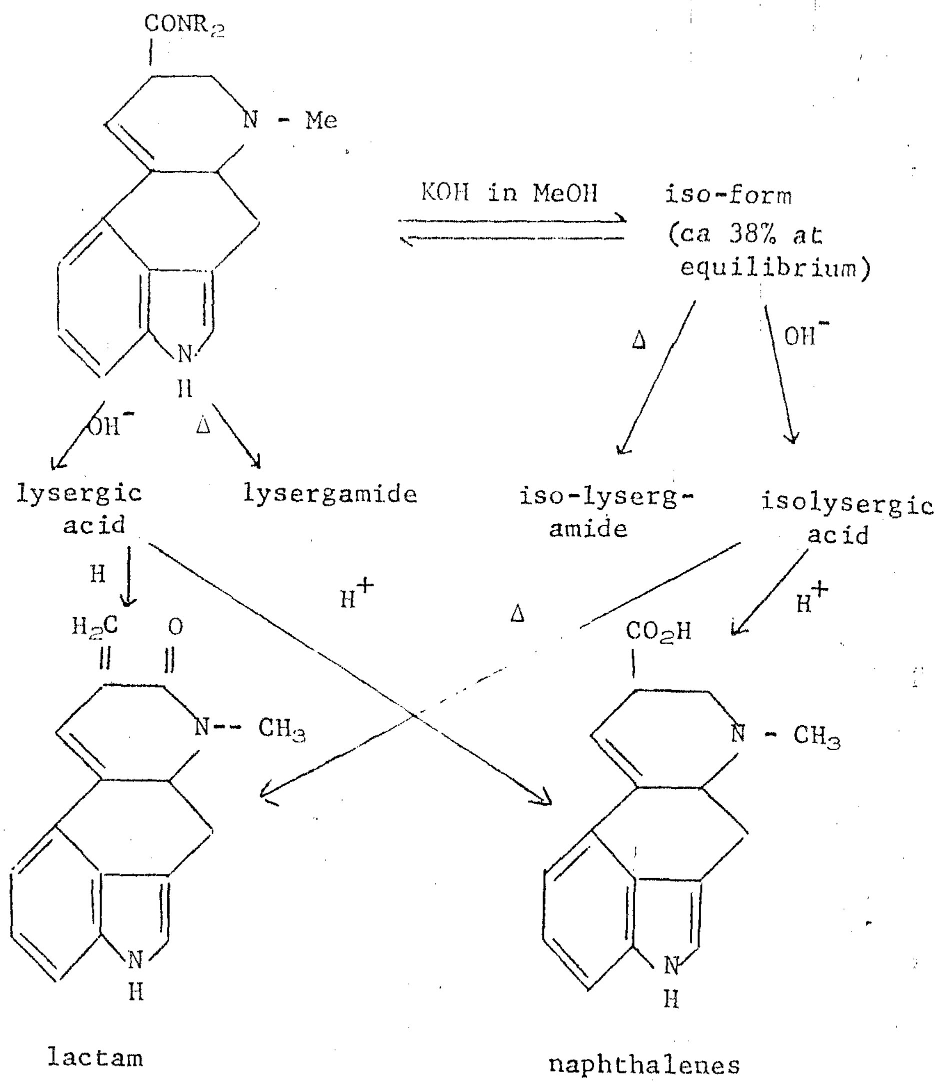
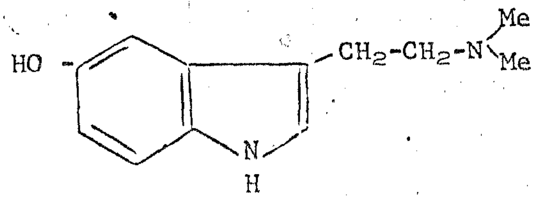


A number of names have been given to LSD: N,N-diethyl-d-lysergamide, N,N-diethyl-d-lysergic acid amide, d-lysergic acid diethylamide, LSD, LSD-25 (the "25" has been attributed to the date of Hofmann's discovery in 1938, 2 May. This Sandoz designation has been used to refer to the base and the tartrate), Delysid (Sandoz registered name for "d-lysergic acid diethylamide tartrate" with the formula of $(C_{20}H_{25}N_3O)_2 \cdot C_4H_6O_6 \cdot CH_3OH$ and a molecular weight of 829.0), "acid", and "L".

Cutting (15) classifies the group "Psychotomimetic Agents and Other Substances Affecting the Mind" into A, epinephrine and related compounds; B, serotonin and related compounds; C, agents related to acetylcholine; D, cannabinols; E, caffeine group; and F, other psychotomimetics. LSD is classified under group B, and a subclassification, "LSD-like compounds", includes the following:



Bufotenine (2): Obtained from a plant (Piptadenia peregrina), a yellow fungus Amanita mappa, and a South American toad (Bufo vulgaris). This and similar hydroxytryptamines have been synthesized by Stoll et al. (16). The article includes ultraviolet and infrared spectra and a spot test (see Chem. Abstr. entry).

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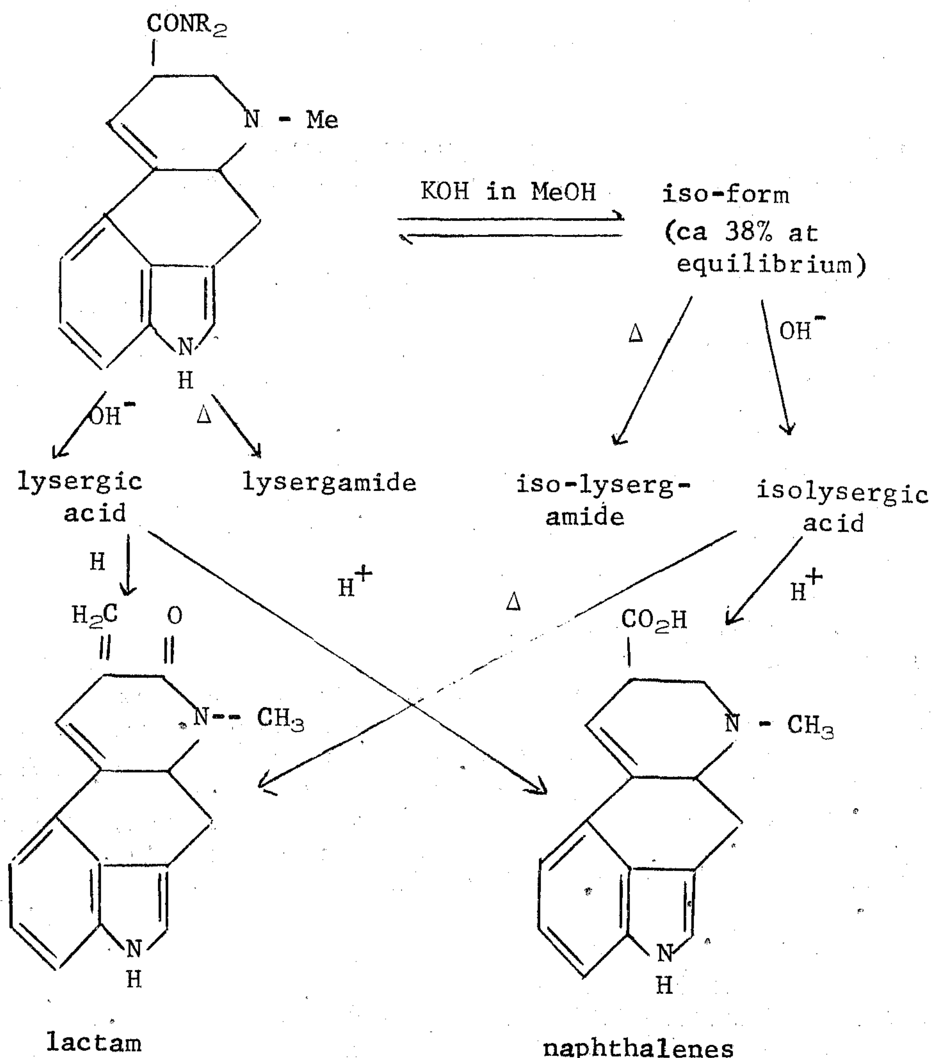

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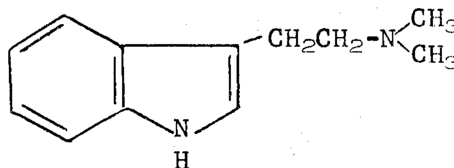
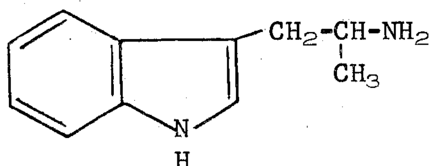
Cohoba (Niopo; Parica) (2): From Acacia niopo, a Central American mimosa; contains bufotenine and other substances. Taken as snuff, produces "drunkenness" and colored visions.

N,N-Dimethyltryptamine: A powerful hallucinogen about 5 times as active as mescaline, but faster and briefer in its effects. Effects appear in 3-5 minutes and disappear in one hour.

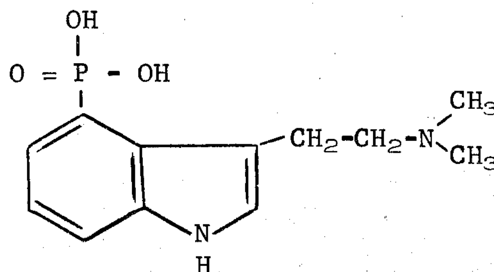


Methyltryptamine: Produces visions.



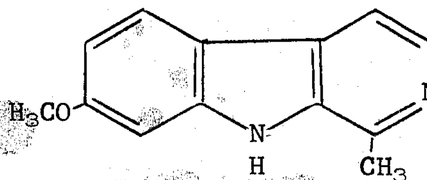
Morning glory seeds; Ololiuqui: Lysergamide (ergine) and isolysergamide have been found in a number of varieties of morning glory seeds (Ipomoea violacea) and in the Mexican bindweed, Ololiuqui (Rivea corymbosa) (17-19). The levels of lysergamide found by Genest (17) in six varieties of morning glory seeds range from 25 to 213 ppm. Ingestion of about 5 grams of seeds (about 125 seeds) of these varieties is required to obtain a psychotomimetic effect (18).

Psilocybin (2): Found in Mexican mushrooms, such as Psilocybe mexicana, P. sempervirens, P. cubensis, Conocybe cyanopus, and Stropharia. It is also found in the North American mushroom, P. pelliculosa. Psilocybin is easily hydrolyzed to 4-hydroxybufotenine or psilocin. Psilocybin is about 1/100 as potent as LSD.



Another subclassification of Cutting's includes LSD-like compounds that have depressive qualities, in addition to hallucinogenic ones:

Harmine (banisterine, yageine, telepathine): From Peganum harmala and other plants, called a psychic sedative.



Caapi (aya huasca, wild rue): From Banistericopsis caapi, a South American jungle vine, contains Harmine. This compound produces frenzy, visions, psychoeroticism, and sleep.

Yagé: From Haemadictyon amazonia, contains harmine. Yagé stimulates and then depresses with drowsy hallucinations.

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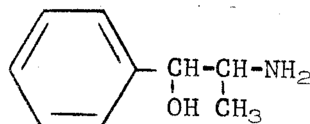
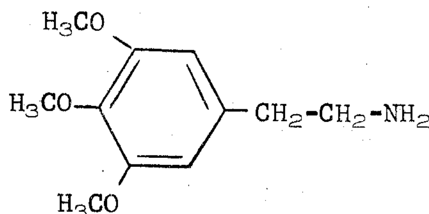
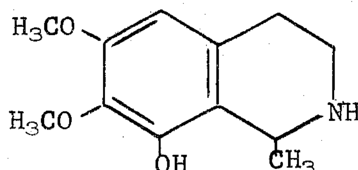
From Group A, the epinephrine-related compounds are

Kat (Khat): Catha edulis, grown in Ethiopia, contains 1% (dried basis) cathine or d-norpseudoephedrine.

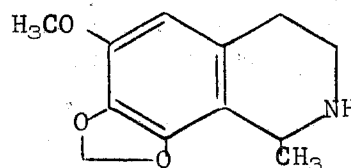


Mescaline (20): About 6.3% present in tops or "buttons" from the Peyote cactus (Lophophora williamsii, L. Lewinii, Anhalonium sp., and many other names) which is found in southwestern U.S. and northern Mexico. Mescaline is associated with a number of alkaloids of the isoquinoline type, both phenolic and non-phenolic; for example:



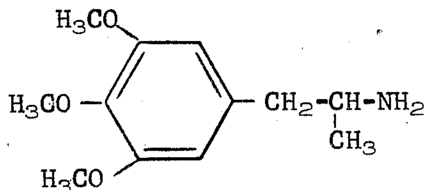


Anhalonidine (5%)

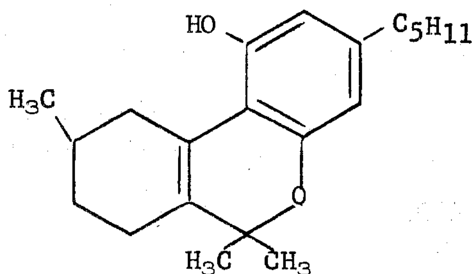


Anhalonine (3%)

Trimethoxyamphetamine: Less stimulating than amphetamine, but more hallucinogenic than mescaline.



From Group D, cannabinols, the compound from Cannabis sativa (indica) that produces the characteristic Cannabis (hashish, marihuana) effect is tetrahydrocannabinal:



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(14) Garbrecht, W. L., J. Org. Chem. 24, 368-372 (1959).

(15) Cutting, W. C., Handbook of Pharmacology, p. 596 ff.

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II. ANALYTICAL BACKGROUND

By Robert J. Martin[1], Donald D. Dechert[1], and Ernest Beyer[2]

The enactment of the "Drug Abuse Control Amendments of 1965" establishes special controls of depressant and stimulant type drugs. This act was enacted to protect the public's health and safety (1). The act defines the potentially dangerous depressant (barbituric or habit-forming) and stimulant (amphetamines or habit-forming because of stimulant effect on the central nervous system) type drugs which may be misused. Psychotoxic drugs which have a potential for abuse because of their hallucinogenic effects are also regulated by the act.

Hoffman (2) discusses four wonder drug plants from Mexico which have far-reaching psychic effects. Peyote (a type of cactus) contains the alkaloid mescaline. Teonanacatol (a certain leaf mushroom, Psilocybe mexicana Heim) contain the alkaloids psilocybin and psilocin plus other alkaloids. Ololiuqui (seeds of the vine, Rivea corymbosa and Ipomoea violacea L) contains the active ingredients of ergot alkaloids (lysergic acid amide and isolysergic acid amide among others). The active ingredients of the fourth-mentioned wonder drug plant, Salvia divinorum, appear to be unstable and have not been identified as of 1964.

Beyerman et al. (3) found by thin layer chromatography that Ipomoea rubro-coerula and Ipomoea pearly gates contain lysergic acid amide, isolysergic acid amide and other indole alkaloids similar to the extracts of Ipomoea violacea L and Rivea corymboso mentioned by Hoffman (2).

Various authors (4-7) have analyzed different species of Ipomoea and Rivea coryboso for the presence of indole alkaloids. Only the Ipomoea violacea (seven varieties) and Rivea corymboso contained the indole alkaloids. The total alkaloid content ranged from 0.005% to 0.079%. Among the indole alkaloids identified were chanoclavine, lysergic acid amide (ergine), isolysergic acid amide (isoergine), ergometrine, penniclavine, tryptophan, and ergometrinine.

Downing (8) discusses the indole alkaloids and their derivatives, the phenethylamines, the piperidine derivatives, the tetrahydrocannabinols, and other psychotoxic agents. The seeds of the leguminous shrubs Piptadenia peregrina and Piptadenia marcocarpa contain N,N-dimethyltryptamine (DMT) and bufotenine; these shrubs grow in the Caribbean Islands and South America. The effective dose of DMT is about 1 mg/kg (i.m.). Bufotenine has been shown to be present in Piptadenia colubrina and as a constituent of the glandular secretion of certain toad species. A psychotomimetic effect of pure bufotenine in man is produced with 2-16 mg/kg (i.v.).

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[1] Los Angeles District.

[2] San Francisco District.

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Two species of mushrooms, Psilocybe mexicana Heim and Stropharia cubensis from Mexico and Thailand contain psilocybin and psilocin. Psilocybin and psilocin produce a psychotomimetic effect in man at a dose of 4-8 mg/man (orally). Psilocybin is the first naturally occuring indole compound containing phosphorus.

The active ingredients of the dried heads of the dumpling cactus, Lophophora williamsii (Anhalonium lewinii), also known as peyote, mescal, or peyotl, is mescaline. The cactus heads can contain up to 6% mescaline. Other cactus from which mescaline has been isolated is the Argentinian Trichocereus terschekii and the Peruvian Trichocereus pachoni. Mescaline must be administrated at an oral dose of between 0.3 and 0.6 grams to obtain the full effect.

Haylin and Watson (9) examined Argyreia nervosa seeds (a tropical wood rose common to Hawaii) and found about 3 mg of alkaloid material/gram of seed. The alkaloids present were ergine, isoergine, and penniclavine. The authors stated that the seed is the best source of ergoline alkaloids discovered to date.

Rye, official source of ergot when bearing the ergot growth formed from the fungus Claviceps purpurea, is a source of lysergic acid. When the infestation occurs naturally it is called natural ergot. When the infestation is brought about artificially it is called cultivated ergot.

Recently this laboratory received a dried weed seed pod from one of the local police departments. The seeds of the pod were being eaten, resulting in hallucinogenic effects. The seed pod was identified as Datura meteloides (10), which reportedly contains atropine, hyoscyamine, and scopolamine. Downing (8) had reported the use of atropine (5-8 mg orally) to produce hallucinations, mood changes, and depersonalizations. However, large doses may cause death (11).

Synthetically prepared compounds which may be used for hallucinogenic effects include N,N-diethyltryptamine (DET), N,N-dipropyltryptamine, N,N-diallyltryptamine, α-methyltryptamine, 1-methyl-3-piperidyl benzilate, 1-methyl-3-piperidyl cyclopentylphenylglycolate, 1-ethyl-3-piperidyl cyclopentylphenylglycolate, 2-diethylaminoethyl cyclopentyl-2-thienylglycolate, 2-diethylaminoethylbenzilate, and d-lysergic acid diethyl amide (LSD). Effective doses range from 0.02 to 60 mg/man, orally (8).

LSD is probably one of the most widely publicized hallucinogenic drugs. It is known by several names: LSD-25, Acid, N,N-d-lysergic acid diethylamide, and Delysid. It can be synthesized from lysergic acid. LSD does not occur naturally. The most effective physiologically active form is the dextrorotatory.

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The following methods for LSD have been reported in the literature: Dal Cortivo et al. (12), Genest and Farmilo (13), and Axelrod et al. (14) describe spectrofluorometric methods for determining LSD. An activation wavelength of 360 mμ and a fluorescence wavelength of 436 mμ were used. The drug was dissolved in 1 ml methanol and 9 ml 0.001N HCl. A standard curve was obtained in our laboratory; it indicates that fluorescence intensity is linear with concentration up to at least 0.2 μg/ml. The maximum sensitivity is 0.01 μg/ml. Spectrofluorometry is much more sensitive than ultraviolet spectrophotometry, which requires a minimum LSD concentration of 10 μg/ml (14).

Radecka and Nigam (15) used gas chromatography as a preliminary cleanup before thin layer chromatography. They found that hydrogenation of the C_9-C_{10} double bond was necessary to prevent decomposition in the gas chromatograph. The column consisted of micro glass beads (60 mesh) coated with 0.2% silicone rubber SE-30. A flame ionization detector was used. The LSD peak overlapped the solvent peak. The authors stated, "The thin layer chromatographic technique was found to be superior to the gas chromatographic technique in that it allowed the characterization of LSD concentrates which failed to produce gas chromatographic peaks."

Genest (16) describes a thin layer chromatographic method using the Photovolt Densitometer to determine the amount of LSD present in the developed spot. The densitometer scans the plate and when it passes over a spot, it draws a peak similar to that obtained from a gas chromatograph. The area under the peak is directly proportional to the amount of LSD spotted. Thin layer chromatographic spots can also be quantitatively measured by scraping off the LSD spot, extracting the drug, and using spectrofluorometry or spectrophotometry as the determinative step (13).

Stoll and Schlientz (17) and Hellberg (18) report that ultraviolet irradiation of acidic, aqueous LSD solutions causes water to add to the C_9-C_{10} double bond. This reaction can be used as an additional quantitation test during the ultraviolet spectrophotometric determination. After the absorbance is determined at 310 mμ, the acidic aqueous solution is irradiated with strong ultraviolet light for several minutes. The solution is scanned as before and the peak will have shifted to 280 mμ, as shown in Figure 1.

The distribution of LSD between immiscible solvents can be used as an identification test (14). LSD is determined in a solution of 2% isoamyl alcohol in heptane. The solution is then extracted with pH 6 buffer and the organic phase is assayed as before. The amount of LSD in the organic phase, after extraction, divided by the amount originally present, is the distribution coefficient. The distribution coefficient for the sample should be within 2% of that for the LSD standard.

The following three analyses are performed at the Los Angeles District at time of receipt of the sample to determine if a controlled drug is present: (1) Presumptive test for ergot alkaloids (Van Urk);

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(2) quantitative measurement by UV spectrophotometry; and (3) identification by TLC, using silica gel G plates developed with acetone:methanol (4 + 1) and UV light and/or p-dimethylaminobenzaldehyde chromogenic agent for visualization.

When we are notified by BDAC that we are "going to court" with a sample containing LSD, we use all or part of the following qualitative and quantitative tests: TLC on aluminum oxide:silica gel G (50:50) with acetone as developing solvent and visualization as given in analysis 3 above; IR spectrophotometry (2-15 μ), using 80-100 μg LSD; microfluorometric assay (spectral curves), analysis done at Division of Pharmaceutical Chemistry; UV irradiation spectral curves, noting change with 1- and 2-minute irradiation intervals; and optical rotatory dispersion (ORD) to determine if the drug is dextrorotatory (New York District used this analysis on as little as 200 μg).

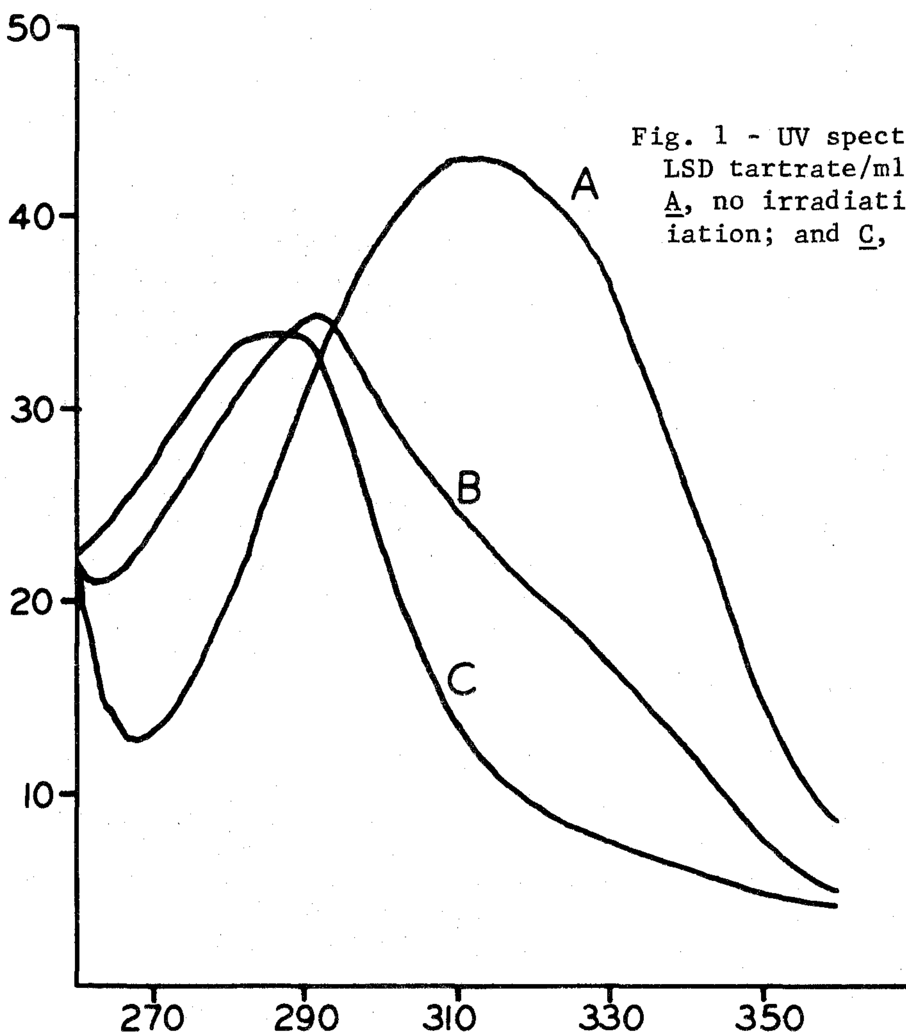

Fig. 1 - UV spectra of LSD (19.9 μg LSD tartrate/ml 10% tartaric acid): A, no irradiation; B, 1-min irradiation; and C, 2-min irradiation.

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III. LOS ANGELES GROUP DISCUSSION

A discussion about reagent blanks for the IR identification of micro amounts of LSD revealed that all the participants were encountering interfering materials in their solvents. The importance of reagent blanks and controls was emphasized.

Recently this laboratory received capsules which contained a green powder with the odor and appearance of a commercial cleanser. The field test on this material gave a negative reaction for LSD. Closer examination of the powder revealed light gray specks dispersed throughout. When these specks were picked out and tested a positive LSD test was obtained. The Comet cleanser seems to mask the *p*-dimethylaminobenzaldehyde color development.

We have received samples of bubble gum, chewing gum, and sponges suspected of containing LSD. The latest samples have been "PEZ" candies with LSD.

The group participation in the preparation and use of the partition column chromatography technique generated a lot of enthusiam and interest. One of the participants demonstrated a microliter syringe which would deliver 0.5 μl of solution at a time.

The question of the effect of time and conditions of storage environment on the stability of LSD was raised by one of the participants. This District plans to initiate a long range study by subjecting various sample forms to varying storage conditions.

Since the conference we have changed the developing solvent for the silica gel G TLC plates to acetone : methanol (4+1); better spots and higher R_f values are obtained.

One participant stated that the content of mescaline in peyote varies with geographical origin. The mescaline content diminishes the closer to Mexico City the plant is grown and increases the farther north the plant is grown.

The major difference noted between the samples analyzed by our chemists and the chemists attending the conference was the amount of sample available for analysis. Usually the police chemist has only one capsule to analyze while we have from 5 to 500 capsules. The number and type of the analyses which may be performed greatly depends on the amount of sample available.

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IV. SAN FRANCISCO GROUP DISCUSSION

A number of questions were repeated throughout the day.

(a) Where can we obtain standards? This was answered by explaining that all the legitimate LSD was under the control of National Institutes of Mental Health, and that we obtain our standards from them through BDAC, Washington, D.C. Requests must be accompanied by (1) the amount desired (not over 200 µg); (2) the use to which it is to be put; and (3) the name and title of the person who will be responsible for it.

(b) What is the source of lysergic acid being used to manufacture LSD? No answer given, although it was generally agreed it was not being synthesized. How much LSD is being prepared illegally? No one could estimate. Several analysts commented on the apparent good quality of the LSD.

(c) What isomers of LSD are physiologically active? Literature was cited that reported only one of the four possible isomers, N,N-diethyl-D-lysergamide, was active.

(d) Has anyone had experience with the synthesis of LSD from lysergic acid? No one had, though several chemists were planning to attempt this when time was available. The presence of certain elements or compounds may make it possible to determine what method of synthesis was used or even to identify batches.

(e) Has a microchemical test been developed? No one knew of such a method. One participant expressed interest in trying to develop one, but he said the development would require about 0.5 g of LSD and was therefore out of the question.

(f) How can you tell the d- from the l-form? The use of optical rotation dispersion was discussed, but since this technique requires the use of an expensive ($38,000) instrument, it will not be readily available. One participant thought that the optical rotation of a solution could be determined microscopically.

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A RAPID IDENTIFICATION TEST KIT FOR MATERIALS CONTAINING ERGOT-TYPE ALKALOIDS

By Donald D. Dechert,
Los Angeles District

Under the "Drug Abuse Control Amendments of 1965" Food and Drug Inspector or Agent may need a test to rapidly identify a substance. The following procedure can be used to determine if the substance contains an ergot-type alkaloid.

Method

Reagents

(a) Test Paper A. - Dissolve 1 g p-dimethylaminobenzaldehyde in 10 ml ethyl alcohol in 10 ml graduated cylinder. Add 1 drop Acid-Ferric Chloride T.S. (USP XVII). Cut Whatman #1 chromatography paper (8 x 8") into 0.25" strips. Dip one end of strip into solution in cylinder; remove and dip opposite end. Let alcohol evaporate spontaneously. When strips are dry, cut into 0.25" squares and place in a small closed vial.

(b) Test Solution A. - Place absolute methyl alcohol (ACS) in a glass dropper bottle.

(c) Test Solution C. - Place sulfuric acid : water (1:1,v/v) into a glass dropper bottle.

Test Procedure

Place 1 piece of Test Paper A in depression of white spot plate. Place 1 drop liquid (aqueous or organic) and small portion of tablet or powder from capsule (about volume of match head) or 1/8-1/4 of sugar cube on top of test paper. Add Solution A (1-10 drops) until test paper is wet. Add Solution C (1-10 drops) to test paper. If effervescence occurs, add Solution C until effervescence ceases; then add 2 drops excess. (Use the least amount of Solutions A and C as possible; the smaller the volumes used, the more sensitive the test.) The formation of a pink or blue color on the paper or in the solution within 5 min indicates the possible presence of the indole structure. If a negative result is obtained, thoroughly mix capsule contents and repeat test. (We have received capsules which contain LSD only in one end of the capsule.) Perform blank tests on piece of Test Paper A and Solutions A and C, omitting test sample, and also on the test sample with Solutions A and C, omitting Test Paper A.

(The 5 min estimation of color development is relative to the concentration of the indole compound present. This test can detect 1 μg of LSD in less than 1 min.)

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Discussion

The test procedure is based on the formation of a complex between *p*-dimethylaminobenzaldehyde and the indole structure. It is suitable for the detection of LSD-ergotamine alkaloids in liquids, powders, tablets, capsules, and sugar cubes.

The above kit has been successfully used by District analysts for six months and by BDAC agents for two months. In all District samples, a positive or negative test was confirmed by TLC identification.

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DETERMINATION OF LSD AND ISO-LSD BY PAPER CHROMATOGRAPHY

By James Look, San Francisco District
(presented by E. Jekabson)

Paper chromatography can be used to identify and quantitatively measure LSD and iso-LSD. Two qualitative tests and one quantitative method are given below.

Qualitative method 1. - Soak Whatman No. 1 chromatographic paper in a solution composed of 1 g benzoic acid, 25 ml formamide, and 75 ml methanol. Blot paper, air-dry for a few minutes, and then spot enough sample to provide ca 10 μg LSD (as salt or free base). Develop paper in the usual ascending manner, using formamide-saturated ether as mobile phase.

Examine paper under UV light (long and short wavelength) or spray paper with 2% p-dimethylaminobenzaldehyde in alcohol, dry, and respray with alcoholic HCl (1:1).

The R_f values of LSD and iso-LSD are about 0.5 and 0.2, respectively.

Qualitative method 2. - An additional test for LSD identification based on degradation of LSD by a base is as follows: Dissolve sample and standard in about 15 ml water and add several drops of ammonium hydroxide. Let solution stand for 3 min and then extract LSD and its degradation products with chloroform. Evaporate chloroform extract just to dryness, dissolve residue in small amount of methanol, and subject methanol solution to paper chromatography as described above.

For positive identification, the sample and standard should have the same number of spots with the same R_f values.

Quantitative method. - Dilute known amount of sample with a definite volume of alcohol (should be kept to a minimum) and spot an amount equivalent to 100 μg LSD. Develop chromatogram, cut out LSD and iso-LSD spots, and extract spots with 10 ml dilute HCl. Extract acidic solution with two 10 ml portions of chloroform and discard chloroform. Make aqueous phase basic with sodium carbonate and extract with four 15 ml portions of chloroform. Evaporate chloroform extract to dryness. Dissolve residue in 5.0 ml 0.1N HCl and determine UV absorbance of LSD and iso-LSD extracts. Calculate percentage of iso-LSD present.

Discussion

It is easier to determine the total amount of LSD in the sample by one of the spectrophotometric methods that measures LSD and iso-LSD together, then determine the iso-LSD content by paper chromatography, and calculate the LSD content by difference.

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Paper chromatography is more accurate than the column method for the determination of iso-LSD because the sample never comes in contact with base. Qualitative test 2, described above, is based upon the very rapid degradation of LSD in the presence of base.

Other paper chromatographic procedures have been reported for ergot alkaloids:

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IDENTIFICATION OF LSD AND LSD TARTRATE BY THIN LAYER CHROMATOGRAPHY

By Ernest Beyer, San Francisco District,
and Donald D. Dechert, Los Angeles District

Thin layer chromatography (TLC) is a useful and relatively inexpensive technique for identifying drugs. It is faster and more sensitive than paper chromatography. Thin layer plates can be coated with aluminum oxide or silica gel adsorbents with readily available equipment (Brinkmann Instruments, Inc., Westbury, N. Y., or equivalent) or precoated thin layer sheets may be purchased (Eastman Distillation Products Industries , Rochester, N. Y., or equivalent). The precoated sheets are available as 100 μ layers of aluminum oxide or silica gel, with or without a fluorescent indicator.

Procedure 1: LSD (tartrate)

Materials

(a) Chromogenic agent. - Add 125 mg p-dimethylaminobenzaldehyde, 65 ml concentrated H_2SO_4, and 2 drops ferric chloride (USP T.S.) to 100 ml volumetric flask. Dilute to volume with water.

(b) TLC plates. - 200 mm, with 0.125 μ groove (No. K41600, Size A, Kontes Glass Co., Vineland, N. J.).

TLC Technique

Apply silica gel slurry to desired number of plates (3 g silica gel + 6 ml water/plate) and proceed as above, using 0.5 - 1.0 μg sample and LSD standards, in chloroform, for spotting. Develop plate in acetone: chloroform (4:1) solvent, remove from tank, and air-dry.

Compare R_f values of blue fluorescent sample and standard LSD spots. (Some samples give various other colored fluorescent spots which are caused by deterioration of the sample but these do not occur in the standard LSD.)

Spray developed plate with chromogenic agent. (LSD and iso-LSD have R_f values of 0.3 to 0.4 and 0.0 to 0.1, respectively.)

Procedure 2: LSD

Materials

(a) Adsorbents. - 30 g silica gel + 60 ml water; 30 g aluminum oxide + 50 ml water; silica gel-aluminum oxide 1+1 mixture, i.e., prepare separate slurries of 15 g silica gel + 30 ml water and 15 g aluminum oxide + 25 ml water, mix, and then combine before spreading; or precoated TLC sheets.

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(b) Chromogenic agent. - Dissolve 1 g p-dimethylaminobenzaldehyde in 10 ml HCl + 90 ml ethanol.

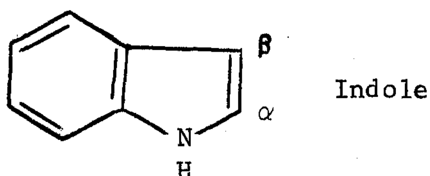
TLC Technique

Prepare solutions of sample and standard in volatile solvent such as acetone. Spot volumes equivalent to 0.5-5 μg LSD about 1.5 cm from bottom of plate, using a syringe or micropipet. Keep spots as small as possible.

Apply desired adsorbent - water slurry to TLC plates. Air-dry prepared plates 15 min, heat in 80° oven for 30 min, and store in desiccator until ready to use.

Develop plate in tank saturated with acetone : methanol (4:1) until solvent front moves three-quarters the length of plate. Remove plate, dry, and observe fluorescent spots under ultraviolet light.

Spray plate with p-dimethylaminobenzaldehyde agent for color development. (Aqua regia vapor may be used to intensify and speed up color development.) LSD gives a blue spot; other indoles with an intact -CH in the α- or β- position to the indole NH group have violet, blue, or purple spots (Look, J., Interbureau By-Lines 3(4), 177-181 (1967)).



Indole

Table 1. Rf values for various adsorbents using acetone : methanol (4:1) as developing solvent

Compound	Silica Gel, 100 μ	Silica Gel + Aluminum Oxide (1+1), 250 μ	Aluminum Oxide, 250 μ
LSD (tartrate)	0.55	0.62	0.74
LSD (free base)	0.55	0.62	0.74
Iso-LSD (free base)	0.45	0.51	0.61
Lysergic acid	0.04	0.02	0.00
Ergotamine tartrate	0.56	0.67	0.70
Ergotamine	0.56	0.75	0.70
Ergoncvine maleate	0.48	0.49	0.55
Ergonovine	0.50	0.49	0.61
Methylergonovine maleate	0.50	0.55	0.64
Methylergonovine	0.48	0.56	0.63
Psilocybin	0.00	0.00	0.00
N,N-dimethyltryptamine	0.10	0.13	0.60
Tryptophan	0.00	0.00	0.00
Indole	0.72	0.80	0.73

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Absorbents with ultraviolet fluorescent indicators can also be used to observe the developed spots. These are particularly useful when alkaloids that do not fluoresce in ultraviolet light, such as N,N-dimethyltryptamine and psilocybin, are being examined.

Discussion

Table 1 lists the $\underline{R}_f$ values obtained for Procedure 2, using all three adsorbent layers. The $\underline{R}_f$ values from a different solvent system are given in Table 2.

Table 2. $\underline{R}_f$ values for various compounds, using acetone : chloroform for developing solvent for silica gel (100 μ) plates

Compound	$\underline{R}_f$
LSD (tartrate)	0.33
Lysergic acid	0.00
Ergotamine tartrate	0.37
N,N-dimethyltryptamine	0.11

The $\underline{R}_f$ values are only approximate, since temperature, humidity, and other factors will change them. As a result, standards must be spotted along with the samples each time. The standards and samples should be approximately the same concentration.

Notes on Procedure

(1) Carefully spot samples and standards to obtain about the same size spots and to avoid making a hole at the spotting point. These factors may influence $\underline{R}_f$ values.

(2) Protect eyes from direct exposure to UV light while examining plates.

(3) Calculate $\underline{R}_f$ values as follows: $\underline{R}_f$ = distance spot moved/distance solvent front moved.

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INFRARED IDENTIFICATION OF LSD IN CAPSULES, LIQUID, SUGAR CUBES, AND TABLETS

By Don Zacharias, Los Angeles District

A rapid infrared spectrophotometric identification procedure for LSD would be useful for the analysis of BDAC samples. The usual sample analyzed contains from 50 to 150 µg LSD/unit, which amount cannot be detected by the usual infrared technique. In the following procedure, LSD is extracted and identified, using a micro KBr disk. Infrared spectra have been obtained on amounts as low as 100-200 µg LSD.

Procedure

Transfer sample portion (equivalent to 250-300 µg LSD) to a separatory funnel, combining units if necessary. Dilute volume to 10 ml with water, add 5 ml 1N $NaHCO_3$(AR), and mix. Check pH (pH paper); if pH is less than 8, add bicarbonate to bring pH to 8 or above. Extract solution with 10 ml portions of chloroform, keeping number and amount of extractions to minimum. Wash combined extracts with 5 ml water and pass combined extracts through 1" anhydrous sodium sulfate into 50 ml beaker. Evaporate extract to ca 1 ml or less on a water bath (not over 30°C) under a gentle flow of prepurified nitrogen.

Grind 60-70 mg KBr (spectral grade) to a fine powder in a mortar. Transfer concentrate to mortar and rinse beaker with ca 0.4 ml chloroform, transferring rinse to mortar. Carefully evaporate chloroform under a gentle flow of nitrogen. Grind resulting mixture to a fine well-mixed powder. Transfer the fine powder to a KBr die containing a microdisk with a 2 x 11 mm slot. Center powder in slot and place ram in die. Use vacuum on die for 1 min and then place die in laboratory press and prepare disk. Remove disk and record spectrum from 2 to 15 µ with a suitable IR recording spectrophotometer.

To obtain spectrum for LSD standard (100 µg LSD/ml 0.1N HCl), add 2 ml to separatory funnel, and proceed as outlined. Compare spectra of sample and standard for identification. Compare the sample and standard LSD spectra.

Discussion

The 30° water temperature is specified since a solution of LSD in chloroform, when allowed to rise above this temperature, may deteriorate.

The KBr-LSD powder must be thoroughly mixed or an opaque disk may result. The powder should be scraped from the sides of the mortar and reground at least twice. If an opaque disk is obtained with the

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first pressing, regrind the disk. More KBr may also be added to obtain a clear disk. The positioning of the KBr mixture in the center of the disk slot may also affect the clarity of the disk. When analyzing sugar cubes, a blank sugar cube disk must be prepared since the sugar extracts alone will give an infrared spectrum. A known amount of standard LSD is added to a sugar cube and treated in the same manner as the sample cube.

Conclusion

The above procedure has been used by three different analysts for samples of capsules, liquids, sugar cubes, and tablets. No difficulties except those mentioned in the discussion were encountered. The procedure is rapid (about 1-2 hours) and specific for the identification of LSD.

Acknowledgments

The author wishes to thank Robert J. Martin and Donald D. Dechert for their assistance and collaboration.

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IDENTIFICATION OF LSD BY INFRARED SPECTROPHOTOMETRY

By Ted M. Hopes, San Francisco District

We do not use infrared spectrophotometry (IR) for routine identification of LSD since paper chromatography is more sensitive, simpler, and, in at least one important aspect, more specific than IR. The difference between the IR spectra of LSD and iso-LSD is the presence or absence of a half-dozen weak absorption bands in the 850-1150 cm^{-1} region; see Table 1. With micro amounts of compounds, it is difficult to bring out this region with enough clarity. The material under analysis could be predominantly the iso form and have relatively little physiological activity, yet appear to have a good LSD spectrum. There is no such doubt with paper or thin layer chromatography. The amounts of iso-LSD and LSD can be easily estimated and/or quantitatively measured. Since LSD deteriorates readily on handling, in most cases paper chromatography has the further advantage that the LSD can be directly transferred to the paper with ethanol. A truer picture of the sample would be expected by this technique than after the extractions and evaporations necessary in IR work. Nevertheless, IR analysis can furnish valuable additional evidence of the identity of a sample.

We use micro beam condensers (devices that use sodium chloride or potassium bromide lenses to concentrate light from the source to pass through a small sample) for all our micro work. A 0.5 x 4.0 mm image of the slit is focused at the sample holder. With a micro disk with dimensions equal to or smaller than the slit image, almost the full power of the source is passed through several micrograms of sample concentrated in about 10 mg KBr. The unabsorbed light is refracted back to normal beam size and focused on the detector. An attenuator in the reference beam permits the equalization of both beams to zero the instrument, i.e., obtain a convenient base line.

Procedure

Quantitatively measure sample in acid solution by UV spectrophotometry. Add ammonia to make solution basic and extract LSD and iso-LSD with small portions of chloroform. Evaporate chloroform to small volume, depending on amount of LSD present. Grind 10 mg dry KBr (reagent grade) to a fine powder in agate mortar, add sample-chloroform solution, and grind slurry until chloroform has evaporated and a dry powder is obtained. Use this powder to prepare microdisks by one of the following methods.

(1) The least expensive method is as follows: Fashion 15 gauge hypodermic needle into paper borer by sawing the tip off flat and sharpening cutting portion. Make two or three punches in piece of blotter paper to form a window ca 1.5 x 4 mm. Tape piece of blotter paper flat onto a stainless steel block with cellophane tape. Fill window with KBr-sample mixture, tamping powder in with flat microspatula. Place a stainless steel block on top of paper, put the two blocks into a press, and

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Table 1. Infrared absorption maxima of LSD and iso-LSD

LSD		iso-LSD	
wavelength[a]	wave number, cm^{-1}	wavelength[a]	wave number cm^{-1}
2.9 sh	3448	2.9 sh	3448
3.06 s	3268	3.06 s	3268
3.39 s	2950	3.39 s	2950
3.5 sh	2857	3.5 sh	2857
3.65 w	2740	3.65 w	2740
6.13 vs	1631	6.13 vs	1631
6.75 sh	1481	6.75 sh	1481
6.89 vs	1451	6.89 vs	1451
7.27 m	1376	7.27 m	1376
7.45 m	1342	7.45 m	1342
7.65 w	1307	--	--
8.00 w	1250	7.98 w	1253
8.12 w	1232	8.09 w	1236
8.25 s	1212	8.25 m	1212
8.62 m	1160	8.60 m	1163
8.90 m	1124	8.85 m	1130
9.00 w	1111	--	--
9.12 w	1096	9.12 m	1096
9.30 w	1075	9.30 w	1075
9.50 w	1053	9.49 sh	1054
--	--	9.70 w	1031
10.02 w	998	10.01 w	999
--	--	10.25 w	976
10.70 w	935	10.88 w	919
11.08 m	902	11.37 w	880
--	--	11.62 w	861
11.78 m	849	11.87 w	842
12.25 w	816	12.25 w	816
12.89 s	776	12.85 s	778
13.39 s	747	13.35 s	749

[a] vs, very strong; s, strong; m, moderate; w, weak; sh, shoulder.

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apply ca 20,000 lb ca 1 min. (The end product should be a transparent disk set in paper that will, with proper alignment in the micro beam condenser, give a reasonable spectrum.)

(2) The other method is simpler and gives better spectra: Press disks with a commercially available microdie. (We can obtain a good spectra of 10-50 μg LSD in 10 mg KBr.)

Discussion

A useful collection of IR spectra has been published by Food and Drug chemists (Hayden, A. L., _et al_., _J. Assoc. Offic. Anal. Chemists_ _45_, 797-900 (1962); _47_, 918-991 (1964); _40_, 1109-1153 (1966)). At present there are 742 spectra of organic and inorganic compounds of pharmaceutical interest in this collection. LSD and iso-LSD are spectra 618 and 655, respectively.

A comparison of KBr disks of LSD and iso-LSD is shown in Table 1. The spectra mentioned above were used for these measurements.

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IDENTIFICATION OF MESCAL BUTTONS (PEYOTE)

By Joseph Levine, Division of Pharmaceutical Chemistry

The hallucinogenic activity of peyote is due principally to the alkaloid mescaline and, to a lesser extent, anhalonine. While mescal buttons can be identified by histological examination, isolation of these alkaloids constitutes proof that the sample is physiologically potent. Demonstration of the presence of other characteristic alkaloids provides an independent identification of the sample.

By the procedure described below, mescaline is readily isolated as its crystalline sulfate; anhalonine as its hydrochloride. The presence of the other alkaloids can be shown by gas chromatography, which also can provide a rough estimate of the mescaline content of the sample.

The principal non-phenolic peyote alkaloids are mescaline, anhalonine, anhalinine, and lophophorine. The principal phenolic alkaloids are anhalamine, anhalonidine, anhalidine, and pellotine. Mescaline sulfate can be obtained from K & K ($9/g); anhalonine hydrochloride, anhalamine hydrochloride, and lophophorine hydrochloride from S. B. Penick for $10 per vial (50-100 mg).

Procedure

Grind several grams of Dry Ice in a blender, add the dry sample (20-30 g), and grind to a fine powder.

Weigh about 20 g powdered sample into a Soxhlet thimble. Cover with 95% alcohol, add 1 ml NH_4OH, and extract with alcohol for 3 hr. Let stand overnight (thimble covered with alcohol) and continue extraction for 3 more hr.

Filter the extract through paper and evaporate just to dryness on a steam bath.

With the aid of $CHCl_3$ and ca 0.5N HCl, dissolve and transfer the residue to a separatory funnel. Shake, and transfer the $CHCl_3$ to a second separatory funnel. Extract with 2 additional portions of HCl and wash the aqueous solutions serially with fresh $CHCl_3$. Discard the $CHCl_3$ washings.

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Carefully add solid Na_2CO_3 in small portions to the combined aqueous solutions until effervescence ceases, finally adjusting to ca pH 8 (check with indicator paper). Extract with four 50 ml portions of $CHCl_3$. Extract the combined $CHCl_3$ twice with ca 0.5N NaOH to remove phenolic alkaloids, filter the $CHCl_3$, and concentrate to ca 30 ml. Transfer to a 50 ml volumetric flask and adjust to volume. Withdraw a 2 ml aliquot for gas chromatography and evaporate the remainder just to dryness on a steam bath. Dissolve the residue in ca 10 ml 95% alcohol and add H_2SO_4 (1 + 2) dropwise until neutral (check by touching glass rod to moist indicator paper). Crystalline mescaline sulfate will then separate. Cool, filter, and wash with cold alcohol.

Evaporate the filtrate to ca 5 ml and add 1-2 drops 2N HCl. Crystalline anhalonine hydrochloride will separate. Filter and wash with cold alcohol.

To recover the phenolic alkaloids, acidify the NaOH extract obtained above, wash with $CHCl_3$, adjust to ca pH 8 with solid Na_2CO_3, and extract with $CHCl_3$.

Identify the mescaline and anhalonine by IR (KBr disks). They can also be identified by measurement of the optical properties of the crystals, or by microscopic observation of characteristic crystals precipitated with platinic chloride.

Perform gas chromatography, using a column of 3% SE-30 and 1% QF-1 on Gas-Chrom P, 80-100 mesh, at a column temperature of 170-190° and 20-24 psi.

Prepare standards as follows: dissolve weighed quantities of the alkaloid salts in water, make the solutions alkaline, and extract with $CHCl_3$. Chromatograph aliquots of these standards of the extracts reserved above, and of the phenolic alkaloids.

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MESCALINE (HYDROCHLORIDE OR SULFATE)

Usual Dosage form	Usual Concentration
Capsules	300 - 500 mg/capsule

Method of Analysis: Spectophotometric - UV

Mescaline salts in capsules are almost always free of diluents. If clean-up or extraction is necessary, take spl. up in 1% tartaric acid, render alkaline with $NaHCO_3$ and extract with $CHCl_3$. Place an accurately weighed portion of the contents of a capsule, approx. 20 mg., into a 100 ml. volumetric flask. Dissolve in water and dilute to volume.

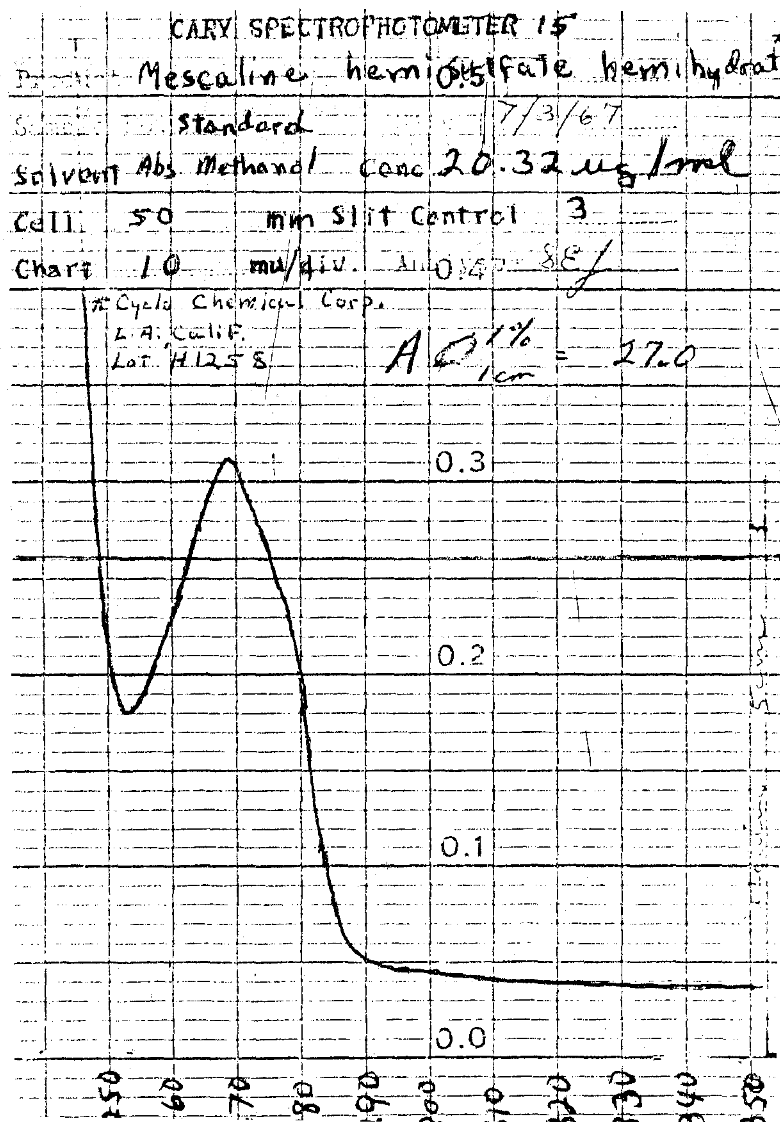
Prepare a std. of Mescaline Sulfate or Hydrochloride at a concentration of approx. 20 mg/100 ml. H_2O.

Blank recording spectrophotometer at 330 mu with H_2O.

Scan ssl. & std. in 1 cm. cells from 330 - 248 mu.

Maximum absorbance: approx. 268 mu.

Melting Points: Hydrochloride 181° C, Sulfate 183 - 186° C



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LSD ANALYSIS

By Donald D. Dechert, Los Angeles District,
and Evalds Jekabsons, San Francisco District

The following summarizes some of the various procedures[1] used in the Food and Drug Administration to assay and identify LSD in various kinds of samples. The methods described are applicable to samples of capsules, liquids, powders, sugar cubes, and tablets. In all procedures, an equivalent amount of LSD or iso-LSD standard should be carried through the same procedure that is being used to analyze the sample.

I. Preliminary Procedures

Inspection and preparation of sample (SF): Examine sample and note dosage form. Analyze individual tablets or capsules (if sample size is large enough), 400 mg powder, or 5 ml liquid. If sample size is limited, reduce amounts. In this case, weigh tablets, grind to a powder, and mix. Use a portion of tablet for analysis and calculate results on whole tablet basis.

Preliminary test (SF): Perform Look's presumptive test (1) on small portion of sample. (A blue color indicates the presence of an indole group.)

Qualitative identification of LSD by paper chromatography (SF): Dilute ca 20 µg LSD with small amount of alcohol and spot extract, as well as ca 10 µg LSD standard, on Whatman #1 chromatographic paper impregnated with formamide-benzoic acid. Develop in ascending technique with formamide-saturated ether as mobile solvent. R_f: LSD = ca 0.5, iso-LSD = 0.25. (See details in paper by E. Jekabsons, pp. 19-20.)

II. Extraction Procedures

Procedure 1 - SF: Transfer portion of sample equivalent to ca 100 ug LSD to separatory funnel with 10 ml water and 2 drops HCl. Extract aqueous layer with three 10 ml portions of $CHCl_3$ and discard $CHCl_3$ extracts. (Note: Save extract if presence of barbiturates is suspected.) Make aqueous layer alkaline with 3-4 drops of concentrated NH_4OH and extract alkaloids with 15 ml portions of $CHCl_3$. Collect extracts in 100 ml beaker and evaporate just to dryness. (A steam bath may be used for evaporation if temperature does not exceed 40°C.) Dissolve residue in 5.0 or 10.0 ml 0.1N HCl.

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[1] The order of mention of methods or district is arbitrary and does not imply any rating of the method; LA - Los Angeles District; SF - San Francisco District.

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Procedure 1 - LA: Transfer sample equivalent to ca 100 μg LSD to separatory funnel with 10 ml water and make aqueous layer alkaline (pH paper) with 1N $NaHCO_3$. Extract aqueous layer with four 20 ml portions of $CHCl_3$, combine $CHCl_3$ extracts in 100 ml beaker, and evaporate extracts to <5 ml, using nitrogen and a warm water bath $<35°C$). Transfer extract to 5 ml volumetric flask and dilute to volume with $CHCl_3$.

Procedure 2 - (SF, LA, and (2)): Thoroughly mix 2 g Celite 545 (acid-washed) and 1 ml 1N $NaHCO_3$ and transfer mixture to chromatographic column (25 x 200 mm) containing glass wool plug. Thoroughly mix 4 g Celite 545, 3 ml 1N $NaHCO_3$, and sample equivalent to 100 μg LSD, transfer mixture to column, and pack column with tamping rod. Elute column with 125 ml water-washed $CHCl_3$, collecting eluate in beaker. Concentrate eluate and dissolve residue in described manner.

Procedure 3 (SF, LA, and (2)): Mix 3 ml 2% citric acid with 4 g Celite 545 (acid-washed); transfer to chromatographic column with glass wool plug. Mix 2 ml water and 2 g Celite and add to column. Pack both layers firmly.

Prepare second column as above, but use 8% citric acid instead of 2% solution.

To prepare sample column, mix portion of sample containing ca 100 μg LSD with enough 1% tartaric acid to provide a mobile liquid or suspension. Add 3 ml $CHCl_3$ to mixture and make alkaline with 10% Na_2SO_4. Quickly add enough Celite to make a fluffy mixture, transfer to a third chromatographic column, and pack firmly.

Arrange column so that eluate from sample column flows onto the 2% citric acid column and then onto the 8% citric acid column.

Add 50 ml water-washed $CHCl_3$ to sample column to separate alkaloid-type substances from water-soluble materials. Then elute 2% column with 50 ml more of water-washed $CHCl_3$, letting eluate pass through 8% column. Finally, elute 8% column with 25 ml water-washed $CHCl_3$, discarding all eluates. The 2% column retains iso-LSD, while the 8% column retains LSD.

(This elution should be monitored by viewing the columns occasionally under a strong source of longwave UV light; LSD and iso-LSD appear as light-colored bands.)

LSD and iso-LSD may be removed from the 8% and 2% citric acid columns by various methods: (a) Strip columns with alcohol or similar solvent and remove alcohol from sample portion, using nitrogen as in Procedure 1 - LA; (b) extrude columns into separate beakers, make each alkaline with $NaHCO_3$, and transfer solutions to separate separatory funnels. Extract alkaline solution with four 20 ml portions of $CHCl_3$; or (c) pack mixture of 5 g Celite and 5 ml concentrated NH_4OH into each column and elute each with 100 ml water-washed $CHCl_3$ (or until fluorescent bands are removed).

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III. Determination Procedures

Colorimetry (SF, LA, and (3)): The color reaction described below depends on the presence of an indole or an α- or β-substituted indole system. The reaction is extremely sensitive to hydrogen-ion concentration, oxidizing agent concentration and type, and p-dimethylaminobenzaldehyde (chromogenic agent) concentration. Therefore, samples and standards should be determined concomitantly.

Pipet aliquot equal to 100 µg LSD into 50 ml Erlenmeyer flask and evaporate to dryness. Pipet 5.0 ml freshly prepared alcoholic tartaric acid solution (1 volume alcohol mixed with 1 volume 1% tartaric acid) and swirl flask contents to dissolve residue. While swirling flask in ice bath, add 10.0 ml p-dimethylaminobenzaldehyde USP T.S. (125 mg in a cooled mixture of 65 ml H_2SO_4, 35 ml water, and 0.05 ml 9% ferric chloride). Let mixture stand 10-15 min for equilibration, with occasional mixing. Determine absorbance of solution at 550 mµ relative to a blank solution consisting of 5.0 ml alcoholic tartaric acid solution and 10.0 ml color reagent. Compare absorbances of sample and standard prepared similarly and calculate quantity of LSD present in sample. (The molar absorptivity of LSD tartrate by this method, accounting for two moles of LSD/mole of tartrate, is 16,300.)

Thin layer chromatography: See procedures described by E. Beyer and D. D. Dechert, pp. 21-23.

Infrared spectrophotometry: See procedures described by D. Zacharias, pp. 24-25, and by T. M. Hopes, pp. 26-28.

Ultraviolet spectrophotometry: Procedure 1 (SF). - Determine UV absorbances of sample and standard solutions from 400 to 230 mµ with recording spectrophotometer; use maximum absorbance at 312 mµ for quantitative calculation. (The molar absorptivity of the tartrate, accounting for 2 moles of LSD/mole of tartrate, was found to be 8,270.) Report results as lysergic acid diethylamide rather than as the tartrate salt, because any pharmacological activity is due to the former compound.

Procedure 2 (LA and (4)): Pipet 4.0 ml $CHCl_3$ extract from extraction or column procedures into a 30 ml beaker. Evaporate just to dryness in warm water bath (not over 35°C) under gentle flow of nitrogen. Dissolve residue in 4.0 ml 0.1N HCl and obtain an ultraviolet spectrum from 380 to 260 mµ versus reference solution of 0.1N HCl. Zero spectrophotometer at 312 mµ. Compare sample and standard LSD spectra and calculate LSD present in sample portion analyzed, using absorbance at 312 mµ.

Reserve rest of 0.1N HCl for additional analysis, if necessary.

Procedure 3 (LA): Pipet 4.0 ml $CHCl_3$ from extraction or column procedures to separatory funnel, add 5.0 ml 10% tartaric acid solution by pipet, and shake contents vigorously 1 min. Let $CHCl_3$ settle and discard $CHCl_3$ layer. Swirl funnel to remove any $CHCl_3$ adhering to sides and again discard $CHCl_3$. Transfer tartaric acid solution to 1 cm

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quartz cells and obtain UV spectrum as in Procedure 2. Zero spectrophotometer at 312 mμ, using a $CHCl_3$-saturated 10% tartaric acid solution in each cell. Read sample and standard solutions against one of these solutions.

Procedure 4 (LA and (5)): Place quartz cell containing standard LSD tartaric acid solution 1" from longwave UV light source. Irradiate solution 1 min and scan in UV region as in Procedure 3. Irradiate solution 1 min more and repeat scan. Carry sample tartaric acid solution through same procedure. Compare standard and sample spectra; note shifting of peaks. (See Fig. 1, p. 13.)

IV. Notes and Comments

(1) Because of the difficulty in obtaining LSD standards, USP ergonovine maleate or USP methylergonovine maleate (available from USP Reference Standards, 46 Park Ave., New York, N.Y. 10016 for $10/25 mg) may be used. The UV-active chromophoric groups and the reactive sites for colorimetric assay are the same. Molar absorptivities have been found to be equivalent (within 1%) for both quantitative procedures.

(2) Whenever iso-LSD is to be determined, care should be taken to prevent LSD from getting in the basic solution because LSD is rapidly converted to the iso-form in the presence of base.

(3) Sodium sulfate may be used to disperse emulsions if a separatory funnel extraction is used.

(4) If the solution is kept in the dark, LSD in dilute acid is stable up to two days.

(5) Protect eyes from direct exposure to UV light source.

References

(1) Look, J., Interbureau By-Lines 3(4), 177-181 (1967).

(2) Alexander, T. G., ibid. 2(4), 149-151 (1966).

(3) Alexander, T. G., ibid. 1(2), 87-89 (1964).

(4) Martin, R. J., private communication, Food and Drug Administration.

(5) Based on work of H. Hellberg [Acta Chem. Scand. 11, 219-229 (1957)] and A. Stoll and W. Schlientz [Helv. Chim. Acta 38, 585-594 (1955).]

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NOMINATION FORM
BUREAU OF DRUG ABUSE CONTROL
SCHOOL FOR LOCAL AND STATE POLICE CHEMISTS

ME______________________________ TITLE________________

)ME ADDRESS____

____

1PLOYER____

USINESS ADDRESS____

ENGTH OF SERVICE____

DUCATION: College or University | Degree | Major

_____________________ ______ ____________

_____________________ ______ ____________

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?lease check technique or equipment used in your laboratory.

___ Paper Chromatography ___ U. V. Spectrophotometer
___ Column Chromatography ___ Infrared Spectrophotometer
___ Thin layer " ___ Nuclear magnetic resonance
___ Gas-liquid " ___ X-Ray
___ Microchemical crystal test ___ Spectrophotofluorometer

Other (specify)____

____

Indicate analytical problem(s) nominee would like to have covered:

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ANNOUNCING A SEMINAR

FOR LOCAL AND STATE POLICE CHEMISTS

SPONSORED BY THE FOOD AND DRUG ADMINISTRATION

BUREAU OF DRUG ABUSE CONTROL

IN COOPERATION WITH THE BUREAU OF SCIENCE

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BDAC'S SCHOOL FOR LOCAL AND STATE POLICE CHEMISTS

PURPOSE

This school is designed to increase the chemist knowledge of the drug abuse problem, and to aid him in the analysis of stimulant, depressant and hallucinogenic drugs.

CONTENT

The program will include instruction in Pharmacology, lectures and laboratory workshop on the analysis of stimulant, depressant and hallucinogenic drugs. Class will be limited to sixteen students.

A schedule of classes and information regarding lodging, etc., will be sent to each student prior to the beginning of the course.

Course No.	Dates
2	February 5 - 9, 1968
3	April 8 - 12, 1968
4	June 17 - 21, 1968

WHO IS ELIGIBLE

Nominees will be selected from State, Municipal and Federal Laboratories who conduct analysis of drug evidence in criminal cases. Nominees must have a minimum of a B.S. degree in Chemistry or related science and be employed full time as a police chemist or criminalist.

Nominees selected must be recommended by the head of his agency and his character, reputation and standing in the community must be beyond reproach.

Nominees must bear the cost of transportation and living expenses. There is no charge for the course.

DATE AND LOCATION

CALENDAR

DATE	Nominations due Field Office Director
Location Address	
DATE	Nominations due BDAC's Training Officer
DATE	Course Commences

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