LSD

ONLINE DAT Lysergic Acid Diethylamide

cobas®

Drug abuse testing

Order information

REF	CONTENT		Analyzers on which **cobas c** pack can be used
20763284 122	ONLINE DAT Lysergic Acid Diethylamide (200 tests)	System-ID 07 6328 4	COBAS INTEGRA 400 plus
20766356 122	ONLINE DAT LSD Calibration/Control Pack LSD Calibrator (1 × 5 mL) LSD Positive Control (2 × 4 mL) LSD Negative Control (2 × 4 mL)		

English

System information

Test LSD, test ID 0-328

Intended use

Lysergic acid diethylamide (LSD) assay is an in vitro diagnostic test for the qualitative detection of LSD and its metabolites in human urine at a cutoff concentration of 0.5 ng/mL on COBAS INTEGRA systems.

The LSD assay provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography or Liquid Chromatography coupled with Mass Spectrometry or Tandem Mass Spectrometry (GC/MS, GC/MS/MS, LC/MS or LC/MS/MS) is the preferred confirmatory method.[1,2] Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

Summary

Lysergic acid diethylamide (LSD, lysergamide, Delysid) is an ergot alkaloid that is a natural product of the rye fungus Claviceps. However, most of the LSD consumed illicitly is derived by synthesis involving the reaction of lysergic acid with diethylamine.[3,4] LSD is a hallucinogenic drug that can cause severe altered states of consciousness, can induce psychotic reactions characterized by hallucinations, and can cause other perceptual disturbances that mimic functional psychosis.[4,5] LSD is a partial agonist at serotonin 5-hydroxytryptamine 2A (5-HT2A) receptors, which primarily mediate the hallucinogenic effects of LSD.[6] Of the four possible synthetic diastereomers of LSD only *d*-LSD has mind altering properties. The *d*-LSD is one of the most potent hallucinogenic agents known to man, but it has a remarkably low acute toxicity.[3,5,7] LSD is usually administered by drug abusers as the tartrate salt in oral doses of 25 to 250 µg.[3] This drug undergoes such rapid and extensive metabolism that only a small fraction of a dose is excreted in human urine as unchanged LSD. Urine from suspected drug abusers contain multiple metabolites including (in order of decreasing concentration) 2-oxo-3-hydroxy-LSD, LSD-o-glucuronide, 2-oxo-LSD, LSD, N-desmethyl-LSD (nor-LSD).[1,2,3] Although iso-LSD is not a metabolite of LSD, it is a major contaminant in many illicit LSD preparations and hence is frequently detected in the urine and other body fluids from LSD abusers.[1]

Test principle

Kinetic interaction of microparticles in a solution (KIMS)[8,9] as measured by changes in light transmission.

In the absence of sample drug, free antibody binds to drug-microparticle conjugates causing the formation of particle aggregates. As the aggregation reaction proceeds in the absence of sample drug, the absorbance increases. When a urine sample contains the drug in question, this drug competes with the particle-bound drug derivative for free antibody. Antibody bound to sample drug is no longer available to promote particle aggregation, and subsequent particle lattice formation is inhibited. The presence of sample drug diminishes the increasing absorbance in proportion to the concentration of drug in the sample. Sample drug content is determined relative to the value obtained for a known cutoff concentration of drug.

Reagents - working solutions

R1 Antibody Reagent (AB)
LSD antibody (goat polyclonal) in buffer and 0.09 % sodium azide.

R2 Sample Diluent (SD)
Buffer containing stabilizer and 0.09 % sodium azide.

R3 (SR) Microparticle Reagent (MP)
Conjugated LSD derivative microparticles in buffer and 0.09 % sodium azide.

R1 is in position C, R2 is in position A and R3 (SR) is in position B.

Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

Reagent handling

Mix all new (non-punctured) **cobas c** packs for 1 minute on a cassette mixer before loading on the analyzer. All in-use **cobas c** packs must also be mixed in the same manner at the beginning of each week (once a week).

Storage and stability

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label
On-board in use at 10-15 °C	55 days

Do not freeze reagents. Reagents that have been frozen should be discarded.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

Urine: Collect urine samples in clean, amber glass or non-transparent plastic containers. Fresh urine samples do not require special pretreatment, but an effort should be made to keep pipetted samples free of gross debris. As a precaution against photo decomposition of LSD, urine samples should be protected from exposure to light.[1] Samples should be within the normal physiological pH range of 5-8. No additives or preservatives are required. It is recommended that urine specimens be stored at 2-8 °C and tested within 5 days of collection.[10]

For prolonged storage, freezing of the sample is recommended.

Centrifuge highly turbid specimens before testing.

Adulteration or dilution of the sample can cause erroneous results. If adulteration is suspected, another sample should be collected. Specimen validity testing is required for specimens collected under the *Mandatory Guidelines for Federal Workplace Drug Testing Programs*.[11]

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Materials provided

See "Reagents – working solutions" section for reagents.

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

Application for urine

Test definition[a)]

Measuring mode	Absorbance
Abs. calculation mode	Endpoint

Reaction mode	R1-S-R2-SR (long test)
Reaction direction	Increase
Reaction start	SR
Wavelength A	800 nm
Test range	0-1.9 ng/mL
Postdilution factor	No
Calc. first/last	65/140
Unit	Abs.

a) On COBAS INTEGRA analyzers, the Lab Unit is ABS, the Lab Unit Factor is 1, the Lab Unit Offset is 0, and the Decimal Position is 3.

Pipetting parameters

R1	50 µL
R2	66 µL
Sample	28 µL
R3 (SR)	40 µL
Total volume	184 µL

Calibration

Calibrator	ONLINE DAT LSD Calibration/Control Pack LSD Calibrator 0.5 ng/mL (LSDST, system-ID 07 3565 5)
Calibration mode	Cutoff
Calibration replicate	Triplicate recommended
Calibration interval	Each lot, every 14 days, and as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

A calibration curve is generated using the ONLINE DAT LSD Calibrator. This curve is retained in memory by the COBAS INTEGRA 400 plus analyzer and recalled for later use.

Traceability: This method has been standardized against a primary reference method (LC/MS/MS).

Note

The calibrator should be assayed within 2 hours after placing on-board the instrument. Under Configuration Calibrator Definition, the STD1 value is 0.000 ABS.

Quality control

Quality control	ONLINE DAT LSD Calibration/Control Pack LSD Positive Control (LSDPC, system-ID 07 6534 1) LSD Negative Control (LSDNC, system-ID 07 6533 3)
Control sequence	User defined
Control after calibration	Recommended

For quality control, use control materials as listed in the “Order information” section. In addition, other suitable control material can be used.

Drug concentrations of the controls have been verified by LC/MS/MS or GC/MS.

The control intervals and limits should be adapted to each laboratory’s individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Note

Controls should be assayed within 2 hours of being placed on-board the instrument. The ONLINE DAT LSD Calibration/Control Pack is supplied as a matched set and must not be interchanged with vials from different kit lots. If control limits are utilized, they must be updated after each calibration. Update the Upper Range of the LSDPC and the Lower Range of the LSDNC to the absorbance value of the LSD CAL. Alternatively, the controls may be run as patients. The controls should recover negative or positive, as appropriate, and the results recorded.

Results

COBAS INTEGRA analyzers report results with the following test flags:

Flag	COBAS INTEGRA	Value range
No flag	Negative	< 0.5 ng/mL
Positive	Positive	≥ 0.5 ng/mL

Results are reported in absorbance values relative to the 0.5 ng/mL cutoff calibrator.

Limitations - interference

See the "Specific performance data" section of this document for information on substances tested with this assay. There is the possibility that other substances and/or factors may interfere with the test and cause erroneous results (e.g., technical or procedural errors).

A preliminary positive result with this assay indicates the presence of LSD and/or its metabolites in urine. It does not measure the level of intoxication.

For diagnostic purposes, the results should always be assessed in conjunction with the patient’s medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.
Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Specific performance data

Representative performance data on the COBAS INTEGRA analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined in an internal protocol by using a series of LSD controls in replicates of 20, once a day, for 5 days. The following results were obtained on a COBAS INTEGRA 700 analyzer.

Repeatability	Mean O.D.	SD	CV %
Level 1	0.950	0.02	1.8
Level 2	0.900	0.03	3.0
Level 3	0.830	0.01	1.7

Intermediate precision	Mean O.D.	SD	CV %
Level 1	0.970	0.02	1.7
Level 2	0.900	0.02	2.2
Level 3	0.830	0.01	1.4

Lower detection limit of the test

0.134 ng/mL

The lower detection limit of the COBAS INTEGRA test for LSD was determined by performing 50 replicate assays on a 0 ng/mL urine which had been previously determined to be drug free. The absorbance results were used to calculate equivalent ng/mL values as follows. A linear regression line was generated from the absorbance values of the drug free urine, the 0.5 ng/mL LSD cutoff calibrator and the 1 ng/mL LSD positive control. The absorbance values of the drug free urine were then substituted into the equation to determine the equivalent LSD concentration.
The mean of 50 replicates plus 2 standard deviations yields the lower detection limit.

Accuracy

1000 assumed negative urine samples were obtained from a clinical laboratory. These samples were simultaneously evaluated for LSD using a COBAS INTEGRA 700 analyzer and the Abuscreen RIA method for LSD. 998 samples were negative and 2 samples were preliminary positive on the COBAS INTEGRA 700 analyzer. 999 samples were negative and 1 sample was preliminary positive (1.03 ng/mL) using the Abuscreen RIA method. The 1 sample that was preliminary positive in both assays was found to contain LSD by GC/MS (GC/MS value = 0.133 ng/mL).

39 urine samples, obtained from clinical laboratories where they screened preliminary positive by Abuscreen RIA and were confirmed positive for LSD by GC/MS, were also evaluated on a COBAS INTEGRA 700 analyzer. All 39 samples were positive with the COBAS INTEGRA LSD assay relative to the 0.5 ng/mL cutoff.

		RIA	
		+	–
COBAS INTEGRA 700 analyzer	+	1	1
	–	0	998

		GC/MS	
		+	–
COBAS INTEGRA 700 analyzer	+	39	0
	–	0	0

Analytical specificity

The specificity of the COBAS INTEGRA LSD assay was determined by generating inhibition curves for each of the compounds listed and determining the approximate quantity of each compound that is equivalent in assay reactivity to the 0.5 ng/mL LSD assay cutoff.

Compound	Approximate ng/mL equivalent to 0.5 ng/mL of LSD	Approximate percent cross-reactivity
Nor-LSD (N-desmethyl-LSD)	1.8	28
2-Oxo-3-hydroxy-LSD	4.4	11
Iso-LSD	11	4.5
Lysergic Acid N-(methyl-propyl) amide	16	3.1
Methysergide Maleate	3191	0.016
Ergonovine Maleate	12500	0.004
Lysergic Acid N-(hydroxy-ethyl) amide	15957	0.003
2-Bromo-α-ergocryptine	29070	0.0017
Ergotamine Tartrate	32468	0.0015
α-Lysergic acid	86207	0.0006
α-Tryptophan	116822	0.0004
Serotonin	211864	0.0002
α-Ergocryptine	750000	0.00006

Drug interference

The following compounds were added to aliquots of pooled normal human urine at a concentration of ≥ 50000 ng/mL. None of these compounds gave a positive response.

Acetaminophen
Acetylsalicylic acid
Aminopyrine
Amitriptyline
Amobarbital
d-Amphetamine
d,l-Amphetamine
l-Amphetamine
Ampicillin
Ascorbic acid
Aspartame
Atropine
Benzocaine
Benzoylecgonine (cocaine metabolite)
Benzphetamine
Butabarbital
Caffeine
Calcium hypochlorite
Chlordiazepoxide
Chloroquine
Chlorpheniramine
Chlorpromazine
Cocaine
Codeine
Dextromethorphan
Dextropropoxyphene
Diazepam
Diphenhydramine
Diphenylhydantoin
Dopamine
Doxylamine
Ecgonine
Ecgonine methyl ester
Ephedrine
d-Ephedrine
l-Ephedrine
Epinephrine
Erythromycin
Estriol
Fenoprofen
Furosemide
Gentisic acid
Glutethimide
Guaiacol glycerol ether
Hydrochlorothiazide
p-Hydroxyamphetamine
Ibuprofen
Imipramine
Isoproterenol
Ketamine
Lidocaine
MDA
MDMA
Melanin
Meperidine
Methadone
d-Methamphetamine
l-Methamphetamine
Methaqualone
Methylphenidate
Methyprylon
Morphine
Naloxone
Naltrexone
Naproxen
Niacinamide
Nordiazepam
Norethindrone
l-Norpseudoephedrine
Oxazepam
Penicillin G
Pentobarbital
Phencyclidine
β-Phenethylamine
Phenobarbital
Phenothiazine
Phenylbutazone
Phenylpropanolamine
d-Phenylpropanolamine
d,l-Phenylpropanolamine
Procaine
Promethazine
d-Pseudoephedrine
l-Pseudoephedrine
Quinidine
Quinine
Secobarbital
Sulindac
Tetracycline
Δ^9THC-9-carboxylic acid
Tetrahydrozoline
Trifluoperazine
Tyramine
Verapamil

Any modification of the instrument as set forth in this labeling requires validation by the laboratory.

References

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11 Mandatory Guidelines for Federal Workplace Drug Testing Programs. Fed Regist 2008 Nov 25;73:71858-71907.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see dialog.roche.com for definition of symbols used):

CONTENT	Contents of kit
→	Volume after reconstitution or mixing
GTIN	Global Trade Item Number

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