CEDIA™ LSD Assay

thermo scientific

IVD **For In Vitro Diagnostic Use**

Rx Only

REF 1732137 (15 mL Kit)

Intended Use

The CEDIA™ LSD Assay is an in vitro diagnostic medical device intended for qualitative and semiquantitative assay of lysergic acid diethylamide (LSD) in human urine.

The assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used to obtain a confirmed analytical result Gas chromatography/ mass spectrometry (GC/MS) is the preferred confirmatory method.[1] Clinical consideration and professional judgement should be applied to any drug of abuse test result particularly when preliminary positive results are used.

Summary and Explanation of the Test

Lysergic acid diethylamide (LSD) is a synthetic derivative of the alkaloid lysergic acid, a compound obtained from ergot, a natural product of the fungus Claviceps purpurea.[2-5] LSD is one of the most potent hallucinogenic agents known.[2,3]

It has strong CNS-stimulant activity, and it is often difficult to differentiate LSD intoxication from stimulant drug overdose or psychosis.[2,6] Intoxication usually lasts 6-12 hours and is dose dependent.[4,5] Users experience perceptual alterations, including time distortion, visual illusions, and sound magnification and distortion.[2,4,5]

LSD is extensively metabolized in the liver by hydroxylation and conjugation,[3,4,5] resulting in inactive metabolites: N-demethyl-LSD, hydroxy-LSD, 2-oxo-LSD and 2-oxo-3-OH-LSD.[7] Urine has been found to be positive for LSD for 24–120 hours after ingestion of 200–400 µg, depending on the sensitivity of the assay used.[3,4]

The CEDIA LSD Assay uses recombinant DNA technology (US Patent No. 4708929) to produce a unique homogeneous enzyme immunoassay system.[8] This assay is based on the bacterial enzyme β-galactosidase, which has been genetically engineered into two inactive fragments. These fragments spontaneously reassociate to form fully active enzyme that, in the assay format, cleaves a substrate, generating a color change that can be measured spectrophotometrically.

In the assay, drug in the sample competes with drug conjugated to one inactive fragment of β-galactosidase for antibody binding site. If drug is present in the sample, it binds to antibody, leaving the inactive enzyme fragments free to form active enzyme. If drug is not present in the sample, antibody binds to drug conjugated on the inactive fragment, inhibiting the reassociation of inactive β-galactosidase fragments, and no active enzyme will be formed. The amount of active enzyme formed and resultant absorbance change are proportional to the amount of drug present in the sample.

Reagents

1 **Antibody Reagent:** Contains piperazine-N, N-bis [2-ethanesulfonic acid], 0.05 mg/L monoclonal antibodies reactive to LSD, buffer salts, stabilizer, and preservative.
2 **ED Reconsititution Buffer:** Contains piperazine-N, N-bis [2-ethanesulfonic acid], buffer salts, and preservative.
2a **ED Reagent:** Contains 3.3 µg/L Enzyme donor conjugated to LSD derivative, 2.78 g/L chlorophenol red-β-D galactopyranoside, stabilizer, and preservative.
3 **EA Reconstitution Buffer:** Contains piperazine-N, N-bis [2-ethanesulfonic acid], buffer salts, stabilizer, and preservative.
3a **EA Reagent:** Contains 0.725 g/L Enzyme acceptor, buffer salts, detergent, bulking agent, and preservative.

Additional Materials Required (sold seperately):

CEDIA LSD Cutoff Calibrator
CEDIA Negative Calibrator
CEDIA LSD Cutoff Calibrator
CEDIA LSD Intermediate Calibrator
CEDIA LSD High Calibrator
MGC Select DAU Control Set

⚠ Precautions and Warnings

DANGER: Powder reagent contains ≤56% w/w bovine serum albumin (BSA), and ≤2% w/w sodium azide. Liquid reagent contains ≤1.0% bovine serum, ≤0.3% sodium azide and ≤0.1% Drug-specific antibody (Mouse).

H317 - May cause allergic skin reaction.
H334 - May cause allergy or asthma symptoms or breathing difficulties if inhaled.
EUH032 - Contact with acids liberates very toxic gas.

Avoid breathing dust/mist/vapors/spray. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/eye protection/face protection. In case of inadequate ventilation wear respiratory protection. If on skin: Wash with plenty of soap and water. IF INHALED: If breathing is difficult, remove victim to fresh air and keep at rest in a position comfortable for breathing. If skin irritation or rash occurs: Get medical advice/attention. If experiencing respiratory symptoms: Call a POISON CENTER or doctor/physician. Wash contaminated clothing before reuse. Dispose of contents/container to location in accordance with local/regional/national/international regulations.

Reagent Preparation and Storage

For preparation of the solutions for Hitachi analyzers, refer below. For all other analyzers, refer to the analyzer specific application sheet.

Remove the kit from refrigerated storage immediately prior to preparation of the solutions.

Prepare the solutions in the following order to minimize the risk of possible contamination.

R1 Antibody solution: Ready to use, no preparation necessary.

R2 Enzyme donor solution: Connect Bottle 2a (ED Reagent) to Bottle 2 (ED Reconstitution Buffer) using one of the enclosed adapters. Mix by gentle inversion, ensuring that all the lyophilized material from Bottle 2a is transferred into Bottle 2. Avoid the formation of foam. Detach Bottle 2a and adapter from Bottle 2 and discard. Cap Bottle 2 and let stand approximately 5 minutes at room temperature (15-25°C). Mix again. Record the reconstitution date on the bottle label.

R3 Enzyme acceptor solution: Connect Bottle 3a (EA Reagent) to Bottle 3 (EA Reconstitution Buffer) using one of the enclosed adapters. Mix by gentle inversion, ensuring that all the lyophilized material from bottle 3a is transferred into Bottle 3. Avoid the formation of foam. Detach Bottle 3a and adapter from Bottle 3 and discard. Cap Bottle 3 and let stand approximately 5 minutes at room temperature (15-25°C). Mix again. Record the reconstitution date on the bottle label.

NOTE 1: The components supplied in this kit are intended for use as an integral unit. Do not mix components from different lots.
NOTE 2: Avoid cross-contamination of reagents by matching reagent stoppers to the proper reagent bottle. The R2 Solution should be yellow-orange in color. A dark red or purple-red color indicates that the reagent has been contaminated and must be discarded.
NOTE 3: The R1, R2 and R3 Solutions must be at the reagent compartment storage temperature of the analyzer before performing the assay. Solutions warmed to room temperature (15-25°C) must be cooled to the reagent compartment temperature prior to use.
NOTE 4: To ensure reconstituted EA reagent stability, protect from prolonged continuous exposure to light.

Store reagents at 2-8°C. **DO NOT FREEZE.** For stability of the unopened components, refer to the box or bottle labels for the expiration date.

R1 Solution: 90 days refrigerated on analyzer or at 2-8°C.
R2 Solution: 90 days refrigerated on analyzer or at 2-8°C.
R3 Solution: 90 days refrigerated on analyzer or at 2-8°C.

Specimen Collection and Handling

Collect urine specimens in plastic or glass containers.

Specimens may be kept at room temperature for up to 4 weeks.[9] For longer storage prior to analysis or for sample retention after analysis, urine specimens may be stored at -20°C.[10]

Laboratories following the SAMHSA mandatory guidelines should refer to SAMHSA "Short-Term Refrigerated Storage" and "Long-Term Storage" requirements.[11]

To protect the integrity of the sample, do not induce foaming and avoid repeated freezing and thawing. An effort should be made to keep pipetted samples free of gross debris. It is recommended that grossly turbid specimens be centrifuged before analysis. Frozen samples should be thawed and mixed prior to analysis. Adulteration of the urine sample may cause erroneous results. If adulteration is suspected, obtain another sample and forward both specimens to the laboratory for testing.

Handle all urine specimens as if they were potentially infectious.

Assay Procedure

Chemistry analyzers capable of maintaining a constant temperature, pipetting samples, mixing reagents, measuring enzymatic rates and timing the reaction accurately can be used to perform this assay. Application sheets with specific instrument parameters are available from Microgenics, part of Thermo Fisher Scientific.

Quality Control and Calibration[12]

Qualitative analysis

For qualitative analysis of samples, use the CEDIA LSD Cutoff Calibrator to analyze results. See the analyzer specific application sheet.

Semiquantitative analysis

For semiquantitative analysis of samples, use the Negative Calibrator and the LSD Cutoff, Intermediate and High Calibrators to analyze results. See the analyzer specific application sheet.

Good laboratory practice suggests that controls be tested each day patient samples are tested and each time calibration is performed. It is recommended that two levels of controls be run; one 40% above the cutoff; the other 40% below the cutoff. Base assessment of quality control on the values obtained for the controls, which should fall within specified limits. If any trends or sudden shifts in values are detected, review all operating parameters. Contact Customer Technical Support for further assistance and for recommendations on suitable control material. All quality control requirements should be performed in conformance with local, state and/or federal regulations or accreditation requirements.

Results and Expected Values

Qualitative results

The CEDIA LSD Cutoff Calibrator, containing 0.5 ng/mL d-LSD, is used as a reference in distinguishing between positive and negative samples. Samples producing a response value equal to or greater than the response value of the calibrator are considered positive. Samples producing a response value less than the value of the calibrator are considered negative. Refer to the analyzer specific application sheet for additional information.

When the qualitative procedure is performed, results of the CEDIA LSD Assay distinguish positive (0.5 ng/mL) from negative samples only. The amount of drug detected in a positive sample cannot be estimated.

Semiquantitative results

The CEDIA LSD Cutoff Calibrator, used in conjunction with the CEDIA Negative and the LSD Intermediate and High Calibrators, can be used to estimate relative concentrations of d-LSD.

Care should be taken when reporting concentration results since there are many other factors that may influence a urine test result such as fluid intake and other biological factors.

When the semiquantitative procedure is performed, results of the CEDIA LSD Assay yield only approximate cumulative concentrations of the drug being tested.

Limitations

1. A positive test result indicates the presence of d-LSD; it does not indicate or measure intoxication.
2. Other substances and/or factors not listed may interfere with the test and cause false results (e.g., technical or procedural errors).

Specific Performance Characteristics

Typical performance results obtained on the Hitachi 911 analyzer are shown below.[13] The results obtained in your laboratory may differ from these data.

Precision

Measured precision studies, using packaged reagents and calibrators, yielded the following results in mA/min with a Hitachi 911 using NCCLS modified replication experiment.

	Within-run Precision			Total Precision		
ng/mL	0.3	0.5	0.7	0.3	0.5	0.7
n	120	120	120	120	120	120
$\bar{x}$ (mA/min)	172	188	202	172	188	202
SD (mA/min)	2.25	2.38	2.91	7.31	7.43	8.30
CV%	1.3	1.3	1.5	4.3	4.0	4.1

Accuracy

Three hundred thirteen urine samples were assayed with the CEDIA LSD Assay on the Hitachi 911 analyzer using a commercially available radioimmunoassay method as a reference. Results were as follows:

		CEDIA +	CEDIA -
RIA	+	81	8*
	-	3†	221

* Samples were tested by GC/MS. The results ranged from 0.06-0.70 ng/mL LSD.
† Samples were tested by GC/MS. The results ranged from 0.05-0.11 ng/mL LSD.

Specificity

The following parent compounds and metabolites when tested with the CEDIA LSD assay yielded the following percent cross-reactivity results:

Compound	Concentration Tested (ng/mL)	% Cross Reactivity
d-LSD	0.5	100.00
Alpha ergocryptine	500,000	0.0
Dihydroergotamine	125,000	0.0
Ecgonine	100,000	0.0
Ecgonine methyl ester	100,000	0.0
Ergonovine	10,000	0.0
Ergotamine	100,000	0.0
Iso-LSD	2,500	0.0
Lysergic acid	100,000	0.0
Lysergol	5,000	0.0
Methysergide maleate	50,000	0.0
Psilocybin	10,000	0.0
Psilocyn	10,000	0.0
Serotonin	1,000,000	0.0
Tryptophan	100,000	0.0

Structurally unrelated compounds were tested with the CEDIA LSD assay and gave a negative response when tested at the concentrations listed below.

Compound	ng/mL	Compound	ng/mL
Acetaminophen	500,000	Ibuprofen	500,000
Acetylsalicylic acid	500,000	Levothyroxine (T4)	50,000
Amoxicillin	100,000	Methamphetamine	200,000
Amphetamine	500,000	Morphine	100,000
Benzoylecgonine	500,000	Nifedipine	500,000
Captopril	500,000	Phencyclidine	500,000
Chlordiazepoxide	100,000	Phenobarbital	500,000
Cimetidine	500,000	Ranitidine	500,000
Codeine	500,000	Salicyluric acid	500,000
Diazepam	500,000	Secobarbital	500,000
Digoxin	100,000	Tolmetin	500,000
Enalapril	500,000	11-nor-Δ^9-THC-COOH	10,000
Fentanyl	40	Verapamil	500,000
Fluoxetine	400,000		

No interference was observed from the following substances added to the normal endogenous concentrations found in urine when tested using the CEDIA LSD Assay:

Substance	Concentration	Substance	Concentration
Acetone	≤ 1.0 g/dL	Hemoglobin	≤ 0.3 g/dL
Ascorbic acid	≤ 1.5 g/dL	Human serum albumin	≤ 0.5 g/dL
Creatinine	≤ 0.5 g/dL	Oxalic acid	≤ 0.1 g/dL
Ethanol	≤ 1.0 g/dL	Riboflavin	≤ 7.5 mg/dL
Galactose	≤ 10 mg/dL	Sodium chloride	≤ 6.0 g/dL
γ-globulin	≤ 0.5 g/dL	Urea	≤ 6.0 g/dL
Glucose	≤ 1.5 g/dL		

Ambroxol, a European expectorant, has a cross-reactivity level of 0.02% which may cause false positives with this assay.

Sensitivity
For the Qualitative application, the limit of detection (LOD) was 0.07 ng/mL. For the Semiquantitative application, the limit of quantitation (LOQ) was 0.11 ng/mL.

References

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11. *Notice of Mandatory Guidelines for Federal Workplace Drug Testing Program: Final Guidelines; Federal Register,* Substance Abuse and Mental Health Administration (SAMHSA), (1994) 110 (June 9):11983.
12. Data on traceability are on file at Microgenics Corporation, part of Thermo Fisher Scientific.
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Glossary:
http://www.thermofisher.com/symbols-glossary

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