



Lithium Enzymatic

REF C4930230D

CE

IVD For in vitro medical device

Use

Kit for measurement of lithium in serum. Enzymatic method.

Summary

Measurements of Lithium are carried out essentially to ensure that proper drug dosage is administered in the treatment of patient suffering from bipolar disorder and to avoid toxicity. For decades, lithium carbonate has remained one of the most effective agents for treatment of patients suffering from bipolar disorder (manic depressive psychosis). Lithium acts by altering intraneuronal metabolism of catecholamines, inhibition of noradrenaline sensitive adenylate cyclase. and reduction in synaptic transmission and increase in neuronal excitability with modification of central nervous system (CNS) amine levels. Recently, studies have also shown that lithium holds promise against Alzheimer's disease. However lithium has many side effects. Over dosage of lithium can cause acute Li+ intoxication, which occurs quite often due to its narrow therapeutic index. For example, serum Li+ levels over 1.5mM (12 hours after a dose) usually indicates a significant risk of intoxication. Therefore the timely and accurate monitoring of serum levels of lithium after a therapeutic dosage is critical.

Principle

Lithium is determined spectrophotometrically through a kinetic coupled enzyme assay system involving Gesani's proprietary phosphatase whose activity is sensitive to lithium (IC50=0.1 mM). Through enzymatic coupling, the phosphatase substrate, adenosine biphosphate (PAP) is converted to hypoxanthine by a series of enzymatic reactions to generate uric acid and hydrogen peroxide (H2O2). H2O2 generated reacts with N-Ethyl-N-(2-hydroxy-3-sulfo-propyl)-3-m-toluidine (EHSPT) and 4-aminoantipyrine (4-AA) in the presence of peroxidase (POD) to form a quinone dye which has maximal absorbance at 556nm. The rate of the quinone dye formation is inversely proportional to the concentration of lithium in serum samples.

Reagents

Reagent 1:Liquid Reagent

Enzymes/substrates liquid containing Good's buffer, phosphatase substrate, 4-AA, enzymes and stabilizers

Reagent 2:Liquid Reagent

Enzymes/substrate liquid containing Good's buffer, enzymes, EHSPT, MgCl2, and stabilizers

Lithium Three point Calibrators Set:

The calibrator is buffer based material and supplied in liquid ready-to-use form.

- Low Level 3 ml
- Medium Level 3 ml
- High Level 3 ml

Reagent Preparation

Liquid Lithium reagents are ready-to-use.

Precaution in Use

The product is not classified as dangerous (DLg. N. 285 art. 28 l. n. 128/1998). However the reagent should be handled with caution, according to good laboratory practice.

Waste Management

Please refer to the local legal requirements.

Specimen Collection and Preparation

The Assay is formulated for use with non-hemolysed serum. No special handling or pretreatment is needed. It is recommended that a standardized 12-hour post dose serum lithium concentration be used to assess adequate therapy. Serum samples should be collected such that testing may be performed as soon as possible after the specimen collection.

Note: Serum specimens and all materials coming in contact with them, should be handled and disposed as if capable of transmitting infection. Avoid contact with skin by wearing gloves and proper laboratory attire.

Note

- The kit, according to this method, must be used in manual procedures. About automatic use follow specific applications.
- Avoid direct light, contamination and evaporation.
- In case of complaint or quality control request, refer to the lot number on the package or to the lot number on the single vials.

Procedure

Wavelength	λ: 550 nm
Working Temperature	37°C
Optical path	1 cm
Reaction	"fixed time"

Reconstitute R 1 and R2 reagents as described in Reagent preparation section and keep the reconstituted R1 and R2 reagents on ice

	BLANK	STD	SAMPLE
Reagent 1	360 µl	360 µl	360 µl
Distilled Water	10 µl	--	--
Sample	--	--	10 µl
Standard	--	10 µl	--
Mix, then incubate for 5' at 37°C. Add:			
Reagent 2	180 µl	180 µl	180 µl
Mix, then incubate for 3' at 37°C. Measure the absorbance values of first reading after 3' from R2 adding (A1) Read a second time after 2' (A2).			

Calculate $\Delta A = A2 - A1$

Reference Values

A trough concentration for 12 hour post dose is expected to be 1.0-1.2 mM. Levels higher than 1.5 mM. 12 hours after a dose indicates a significant risk of intoxication. Reference values are considered indicative since each laboratory should establish reference ranges for its own patient population. The analytical results should be evaluated with other information coming from patient's clinical history.

ANALYTICAL PERFORMANCES

Linearity

The assay has a linear range from 0.1-3.0 mM

"Intra-Assay" precision (within-Run)

Determined on 20 samples for each control (N-H) (Normal- High). Results:

MEAN (mmol/l)	N = 87.15	H = 125.15
S.D.	N = 2.26	H = 1.93
C.V.%	N = 2.60	H = 1.54

"Inter-Assay" precision (between-Run)

Determined on 20 samples for each control (N-H) (Normal- High). Results:

MEAN (mmol/l)	N = 1.00	H = 2.30
C.V.%	N = 4.7	H = 3.3

Interferences

The assay is not interfered by the following substances at indicated concentrations: Na+ 200mM, NH4+: 0.5 mM, Ca2+ 4.0 mM, Mg 2+ 2.0 mM, ascorbic acid 5.0 mM, 0.25mM Zn2+, 0.25mM Fe3+, 0.25mM Cu2+, 10mM K+, triglyceride 250mg/dl and bilirubin 45mg/dl.

For a comprehensive review of interfering substances, refer to the publication by Young.

Quality controls

It's necessary, each time the kit is used, to perform quality controls and to check that values obtained are within the acceptance range provided in the insert. Each laboratory should establish its own mean and standard deviation and adopt a quality control program to monitor laboratory testing.

Bibliography

- Kaplan, L.A., Pesce, A.J.: "Clinical Chemistry", Mosby Ed. (1996).
- Young D.S., Effects of Drugs on Clinical Laboratory Tests, AACC Press, Washington, DC 5th ed. 2000.
- Schoenfeld R.G., Loewell C.S.: Clinical Chemistry (1964), 10, 533.

Symbols

CE CE Mark (requirement of 98/79 regulation)

IVD in vitro medical device

LOT Batch Code

Use by

Storage temperature limits

Read instruction for use

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Lithium LR

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