LITHIUM

OSRT056 | **2 x 16 mL Reagent** | **R1**
1 x 3 mL Standard

Intended Use
Reagent for the quantitative determination of Lithium concentrations in human serum and plasma on the Beckman Coulter AU® Chemistry analyzers.

Summary[1,2]
Lithium is widely used in the treatment of manic depressive psychosis. Administered as Lithium Carbonate, it is completely absorbed by the gastro-intestinal tract, peak serum levels occur 2 to 4 hours after an oral dose. The half life in serum is 48 to 72 hours and it is cleared through the kidneys (excretion parallels that of sodium). Reduced renal function can prolong clearance time. Lithium acts by enhancing the uptake of neurotransmitters which produces a sedative effect on the central nervous system. Serum Lithium concentrations are carried out essentially to ensure compliance and to avoid toxicity.
Early symptoms of intoxication include apathy, sluggishness, drowsiness, lethargy, speech difficulties, irregular tremors, myoclonic twitchings, muscle weakness and ataxia. Levels higher than 1.5 mmol/L (12 hours after a dose) indicate a significant risk of intoxication.

Methodology[1]
Lithium can be determined by atomic absorption spectrophotometry, flame emission photometry or ion - selective electrode. These methods require specific and often dedicated instrumentation.
The Beckman Coulter Lithium reagent is a spectrophotometric method which can be readily adapted to automated clinical chemistry analyzers. Lithium present in the sample reacts with a substituted porphyrin compound at an alkaline pH, resulting in a change in absorbance which is directly proportional to the concentration of Lithium in the sample.

System Information

For AU400/400e/480, AU600/640/640e/680 and AU2700/5400 Beckman Coulter AU Analyzers.

Reagents
Active ingredients

Lithium Reagent	
Sodium hydroxide	0.5 mol/L
EDTA	50 µmol/L
Substituted Porphyrin	15 µmol/L
preservative	
surfactant	
Lithium Standard	
Lithium chloride	1.00 mmol/L

Precautions:
1. For in vitro diagnostic use. Do not ingest. Harmful if swallowed. Avoid contact with skin and eyes. If spilled, thoroughly wash affected areas with water.
2. Contains sodium azide (0.1% W/V). Sodium azide preservative in diagnostic reagents may react with lead joints in copper drain lines to form explosive compounds. Even though the reagent contains minute quantities of sodium azide, drains should be well flushed with water when discarding the reagent.

Preparation of reagent
Reagent and standard are supplied ready to use.

Stability and storage
1. The unopened reagents and standard are stable until the expiration date when stored at 2 - 8°C
2. Once opened the reagents and standard are stable in the bottles provided until the expiry date stated, provided that they are capped when not in use and stored at 2 - 8°C. When stored on board the reagent is stable for 2 weeks.

Indications of Reagent Deterioration:
- Turbidity;
- Failure to recover control values within the assigned range;
  and/or
- Color of reagent is light purple.

Specimen Collection and Preparation [1,2,3]
It is recommended that a standardized 12-hour post dose serum Lithium concentration be used to assess adequate therapy. Peak concentration is reached 2 to 4 hours after oral dose.

Use only serum or EDTA plasma. Serum or EDTA plasma should be separated from cells if storage of more than 4 hours is anticipated.

For analyzers which do not have automatic dilution, samples, controls and calibrators must be prediluted 1:10 with distilled or deionized water.

Sample Storage and Stability:
Samples are stable for one week at 2 - 8°C or > 1 year at -20°C.[4]

Interfering substances:
1. The reagent is light sensitive and will absorb atmospheric carbon dioxide. It is recommended that the reagent be stored capped and in a dark container when not in use for prolonged periods of time (eg. overnight).
2. Studies to determine the level of interference from other cations normally present in serum were carried out in the presence of a lithium concentration of approximately 1 mmol/L and the following results were obtained:
   No significant interference (<5% deviation from assigned Lithium concentration) from

Sodium:	Up to 200 mmol/L;
Potassium:	Up to 8.00 mmol/L;
Calcium:	Up to 4.00 mmol/L (16 mg/dL);
Magnesium:	Up to 2.00 mmol/L (4.86 mg/dL);
Iron:	Up to 200 µmol/L (1,117 µg/dL);
Zinc:	Up to 250 µmol/L (1,625 µg/dL);
Copper:	Up to 250 µmol/L (1,588 µg/dL);

   was observed with this method.

Lithium

3. Studies to determine the level of interference from Bilirubin, Lipemia and Hemoglobin in the presence of a lithium concentration of approximately 1 mmol/L were carried out and the following results were obtained:

Free Bilirubin:	Interference is less than 10% at 45 mg/dL Free Bilirubin
Conjugated Bilirubin:	Interference of less than 10% at 45 mg/dL Conjugated Bilirubin
Lipemia:	Interference is less than 10% at 2000 mg/dL Triglyceride
Hemoglobin:	Interference is less than 5% at 2 g/L Hemoglobin

Procedure

Materials Provided:
Beckman Coulter Lithium Reagent
Beckman Coulter Lithium Standard

Suggested Analytical Parameters:
Refer to the Methodology Section located in the respective analyzer's Operator's Manual.

Calibration:
The calibration frequency for this procedure is 7 days. Calibration of this lithium procedure is accomplished by use of Beckman Coulter Lithium standard provided in the kit. The lithium standard is traceable to NIST SRM3129.
Recalibration of this procedure is required when a reagent lot number has changed or there is an observed shift in control values, if a critical part of the analyzer is replaced or, if a major preventative maintenance procedure was performed on the analyzer.

Quality Control:
Two levels of chemistry control sera should be analyzed routinely with each group of unknown samples, at least once per day.

Results:
Results in mmol/L will be automatically printed for each sample assayed.

Dynamic Range

The Beckman Coulter lithium procedure is linear from 0.1 mmol/L to 5.0 mmol/L.

Expected Values[1,2]

12 hour post dose trough concentration: 1.0 - 1.2 mmol/L
Minimum effective concentration : 0.6 mmol/L
Values > 1.5 mmol/L 12 hours after dose indicates a significant risk of intoxication.

The quoted values should serve as a guide only. It is recommended that each laboratory verify this range or derives a reference interval for the population it serves[5].

Specific Performance Characteristics

The following data was obtained using the Beckman Coulter AU analyzers according to established procedures. Results obtained in individual laboratories may vary.

Precision:[6]
Estimates of precision, based on CLSI recommendations[7], are less than 3% within run and total precision is less than 5% on the AU Chemistry Analyzers. Assays of control sera products were performed and the data produced following the CLSI guidlines above.

N= 80		WITHIN RUN		TOTAL
Mean (mmol/L)	SD	CV%	SD	CV%
0.57		0.005	0.9	0.011 1.9
1.83		0.012	0.7	0.024 1.3

Method comparison:[6]
The following data below demonstrates representative performance on AU analyzers. A comparison of this Beckman Coulter lithium method (Method 1) vs NOVA ISE (Method 2) was run on an AU2700/AU5400 utilizing 55 patient serum samples. The resulting data is as follows:

Correlation Coefficient:	r = 0.9959
Regression equation:	Method 1 = 1.01X - 0.010
Range of patients:	0.11 - 1.72 mmol/L

Analytical Sensitivity (Lower Detection Limit):
The lowest detection limit (LDL) for this method was determined by assaying 11 replicates of a serum substitute material (SERASUB™) that does not contain Lithium.
The mean and standard deviation were determined and LDL was calculated using the formula:

$$LDL = \overline{x} + (2 \times s)$$

Where: $\overline{x}$ = mean value of replicates
s = standard deviation of replicates (n - 1).

When run as recommended the lowest detection limit is 0.04mmol/L.

References

1. Tietz Fundamentals of Clinical Chemistry, Sixth Edition Saunders Elservier Inc., 2008 pg 555, 556, 868.
2. Amdisen A. "Serum Lithium determinations for Clinical use." Scand Jnl Clin Lab Invest. 1967; 20:104-8.
3. Young DS. "Effects of Preanalytical Variables on Clinical Laboratory Test" 2nd Ed. 1997, pg 3-360.
4. Tietz NW "Blood Gases and Electrolytes in Fundamentals of Clinical Chemistry, Philadelphia W.B. Saunders Co., 1976 pg 899-901.
5. Wachtel M et al, "Creation and Verification of Reference Intervals." Laboratory Medicine 1995; 26:593-7.
6. Data is on file for specific AU analyzers.
7. Clinical and Laboratory Standards Institute. User evaluation of Precision Performance of Clinical Laboratory Devices. CLSI:2004, CLSI Publication EP5-A2.

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