OSRT056 2 x 16 mL Reagent 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
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.

Methodology
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
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.

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.
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


Lithium

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
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.

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
Estimates of precision, based on CLSI recommendations, 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 guidelines above.

<table>
<thead>
<tr>
<th>N</th>
<th>80</th>
<th>WITHIN RUN</th>
<th>TOTAL</th>
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</thead>
<tbody>
<tr>
<td>Mean (mmol/L)</td>
<td>SD</td>
<td>CV%</td>
<td>SD</td>
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<td>0.57</td>
<td>0.005</td>
<td>0.9</td>
<td>0.011</td>
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<tr>
<td>1.63</td>
<td>0.012</td>
<td>0.7</td>
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Method comparison
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:

\[
LDL = \bar{x} + (2 \times s)
\]

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

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

References
6. Data is on file for specific AU analyzers.

Corrosion
Signal Word: Danger
Hazard Statements
Causes severe skin burns and eye damage
Precautionary Statements - Prevention
Do not breathe dust/fume/gas/ mist/vapors/spray
Wash face, hands and any exposed skin thoroughly after handling
Wear protective gloves/protective clothing/eye protection/face protection
Precautionary Statements - Response
Immediately call a POISON CENTER or doctor/physician
Specific treatment (see supplemental first aid instructions on this label)
Eyes
IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
Immediately call a POISON CENTER or doctor/physician
Skin
IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower
Wash contaminated clothing before reuse
Inhalation
IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
Immediately call a POISON CENTER or doctor/physician
Ingestion
IF SWALLOWED: Rinse mouth. DO NOT induce vomiting
Precautionary Statements - Storage
Store locked up
Precautionary Statements - Disposal
Dispose of contents/container to an approved waste disposal plant
Hazards not otherwise classified (HNOC)
Not applicable
Unknown Toxicity
0.004% of the mixture consists of ingredient(s) of unknown toxicity
Other information
No information available

Manufactured in USA for Beckman Coulter, Inc., 250 S. Kraemer Blvd., Brea, CA 92821.