Development and Validation of a Matrix-matched Assay to Measure Iodine in Serum by Inductively Coupled Plasma-Mass Spectrometry

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Abstract

Background: Iodine is an essential element generally monitored in urine for the assessment of proper nutritional status. Although acute toxicity of iodine is rare, exposure to excess iodine can occur in individuals taking iodine containing medications such as amiodarone, in cases of excess supplementation, use of iodinated contrast agents in radiological studies or through adherence to alternative diets rich in seaweed. Traditionally, these patients are monitored by the assessment of thyroid function; however, determination of iodine in serum is important in the differential diagnosis of unexplained thyroid dysfunction.

Methods: Samples were prepared using 100 µL standards, controls, or patient sample and 4.9 mL diluent containing 1% ammonium hydroxide. Rhodium and indium were used as internal standards. Serum was added to all four calibrators (5-1000 µg/L) to achieve a matrix matched method. Diluted samples were analyzed on an Agilent 7700x Inductively Coupled Plasma – Mass Spectrometry (ICP-MS) system with a Cetac ASX-500 autosampler with ASXpress Plus upgrade.

Results: The method was linear from 1-1750 µg/L with intra and inter assay imprecision of 5.1% or less at two different concentrations spanning the linear range. Accuracy was evaluated with 41 patient correlation samples ranging from 41 to 1197 µg/L with an outside reference laboratory. The samples correlated with an r² of 0.999 and a linear regression equation of y = 0.993x + 1.645. Carryover was assessed by sampling subsequent sets of two high samples (1000 µg/L) followed by two low samples (5 µg/L). Percent carryover was determined to be less than 0.093%.

Conclusions: The method described for serum iodine measurements was validated based upon requirements for high complexity testing in CLIA certified clinical laboratories. The method uses matrix-matched calibrators to ensure accuracy and to comply with the College of American Pathologists recommendations and guidelines.

Key Words: Iodine, Serum, Matrix Matched, Inductively Coupled Plasma – Mass Spectrometry, ICP-MS

Iodine Overview & Clinical Utility

- Essential element utilized by the thyroid gland to make thyroid hormones: Triiodothyronine (T3) and Thyroxine (T4)
- Iodine deficiency & toxicity are both possible

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>Excess</th>
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| Acute Toxicity   | 30% of world’s population is deficient
| Autoimmune Thyroiditis | Growth and development abnormalities
| Hypothyroidism & Goiter | Hypothyroidism & Goiter

- Recommended Daily Allowance: ~90 – 150 µg/day dependent on age.
- Pregnant or breastfeeding women need 220-290 µg/day

Sources of Iodine

<table>
<thead>
<tr>
<th>Verified Sources</th>
<th>Natural Sources</th>
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<tbody>
<tr>
<td>Salt, 1 gram</td>
<td>Kelp/Seaweed, ½ ounce (7g) dried</td>
</tr>
<tr>
<td></td>
<td>Certain seafood (Cod), 3 ounces</td>
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<tr>
<td></td>
<td>Milk, 1 cup</td>
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Supplements

- Multivitamin (Potassium Iodide): 150 µg Iodine

Clinical Specimen Types

<table>
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<tr>
<th>Deficiency</th>
<th>Serum/Plasma</th>
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| Monitor individuals on iodine-containing medications | Determine nutritional status

Results

- Sensitivity
  - Limit of Quantitation at 5 µg/L (n=4 for 5 days)
  - CV < 5%
- Accuracy
  - Limit of Blank – Diluent only (n=4 for 5 days)
  - LOQ = 0.97 µg/L
- Sample Stability
  - Stable at -20°C, 4°C, and 25°C for 30 days
- Carryover
  - High L, H2, Low1, L2, H1, H2, L1, L2, H1, H2, L1, L2
  - H = 1000 µg/L
  - L = 5 µg/L
  - Percent Carryover = 100 * [(L1_avg – L2_avg) / H2_avg]
  - Percent Carryover = 0.093%
- Instrument Conditioning

Conclusions

- The method correlated well with an outside reference laboratory and was proven to be stable and robust.
- Iodine in serum is a suitable specimen type for monitoring iodine overload from a variety of sources.

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