

Iodide Assay by Ion Chromatography

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PURPOSE

Potassium iodide (KI) is used to treat overactive thyroid and to protect the thyroid gland from the effects of radiation from inhaled or swallowed radioactive iodine. The effectiveness of KI as a specific blocker of thyroid radioiodine uptake is well-established. When administered in the recommended dose, KI is effective in reducing the risk of thyroid cancer in individuals or populations at risk for inhalation or ingestion of radioiodines. Currently, in the USP Potassium Iodide Monograph, iodide identification is performed by wet chemistry and assay by manual titration. Manual titration has a history of reduced precision and accuracy. As part of USP's global monograph modernization initiative, an alternative selective and sensitive method was developed and validated – ion chromatography (IC). The proposed IC method can also be used for the identification test as an alternative to wet chemistry.

METHOD

The current assay of KI is based on manual titration against potassium iodate under acidic condition using an Amaranth indicator until the red color changes to yellow. This method using a visual indication is difficult to follow, has poor precision and inaccurate results. Ion chromatography, on the other hand, is well-suited for the separation of mono and divalent anions, and organic acids in the presence of complex sample matrices. A Metrosep A Supp 17 100/4.0 mm column with L91 packing was identified as the most suitable for the separation of iodide. Two different methods based on UV detection and conductivity detection after suppression were tested for the iodide assay. Suppressed conductivity detection was found to be precise and accurate and allowed the simultaneous detection of other impurities such as chloride and sulfate. The suppressed conductivity detection-based IC method was fully validated as per USP <1225> validation of compendial methods.

RESULTS

Method validation elements like specificity, linearity, system suitability, solution stability, accuracy and precision, and intermediate precision were investigated for the potassium iodide assay. The validation results met the acceptance criteria and are summarized in Table 1. The data demonstrated that the assay procedure can be used for the identification of iodide in potassium iodide.

Specificity was checked with diluent, resolution solution, standard solution, and sample solution to ensure no interference or co-elution with the iodide peak (Figure 1). The linearity of iodide was investigated over the concentration range from 3.0 mg/L to 22.5 mg/L of iodide covering 20% to 150% of the expected iodide concentration. The correlation coefficient was found to be 0.9999 and the calculated Y-intercept bias was 0.73% of the 100% linearity level response (Figure 2). The potassium iodide sample assay chromatogram is shown in Figure 3. The instrumentation used and the chromatographic conditions are summarized in Figure 4.

DATA

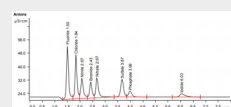


Figure 1: Resolution Solution - Mixed Standard Anion

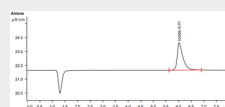


Figure 3: Sample - Sigma Aldrich, Potassium Iodide $\geq 99\%$ Assay, Part# 221944, Lot# MKBX 6865V

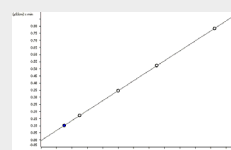


Figure 2: Linearity Iodide from 20% to 150% (3.0 µg/mL – 22.5 µg/mL)

| KF Assay Validation Data Summary | | | |
|--|--|--|--------|
| Iodide Assay in Potassium Iodide Using Suppressed Conductivity | | | |
| Analyst 1 | Metrosep A Supp 17 – 100/4.0, p/n 6.01032.410, S/N 0044.1002 | | |
| Parameters | USP Requirement | Metrohm Procedure | Status |
| Columns (L91) | NA | A Supp 17 100/4.0 (L91)/Supp 17 Guard/4.0 (L91) | ✓ |
| Eluent | NA | 10 mM Na ₂ CO ₃ | ✓ |
| Flow Rate | NA | 1.0 mL/Min | ✓ |
| Detection | NA | Suppressed Conductivity/No CO ₂ Suppression | ✓ |
| Injection Volume | NA | 20 µL | ✓ |
| Run Time | NA | 10 minutes | ✓ |
| Column Temperature | NA | 45°C | ✓ |
| Working Standard Concentration | NA | 15 mg/L Iodine | ✓ |
| Sample Concentration | NA | 15 mg/L Iodine | ✓ |
| Specificity | | | |
| Blank | No interference with iodine peak | No interference with iodine | ✓ |
| Tailing | Iodine tailing is NMT 2.0 for standard | 1.75 | ✓ |
| Interference/Co-elution | Resolution of the nearest peak from iodine is NLT 2.0 for resolution standard | 6.5 between phosphate and iodine | ✓ |
| Critical Pair | Resolution between iodine and adjacent impurity peak should be NLT 1.5 | None | ✓ |
| Suitability | | | |
| 15.0 mg/L Iodine Standard | Six replicate injections RSD in NMT 1.0% | 0.41% | ✓ |
| Solution Stability | | | |
| 15.0 mg/L Iodine Standard & Sample | The change in peak is NMT 1.0% from the initial time point (µS/cm*min) | Maximum 0.58 for standard and 0.77 for sample | ✓ |
| Linearity | | | |
| Linearity solutions ranging from 20%-150% (3/5,10/15/22.5 mg/L) | Correlation coefficient is NLT 0.999 | 0.99999 | ✓ |
| | Y-intercept | 0.003808 | ✓ |
| | Y-intercept bias: $\pm 2.0\%$ of 100% linearity level response | 0.73% | ✓ |
| Repeatability and Accuracy | | | |
| Accuracy/Precision sample solution in triplicate at 80, 100 & 120% levels (12, 15 & 18 mg/L) analyzed against standard | The average assay result should be (1) 100 \pm 2% of the manufacturer's CoA value or (2) 99.0% and NMT 101% of the monograph specification | Average assay result was 100% | ✓ |
| | The RSD of the nine assay results should be NMT 1.0% | RSD of nine assay results was 0.86% | ✓ |
| Intermediate Precision | | | |
| Analyst 2 | Metrosep A Supp 17 – 100/4.0, p/n 6.01032.410, S/N 0082.1017 | | |
| Specificity | | | |
| Blank | No interference with iodine peak | No interference with iodine | ✓ |
| Tailing | Iodine tailing is NMT 2.0 for standard | 1.6 | ✓ |
| Interference/Co-elution | Resolution of the nearest peak from iodine is NLT 2.0 for resolution standard | 6.87 between phosphate and iodine | ✓ |
| Suitability | | | |
| 15.0 mg/L Iodine Standard | Six replicate injections RSD is NMT 0.5% | 0.16% | ✓ |
| Repeatability and Accuracy | | | |
| Accuracy/Precision sample solution in triplicate at 80, 100 & 120% levels (12, 15 & 18 mg/L) analyzed against standard | The average assay result should be (1) 100 \pm 2% of the manufacturer's CoA value or (2) 99.0% and NMT 101% of the monograph specification | Average assay result was 100.1% | ✓ |
| | The RSD of the nine assay results should be NMT 1.0% | RSD of nine assay result was 0.84% | ✓ |
| Sample Assay Test | | | |
| Analyze sample solutions in duplicate using the drug products against standard | The average assay result should be NLT 99.0% and NMT 100.5% of the monograph specifications | Sigma assay result was 98.9%/CoA 99.5% Lab Chem assay result was 100.6%/CoA 99.8% | ✓ |

Table 1: Validation summary

INSTRUMENT

- Metrohm 940 Professional IC Vario
- Detection: Conductivity Detection after Suppression
- Column Temperature: 45° C
- Flow Rate: 1.0 mL/min
- Injection Volume: 20 µL
- Eluent : 10mM Na2CO3
- Column: Metrosep A Supp 17-100/4.0, packing L91



Fig 4. Ion Chromatography Instrument Used for Iodide Assay

CONCLUSION

A single IC procedure for iodide assay and identification in potassium iodide salt was developed and validated. A single chromatographic method for assay and identification simplifies the overall QA/QC workflow. A Metrosep A Supp 17 100/4.0 mm column with L91 packing with optimized chromatographic condition is suitable for fast and reliable identification and quantification of iodide in potassium iodide salt and can be utilized for iodide assay in other OTC formulations such as potassium iodide oral solution and potassium iodide tablets.

Metrohm USA, Inc¹, United States Pharmacopeia²

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