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ADVANCED ANALYTICAL APPROACH FOR THE QUANTIFICATION OF POTASSIUM IODIDE IN HERBAL FORMULATIONS AND PHARMACEUTICAL SAMPLES BY USING INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY (ICP-MS)

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ABSTRACT: This research demonstrates the use of inductively coupled plasma-mass spectrometry (ICP-MS) following microwave digestion in the estimation of the quantity of iodine in pharmaceutical samples and herbal formulations. The samples were dissolved in 4 mL of a 2% Tetra-methyl-ammonium-hydroxide solution, and iodine was used as a reference standard. Collectively, the findings show that the method was linear with calibration curves ranging from 1 ppb to 100 ppb. The recoveries of the examined samples fell between 98 and 115%. The precision of repeatability for iodine concentration ranged from 2.11% to 2.85% for intermediate precision. The present method is robust according to the percentage of RSD of robustness test under various modified conditions. For herbal formulations and pharmaceutical samples, validated methods were proved to be applicable, sensitive, accurate, and reliable.

INTRODUCTION: Iodine is a vital trace element with significant effects on environment research and human health. ICP-MS, or Inductively coupled plasma mass spectrometry has become an extremely effective analytical method for accurately and sensitively determining the amount of Iodine present in a variety of sample matrices like Pharmaceuticals, food, herbal drugs, and nutraceuticals. The protocol involves a preparation of the materials through digestion techniques and incorporation into the ICP-MS equipment. Because of its characteristic low detection limits, large dynamic range, and high sensitivity, ICP-MS is used for the quantitative determination of iodine at trace levels.

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Calibrations of the standards by using standard reference materials ensure accuracy and reliability. ICP-MS measures the trace element Iodine in biological samples such as human tissues or fluids, aiding in research on the function of thyroid hormones (thyroxine (T3) and triiodothyronine (T4)), for instance, which is synthesized from it. The versatility of ICP-MS allows for the analysis of multiple elements simultaneously, thus providing a comprehensive view of the distribution of Iodine and its interaction with other elements in various samples. Moreover, the method introduces another level of detail to the research by the differentiation of various species of Iodine [1-5].

This paper emphasizes the importance of ICP-MS in Iodine quantification and its contribution to human health, environmental monitoring, and industrial applications. The thorough understanding of Iodine dynamics in many systems made possible by ICP-MS analysis aids in the creation of strategies for better Iodine management and its

effects on the environment and public health. For estimation of iodine, many traditional methods are available such as,

Titration Methods: Iodometric method: Involves titrating iodine with a standardized solution for example sodium thiosulphate. This method is widely used but may have limitations in terms of sensitivity and specificity.

Colorimetric Methods:
Starch-Indigo Carmine Method: This method relies on the formation of a blue complex between iodine and starch, with the endpoint detected visually or spectrophotometrically.

Arsenite-Cerium (IV) Method: Arsenite is used to reduce iodine to iodide, and the excess arsenite is titrated with cerium (IV) sulfate. The method is based on the decrease in the cerium (IV) concentration.

Gravimetric Method:
Silver Nitrate Gravimetric Method: Iodide is precipitated as silver iodide, which is then weighed. This method is less commonly used due to challenges in achieving high precision [6].

Advancements in Iodine Estimation:
Inductively Coupled Plasma Mass Spectrometry (ICP-MS): High Sensitivity: ICP-MS allows for the determination of iodine at trace levels with high sensitivity, offering a wide dynamic range for accurate quantification.

Multi-Elemental Analysis: ICP-MS enables simultaneous analysis of multiple elements, providing a comprehensive understanding of iodine interactions in complex matrices.

Ion Chromatography (IC):
Selective Detection: IC coupled with various detectors, such as conductivity or amperometry detectors, allows for selective and sensitive detection of iodine species, including iodide and iodate.

Inductively Coupled Plasma Optical Emission Spectrometry (ICP-OES):
Multi-Element Analysis: Similar to ICP-MS, ICP-OES allows for the simultaneous analysis of multiple elements, providing a holistic view of iodine in various samples.

High-Performance Liquid Chromatography (HPLC):
Species Differentiation: HPLC coupled with UV or fluorescence detection enables the separation and quantification of different iodine species, offering insights into the bioavailability and environmental fate of iodine.

X-ray Fluorescence (XRF):
Non-Destructive Analysis: XRF allows for non-destructive elemental analysis, including iodine, in solid samples, making it useful for a range of applications, such as geological studies.

Molecular Techniques:
Molecular Probes and Sensors: Advances in molecular biology have led to the development of molecular probes and sensors for iodine, allowing for selective and real-time monitoring in biological samples.

These advancements offer increased accuracy, precision, and the ability to analyse complex sample matrices, addressing some limitations of traditional methods. The choice of method depends on the specific requirements of the analysis and the nature of the samples being investigated.

Given that the conventional techniques are not very appropriate for iodine trace level analysis. This experiment performed on a herbal formulation used to treat thyroid mal functions with around 150ppm content of Iodine describes the development and validation of an ICP-MS method for the estimation of potassium iodide at the trace level [7-10].

MATERIALS AND METHODS:

Chemicals and Reagents: Tetra Methyl Ammonium Hydroxide 0.1M (AR Grade)**,** Milli-Q water or equivalent (Grade-HPLC Grade)**,** Iodine Crystals (Grade-AR).

Instruments Details: Electronic balance which can accurately read minimum up to 0.1mg. ICP-MS instrument (Make-Perkin Elmer Model-300x). Microwave digester (Make-Anton Paar, Model-Multiwave Go). Micro pipette with adjustable range from 10-100 µL. Micro pipette with adjustable range from 100-1000 µL.

Glass wares/ Apparatus Details: All the apparatus used are Class A grade.

Operation of Microwave Digestion System and ICP-MS:

ICP-MS Parameters:

No of sweeps/ reading: 75

No of reading/replicate: 1

No of replicates: 3

Scan mode: Peak hopping, Dwell time per amu (ms) 50.

Sr. no.	Element	Mass	Mode	Cell gas	Rpq value
1.	Iodine	126.9	KED	3.5	0.25

Peristaltic Pump Program:

Details	Time (sec)	rpm
Sample flush	60*	-48.0
Read delay	40	-20.0
Wash	60*	-48.0

Microwave Digestion Parameters: Program the instrument as per the appropriate microwave digester system using below program:

Power controlled digestion parameters for Anton Paar 12 Vessels

S. no.	Ramp (mm: ss)	Temperature (°C)	Time (minutes)
1	10:00	80	90
2	10:00	80	30

Procedure:

Preparation of Standards:

Preparation of 2% Tetra Methyl Ammonium Hydroxide Solution using 0.1M Solution: Transfer accurately 20 ml of Tetra Methyl Ammonium Hydroxide in to 1000 ml polypropylene volumetric flask containing about 500 ml of Milli-Q water and make up the volume to 1000 ml with Miili-Q water.

Preparation of 2M Sodium Hydroxide Solution: Dissolve 40 g of Sodium Hydroxide in 500mL of water to get 2M solution.

Preparation of Standard Stock Solution-A (1000 ppm of Iodine Standard): Weigh accurately 50 mg of Iodine crystals into a 50 ml polypropylene tube or volumetric flask and add 0.5ml of 2M NaOH, mix well and make up the volume to 50ml with 2% Tetra Methyl Ammonium Hydroxide.

Preparation of Standard Stock Solution-B (1 ppm of Iodine Standard): Pipette out 0.05ml of Standard stock solution-A into a 50 ml poly propylene tube or volumetric flask and make up the volume to 50ml with 2% Tetra Methyl Ammonium Hydroxide.

Preparation of Standard Stock Solution-C (10 ppm of Iodine Standard): Pipette out 0.5ml of Standard stock solution-A into a 50 ml poly propylene tube or volumetric flask and make up the volume to 50ml with 2% Tetra Methyl Ammonium Hydroxide.

Preparation of Calibration Standards:

Standard Blank: 2% Tetra Methyl Ammonium Hydroxide.

Details	Concentration of Iodine (ppb)	Volume of Standard stock (ml)	Volume made using 2% TMAH (ml)
Standard-1	1	0.05 (B)	
Standard-2	5	0.25 (B)	50
Standard-3	10	0.5 (B)	
Standard-4	25	0.125 (C)	
Standard-5	50	0.25(C)	
Standard-6	75	0.375 (C)	
Standard-7	100	0.5 (C)	

Preparation of Sample:

Washing Cycle: Before each cycle of sample digestion, wash the Teflon vessels with Milli-Q water 2-3 times and carryout one digestion cycle using 4 ml of 2% TMAH with respective microwave digester program. Discard the digested water, wash the above tubes by filling the entire tube with Milli-Q water for 2-3 times and discard.

Preparation of Sample: Weigh accurately 500mg (±10%) of the homogeneous sample into the Teflon vessel of microwave digestion system. Add 4 ml of Tetra Methyl Ammonium Hydroxide (2%) and 6ml Milli-Q water. Swirl gently to complete the wetting. Keep for Pre-Digestion for about 20 minutes. Close and keep the vessel inside the microwave digester system.

Digest the sample with respective microwave digester program mentioned above. After the digestion, allow the vessel to cool to 35°C and open the vessels inside fume hood. Transfer the solution quantitatively into a 50ml poly propylene tube or volumetric flask. Wash the lid and Teflon vessel with Milli-Q water. Transfer washed portions into the same 50ml tube or flask and make up to 50ml with Milli-Q water. Centrifuge the above solution for 5 minutes at 3000 rpm and then take 1 ml of supernatant and make up to 50 ml with 2% Tetra Methyl Ammonium Hydroxide and aspirate this solution in to the ICP-MS system and consider the results for Iodine.

Sample Blank: Prepare the sample blank solution without sample using 4 ml of Tetra Methyl Ammonium Hydroxide (2%) and 6ml Milli-Q water and follow the same procedure as mentioned under sample preparation.

Precautions: Kindly ensure there are no acid traces during entire analysis because this may lead to erroneous results.

Analytical Method Validation Parameters:

System Suitability: To ensure the system efficiency, perform the daily verification of the instrument found satisfactory, the obtained results should be well within the pre-defined limit.

Specificity: The specificity of the developed ICP-MS method for the determination of Iodine was investigated as below.

Non-interference of Placebo: Placebo solution was prepared in the same way as the sample solution and analysed. The placebo was spiked with 20ppb concentration of Iodine and checked for its intensity obtained.

Linearity: The linearity was analysed through the standard curves ranging from 1 ppb to 100 ppb by diluting appropriate amounts of Iodine crystal stock solution (1000 ppm) with diluent. The calibration curves were plotted with the following concentrations (1, 5, 10, 25, 50, 75, and 100 ppb). The linearity was evaluated by linear regression analysis.

Accuracy: Accuracy study of the method was carried out for both sample and placebo solutions. Solutions corresponding to 50, 100 and 150% of the nominal analytical concentration in triplicate were compared with reference standard solution of Iodine. The percent recoveries (mean ± %RSD of three replicates) were calculated.

Precision: Precision of the method was determined by repeatability (intraday precision) and intermediate precision (interday precision) of both standard and sample solutions. Precision was determined in six replicates of both standard and sample solution the results were expressed as %RSD of the measurements.

Robustness: The robustness of the current method was tested by weight variation and the amount of 2%TMAH used. The %RSD of robustness testing under these conditions was calculated in all cases.

RESULTS AND DISCUSSION:

Method Validation:

System Suitability: The results of the instrument parameters as defined under daily performance check are well within the pre-defined limits, indicating the good performance of the system.

Specificity: Spiked placebo and samples showed recovery of 90-110 % which shows there is no interference by other metals and the method is specific to Iodine estimation.

Linearity: The regression equation for Iodine standard was found by plotting intensity (y) versus the concentration (x) studied from 1 ppb to 100 ppb, and the correlation coefficient (R^2=0.999) was highly significant. The method is linear with respective to standard and sample.

TABLE 1: TABLE FOR THE LINEARITY OF THE IODINE CONCENTRATION (PPB) AGAINST OBSERVED INTENSITIES

Concentration (ppb)	CPS
1	935
5	4863
10	10245
25	25547
50	52333

75	80475
100	109660

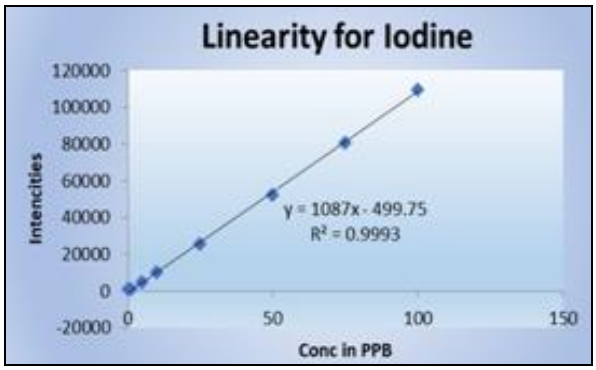

FIG. 1: GRAPHICAL REPRESENTATION FOR THE LINEARITY OF THE IODINE CONCENTRATION (PPB) AGAINST OBSERVED INTENSITIES

Accuracy: The placebo was spiked with respect to 75ppm, 150ppm and 225ppm quantity of Iodine standard solution and the results are expressed as percentage recoveries of the Iodine in the sample (mean ± %RSD) is demonstrated in **Table 2**, indicating good accuracy of the proposed method. The range of the percentage recovery for the 50% spiked sample is 105.81 to 114.46; for the 100% spiked sample, it is 105.32 to 105.44; and for the 150% spiked sample, it is 101.26 to 98.27. These results amply demonstrate the accuracy of the derived approach.

TABLE 2: % RECOVERY OF THE IODINE ANALYSED IN SPIKED SAMPLE AT THREE

Accuracy	Conc. Spiked in ppm	Conc. in PPM	% Recovery
Accuracy 50 % Spiked Sample-1	75	79.360	105.81
Accuracy 50 % Spiked Sample-2	75	82.145	109.53
Accuracy 50 % Spiked Sample-3	75	85.843	114.46
Accuracy 100 % Spiked Sample-1	150	157.981	105.32
Accuracy 100 % Spiked Sample-2	150	159.967	106.64
Accuracy 100 % Spiked Sample-3	150	158.164	105.44
Accuracy 150 % Spiked Sample-1	225	227.824	101.26
Accuracy 150 % Spiked Sample-2	225	223.603	99.38
Accuracy 150 % Spiked Sample-3	225	221.097	98.27

Precision: The values of %RSD for intraday and interday variation are given in **Table 3 & 4**. In both cases, %RSD values were found well within 2% limit, indicating that the current method is repeatable.

TABLE 3: RESULTS FOR THE METHOD PRECISION

Method Precision	Conc. in PPM	%RSD
Method Precision-1	131.500	2.11
Method Precision-2	130.267	
Method Precision-3	137.289	
Method Precision-4	129.708	
Method Precision-5	130.521	
Method Precision-6	131.389	

TABLE 4: RESULTS FOR THE INTERMEDIATE PRECISION

Intermediate precision	Conc. in PPM	%RSD
Intermediate Precision-1	139.368	2.85
Intermediate Precision-2	150.830	
Intermediate Precision-3	145.639	
Intermediate Precision-4	146.769	
Intermediate Precision-5	148.613	
Intermediate Precision-6	150.232	

Robustness: The % of RSD of robustness testing under different altered conditions is given in **Table 5**, indicating that the current method is robust.

TABLE 5: % RSD FOR THE ROBUSTNESS PARAMETER

±1ml of TMAH	Conc. In ppm	%RSD
Robustness 3ml TMAH-Sample-1	162.626	7.95
Robustness 3ml TMAH-Sample-2	160.756	

Robustness 5ml TMAH-Sample-1	167.120	9.22
Robustness 5ml TMAH-Sample-2	169.973	
±10%weight of sample	**Conc. In ppm**	**%RSD**
Robustness 450mg Weight-Sample-1	162.126	7.86
Robustness 450mg Weight-Sample-2	160.216	
Robustness 550mg Weight-Sample-1	165.120	8.55
Robustness 550mg Weight-Sample-2	164.973	

CONCLUSION: The developed inductively coupled plasma mass spectrometry (ICP-MS) method for the Estimation of potassium Iodide is precise, accurate, reproducible, and highly sensitive. The developed method was validated against USP and ICH guidelines [11]. Hence, this method can be used for the routine determination of Iodine in pure and herbal formulations.

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REFERENES:

1. Umesh Kapil: Health Consequences of Iodine Deficiency. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3074887/#b5-squmj-07-267
2. Kulkarni PS, Dhar SD & Kulkarni SD: A rapid assessment method for determination of iodate in table salt samples. J Anal Sci Technol 2013; 4: 21. https://doi.org/10.1186/2093-3371-4-21
3. Michael B Zimmermann and MD Kristien Boelaert: MD. Iodine deficiency and thyroid disorders https://www.thelancet.com/journals/landia/article/PIIS2213-8587(14)70225-6/fulltext?rss%3Dyes=&code=lancet-site
4. Khurana I: Textbook of Medical Physiology. India: Reed Elsevier 2006.
5. Pal GK: Textbook of Medical Physiology. India: Ahuja Publishing House 2007.
6. Alexandr Shimolin and Alena Sobina: Purity determination of potassium iodate by high-precision coulometric titration: New measurement procedure implementation. 2017 2nd International Ural Conference on Measurements (UralCon).
7. Elemental Analysis Manual for Food and Related Products
8. http://www.fda.gov/Food/FoodScienceResearch/LaboratoryMethods/ucm2006954.htm
9. Kaare Julshamn, Lisbeth Dahl and Karen Eckhoff: Determination of iodine in seafood by inductively coupled plasma/mass spectrometry. Journal of AOAC International 2001; 84(6): 1976–1983, https://doi.org/10.1093/jaoac/84.6.1976
10. Yanxia Zeng and Xiashi Zhu: Rapid determination of iodine content in drinking water by isopropyl sensitization and inductively coupled plasma mass spectrometry (ICP-MS). E3S Web Conf 2021; 245: 03004. DOI: https://doi.org/10.1051/e3sconf/202124503004
11. Geraldine Landon: Validation and comparison of two calibration methods for the measurement of stable iodine in the urinary matrix by ICP-MS: standard addition vs. External Calibration. American Journal of Analytical Chemistry 2017; 8(4): 4.
12. ICH Guidelines Q2 (R1). Validation of Analytical Procedures: Text and Methodology Q2(R1).

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