Macedonian pharmaceutical bulletin, 68 (Suppl 1) 47-48 (2022)
Online ISSN 1857 - 8969
*DOI:*10.33320/maced.pharm.bull.2022.68.03.019
Short communication

Optimization for method for elemental impurities in ultra-pure waters

Cvetanka Janakieva Bashevska*, Darko Bachvarovski, Bisera J. Trajkovska, Andrea Alagjozovska, Tatjana Bogovska, Hristina Babunovska

[1] *ALKALOID AD-Skopje, Pharmaceutical, Chemical and Cosmetics Company*
Aleksandar Makedonski 12, 1000 Skopje, North Macedonia

Introduction

Heavy metals are widespread pollutants of great environmental concern as they are no degradable, toxic and persistent. Heavy metals and some trace elements are biologically toxic and can affect and threaten the health of human being.

The elements included in ICH guideline Q3D (R2) on elemental impurities are placed into three classes based on their toxicity (PDE) and likelihood of occurrence in the drug product. The classification scheme is intended to focus the risk assessment on those elements that are the most toxic. The elemental impurity classes are:

Class 1: As, Cd, Hg, and Pb;

Class 2: (*Class 2A)*: Co, Ni and V;

(*Class 2B)*: Ag, Au, Ir, Os, Pd, Pt, Rh, Ru, Se and Tl;

Class 3: Ba, Cr, Cu, Li, Mo, Sb, and Sn.

Other elements: Al, B, Ca, Fe, K, Mg, Mn, Na, W and Zn.

Inductively coupled plasma optical emission spectrometry (ICP-OES) is a technique typically used for the determination of trace metals. The inductively coupled plasma generates excited atoms which emit electromagnetic radiation at characteristic wavelengths for a particular element. These atomic emission lines are sharp and can usually be resolved from other elements. It is a type of emission spectroscopy that uses the inductively coupled plasma to produce excited atoms and ions that emit electromagnetic radiation at wavelengths characteristic of a particular element. The intensity of this emission is in direct correlation with the concentration of the element within the sample.

Water is one of the major commodities used by the pharmaceutical industry. Different grades of water quality are required depending on the different pharmaceutical uses. Control of the quality of water, is a major concern and the pharmaceutical industry devotes considerable resource to the development and maintenance of water purification systems (EMA/CHMP/CVMP/QWP/496873/2018).

This study is aimed at development and optimization of an analytical method for the determination of heavy metals from pharmaceutical water by ICP-OES. ICP-OES is an analytical technique that enables rapid, sensitive multi-elemental determinations. Most trace elements in water are present in low concentrations which approach the detection limit of the instrument.

Materials and methods

In this study several elemental impurities were determined: Class 1(As (188.980 nm), Cd (226.502 nm), Pb (220.353 nm) Hg (184.887 nm)), Class 2A (Co (228.615 nm), V (292.401 nm), Ni (231.604 nm)) and other elements (Al (396.152 nm), Cu (327.395 nm) and Fe (238.204 nm)) at their characteristic wavelengths. Instrument used was Agilent 5100/5110 VDV ICP-OES.

Sequence for analyze included blank, calibration blank, samples (samples of waters from 6 different control points from different systems), 0.01ppm Mercury Standard, 0.01ppm Vanadium standard, 0.01ppm Calibration standard and 0.01ppm Iron standard. All chemicals and reagents used were of analytical reagent grade.

Blank solution: 5% HNO_3.

*cjanakieva@alkaloid.com.mk

Calibration Blank solution: Calibration Blank Solution for ICP-OES (5% HNO_3) is intended for use as a calibration blank solution or zero concentration standard.

Standard preparation: The standard solutions at three concentration levels were prepared from high purity ICP Standards Stock solution.

0.01 ppm calibration solution: In 50 mL volumetric flask add 1 mL of *ICP-OES Wavelength Calibration Solution* (50 mg/L Al, As, Ba, Cd, Co, Cr, Cu, Mn, Mo, Ni, Pb, SE, Sr, Zn and 500 mg/L K in 5% HNO_3) and dilled to the mark with 5% HNO_3. Dilute 1 mL of this solution to 100 mL with 5% HNO_3.

0.01 ppm Vanadium solution: In 10 mL volumetric flask add 1 mL of *Vanadium ICP Standard* (1000 mg/L V in 2-3% HNO_3) and diluted to the mark with 5% HNO_3. Dilute 1 mL of this solution to 100 mL with 5% HNO_3. Dilute 1 mL of this solution to 100 mL with 5% HNO_3.

0.01 ppm Mercury solution: In 10 mL volumetric flask add 1 mL of *Mercury ICP Standard* (1000 mg/L Hg in 10% HNO_3) and diluted to the mark with 5% HNO_3. Dilute 1 mL of this solution to 100 mL with 5% HNO_3. Dilute 1 mL of this solution to 100 mL with 5% HNO_3.

0.01 ppm Iron solution**:** In 10 mL volumetric flask add 1 mL of *Iron ICP Standard* (1000 mg/L Fe in 2-3% HNO_3) and diluted to the mark with 5% HNO_3. Dilute 1 mL of this solution to 100 mL with 5% HNO_3. Dilute 1 mL of this solution to 100 mL with 5% HNO_3.

Sample preparation: The samples did not require any pre-treatment. Test solution was directly injected. Direct measurement of the ultra-pure water samples.

Alkaloid AD have five systems for production ultra-pure water from different manufacturers. All our ultrapure water systems are suitable for the production of ultrapure water. Systems for production ultra-pure water are USF, Gettinge, Werner, Ion pure and WFI.

Water for analysis was taken from 6 control points from different objects. In all objects water may be present as an excipient or used for reconstitution of products, during synthesis, during production of the finished product or as a cleaning agent for rinsing vessels, equipment, primary packaging materials etc.

Method parameters

The performance characteristics of an ICP is a function of a variety of instrumental parameters. Current instrumentation has many parameters that are fixed by the manufacturer. The purpose of this section is to point out the key parameters that were require adjustment. Instrument method was made with following modifications and adjustments in parameters:

Stabilization time(s): 20, RF power (kW): 1.20, Nebulizer flow (L/min): 0.70, Plasma flow (L/min): 12.0, Aux flow (L/min): 1.00-for viewing mode Axial. Compare with modification and adjustments in parameters for Radial viewing mode: Stabilization time(s): 20, RF power (kW): 1.20, Nebulizer flow (L/min): 0.70, Plasma flow (L/min): 15.0, Aux flow (L/min): 1.20.

ICP Spectrometers are available in radial and axial viewing mode configurations, we choose axial view because that was best choose for determination low concentration recommended from manufacture. Also samples were measured with radial view for comparison. Wavelengths for elemental impurities were same for axial and radial viewing mode measurements.

Results and discussion

Control of elemental impurities is one part of the overall control strategy for a drug product that assures that elemental impurities do not exceed the permitted daily exposure (PDE), i.e the maximum acceptable intake of elemental impurity in pharmaceutical products per day.

ICP-OES can help to examine the purity of ultra-pure water (UPW) down to 10 part per billion (µg/L) and lower. This method detect and quantify elemental impurities Class 1: As, Cd, Pb, Hg; Class 2A: Co, V, Ni and other elements Al, Cu, Fe in water at low concentrations. The concentrations found in all the samples were similar like in blank and Standard solution down to 10 part per billion (µg/L) and lower.

Conclusion

ICP-OES is an excellent analytical technique for detecting a large number of elements in water. All measurements were performed on Agilent 5100/5110 VDV ICP-OES. All results from samples were below 0.01ppm compared with standard solution.

References

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