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speedwave XPERT
Pharma & Cosmetic

Application Note XP1
Microwave Digestion of Herbal Medicine

Summary

A sample preparation method to determine trace elements in herbal sleeping medicine is introduced below. Herbal tablets containing dry extract of valerian roots, silicon oxide, titanium oxide, calcium carbonate, magnesium stearate and various other ingredients are digested using speedwave XPERT in DAK-100 vessels. During the digestion, the reaction temperature is controlled via contactless in-situ temperature sensor (DIRC) to ensure efficient digestion.

Introduction

Herbal medicines are required to be effective and safe in terms of their compositions. To ensure their safety, toxic contaminants and elemental impurities must be analysed. United States Pharmacopeial Convention (USP), International Conference on Harmonization (ICH) and World Health Organization (WHO) support quality control and verification for these products [refs, 1,2,3] by publishing ICH-Guideline Q3D ("Elemental Impurities"), USP <232> or <2232> ("Elemental Impurities- Limits"), USP <233> ("Elemental Impurities – Procedures") and quality control methods for these products. They suggested microwave digestion in closed vessels before ICP-OES or ICP-MS analysis to enhance the quantitative recovery of all the regulated analytes (e.g. Cd, Pb, As and Hg). [1,2,3]

Currently, there are strict regulations for pharma corporations in the US market. The compliance with the pharma regulations of Food and Drug Administration (FDA) and Good Manufacturing Practices (GMP) is implemented in our 21 CFR Part 11 software upgrade package and a qualification package including IQ and OQ documentation. For further information, please see our white paper for the 21 CFR Part 11 software upgrade package in our website.[ref, 4]

This application note serves as a guideline to show the ability of speedwave XPERT for safe, efficient and fast microwave digestions of herbal medical tablets. Further validation protocol is not in the scope of this study.

Instrumentation

	Rotor and Vessel Type	Liner Type		
Microwave Digestion	☐ DAP-40X			☐ MiniVessels
	☐ DAP-60X	☐ DAQ-20H		☐ MiniVessels
	☐ DAP-100X	☐ DAQ-22H	☐ DAC-17	☐ MiniVessels
	☑ DAK-100X		☐ MultiTube	☐ MiniVessels
Accessories	☑ speedwave XPERT Pharma Package			

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Procedure

Sample Amount	500 mg
Sample Preparation	The herbal sleeping medicine is purchased from drugstore. The tablets are grinded in a mortar by using a pestle before weighing.
Reagents [2]	6 ml HNO_3 (65%), 2 ml H_2O_2 (35%) and 2 ml HF* (40 %) * for complete digestion
Experiment	Weigh sample into the vessel by using weighing cups. Add the reagent/s. Swirl the mixture carefully or stir with a clean PTFE bar. Keep the vessel in the fume hood 1 hour for pre-reaction. Seal and close the vessels as described in the operation manual. Start the digestion according to the following temperature program. Allow the vessels to cool down to room temperature and open them carefully as described in the operation manual. [1] Transfer the sample into centrifugal tubes and dilute them to a volume of 25 ml before analysis.

Temperature Program [2]	**Step**	**T [°C]**	**p [bar]** [3]	**Ramp [min]**	**Hold [min]**	**Power [%]** [4]
	1	170	60	15	5	60
	2	210	60	10	30	80
	3	50	60	1	10	0

Results

Clear and colorless solutions when HF is used (complete digestion).
Colorless solutions with white precipitates of SiO_2 and TiO_2 when HF is excluded (acid leaching).

Discussion

In this application, the herbal sleeping tablets are digested in oxidizing acid mixture to break down the complex organic matrix. When the matrix is destroyed with the help of concentrated acids at high temperatures, the elements are extracted in the digested solution (acid leaching). Since the tablets contain SiO_2 and TiO_2, using HF provides complete digestion of these constituents. Both of these sample preparation procedures are commonly used for medical tablets and are applicable to recover regulated analyte concentrations. In case of analyzing elemental impurities, such as Ag, Ba, Sb, Fe and Al, addition of 1 ml HCl (37%) is suggested after microwave digestion to enhance the recovery of these analytes.

Digestion procedures with HF are required further treatment to prevent etching of HF intolerant sample introduction system of analysis techniques. If your analysis technique doesn't have HF tolerant systems, please conduct complexation of HF with boric acid (Technical note_TN1).

Although this application is conducted in high pressure DAK-100 vessels (withstand up to 100 bar), the same experimental procedure can be applied in DAP-100 vessels (withstand up to 40 bar) by reducing the sample weight to 250 mg.

To conclude, this work demonstrates the ability of the speedwave XPERT to digest herbal sleeping medicine in DAK-100 vessels for measuring elemental impurities according to ICH-Guideline and USP Chapters. To meet the technical requirements for CFR 21 Part 11 compliance, please use our 21 CFR Part 11 software upgrade package in speedwave XPERT and a qualification package including IQ and OQ documentation.

References

[1]https://www.usp.org/sites/default/files/usp/document/our-work/chemical-medicines/key-issues/c232-usp-39.pdf (accessed Oct, 01, 2020)
[2] https://www.usp.org/dietary-supplements-herbal-medicines (accessed Oct, 01, 2020)
[3] https://www.who.int/medicines/publications/qas_herbalmed/en/
(accessed Oct, 01, 2020)
[4]https://www.berghof-instruments.com/en/insights/article/compliance-to-fda-21-cfr-part-11-of-speedwave-xpert/

Notes

[1] To avoid foaming and splashing, wait until the vessels have cooled to room temperature (about 20 min). Carefully open the digestion vessel in a fume hood wearing hand, eye and body protection, since a large amount of fumes will be produced during the digestion process.
[2] This application serves only as a guideline and may need to be optimized for your sample.
[3] Pressure is the maximum value given to the program that is limited by the vessel and/or rupture disc specifications.
[4] This application is outlined for 4 samples. Increase or decrease the power by 10% per sample, when using more or less sample. Minimum is 40% independent of the sample number.