

# Application Note XP2

## Microwave Digestion of Cold and Flu Medicine

### Summary

A sample preparation method to determine trace elements in cold and flu medicine (Grippostad C) is introduced below. The samples containing paracetamol, chlorphenamin, ascorbic acid, coffein 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

Pharmaceutical products 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) and International Conference on Harmonization (ICH) support quality control and verification for these products <sup>[ref.1,2]</sup> by publishing ICH-Guideline Q3D ("Elemental Impurities"), USP <232> ("Elemental Impurities- Limits") and USP <233> ("Elemental Impurities – Procedures") 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, Hg...etc). <sup>[ref.1,2]</sup>

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. <sup>[ref. 3]</sup>

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

### Instrumentation

	Rotor and Vessel Type	Liner Type	
Microwave Digestion	<input type="checkbox"/> DAP-40X		<input type="checkbox"/> MiniVessels
	<input type="checkbox"/> DAP-60X	<input type="checkbox"/> DAQ-20H	<input type="checkbox"/> MiniVessels
	<input type="checkbox"/> DAP-100X	<input type="checkbox"/> DAQ-22H	<input type="checkbox"/> MiniVessels
	<input checked="" type="checkbox"/> DAK-100X	<input type="checkbox"/> MultiTube	<input type="checkbox"/> MiniVessels
Accessories	<input checked="" type="checkbox"/> speedwave XPERT Pharma Package		

Procedure						
<b>Sample Amount</b>	500 mg					
<b>Sample Preparation</b>	The cold flu medicine is purchased from pharmacy. The capsule shells of the medicine are opened and powder is taken as a sample for the digestion.					
<b>Reagents <sup>[2]</sup></b>	6 ml HNO <sub>3</sub> (65%), 2 ml H <sub>2</sub> O <sub>2</sub> (35%) and 2 ml HCl (37 %)					
<b>Experiment</b>	<p>Weigh sample into the vessel by using weighing cups. Add the reagent/s.</p> <p>Swirl the mixture carefully or stir with a clean PTFE or glass bar.</p> <p>Keep the vessel in the fume hood at least 10 minutes for pre-reaction.</p> <p>Seal and close the vessels as described in the operation manual.</p> <p>Start the digestion according to the following temperature program.</p> <p>Allow the vessels to cool down to room temperature and open them carefully as described in the operation manual. <sup>[1]</sup></p> <p>Transfer the sample into centrifugal tubes and dilute them to a volume of 25 ml before analysis.</p>					
<b>Temperature Program <sup>[2]</sup></b>	<b>Step</b>	<b>T [°C]</b>	<b>p [bar] <sup>[3]</sup></b>	<b>Ramp [min]</b>	<b>Hold [min]</b>	<b>Power [%] <sup>[4]</sup></b>
	1	160	60	10	5	60
	2	190	60	10	5	80
	3	200	60	5	10	80
	4	50	60	1	10	0
<b>Results</b>	Clear and colorless solutions.					
<b>Discussion</b>	<p>In this application, cold flu tablets are digested in oxidizing acid mixture to break down the organic matrix. When the matrix is destroyed with the help of concentrated acids at high temperatures, the elements are extracted in the digested solution. To enhance the recovery and solubility of some analytes, such as Ag, Ba, Sb, Fe and Al, HCl is also used as reagent.</p> <p>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.</p> <p>To conclude, this work demonstrates the ability of the speedwave XPERT to digest cold flu medicine powder 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.</p>					
<b>References</b>	<p>[1] <a href="https://www.usp.org/sites/default/files/usp/document/our-work/chemical-medicines/key-issues/c232-usp-39.pdf">https://www.usp.org/sites/default/files/usp/document/our-work/chemical-medicines/key-issues/c232-usp-39.pdf</a> (accessed Oct, 01, 2020)<sup>2</sup></p> <p>[2] <a href="https://www.ich.org/page/quality-guidelines">https://www.ich.org/page/quality-guidelines</a> (accessed Oct, 02, 2020)</p> <p>[3] <a href="https://www.berghof-instruments.com/en/insights/article/compliance-to-fda-21-cfr-part-11-of-speedwave-xpert/">https://www.berghof-instruments.com/en/insights/article/compliance-to-fda-21-cfr-part-11-of-speedwave-xpert/</a></p>					
<b>Notes</b>	<p>[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.</p> <p>[2] This application serves only as a guideline and may need to be optimized for your sample.</p> <p>[3] Pressure is the maximum value given to the program that is limited by the vessel and/or rupture disc specifications.</p> <p>[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.</p>					