



DIGESTION OF PHARMACEUTICAL SAMPLES

Sample preparation for trace metal analysis of pharmaceutical matrices, using microwave digestion system

Introduction

The new USP chapters <232> and <233> for the measurement of inorganic contaminants in pharmaceutical samples will be implemented on January 1, 2018. While samples that are soluble in aqueous and organic solvents may be analyzed directly, a large proportion of samples will require digestion. In fact, digestion may be preferred for ICP-MS analysis even if the sample is soluble in organic solvent. Closed-vessel digestion is stipulated by USP and it is expected that microwave digestion will be the predominant digestion technique used: its high pressure and temperature capability offer greater digestion power than traditional hot plate digestion techniques.



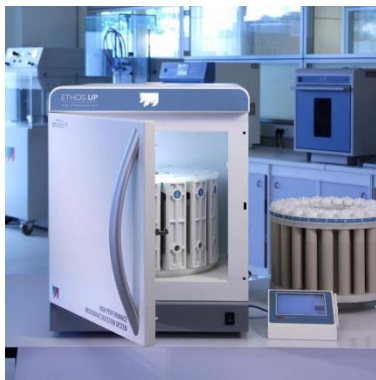
Milestone's Ethos UP microwave digestion system incorporates all the benefits of closed vessel microwave digestion while making sample preparation fast, easy, and effective.

This application report evaluates the digestion quality of **magnesium stearate, capsules, and a dietary supplement** in the measurement of mercury, arsenic, cadmium and lead content.

APPLICATION NOTE



Instrumentation



The ETHOS UP exceeds the requirements of many pharmaceutical labs thanks to its unique benefits, such as:

- High productivity
- Ease of use
- High safety
- High flexibility

Available in multiple configurations, the Milestone Ethos UP is a high-performance, flexible platform used in a wide array of applications and industries.

For trace metals analysis in the pharmaceutical industry, Milestone's SK-15 high pressure rotor is an excellent solution.

SK-15 High Pressure Rotor



The SK-15 high pressor rotor has the ability to digest large amounts of sample and operate at both high temperature and pressure. Digestions are monitored in real-time via direct temperature monitoring. This ensures optimal temperature is achieved and superior digestion accomplished.

APPLICATION NOTE

The SK-15 utilizes Milestone's unique vent-and-reseal technology for controlling and limiting the internal pressure of each vessel, while minimizing the loss of volatiles. These superior temperature and pressure capabilities allow for the digestion of even the most difficult samples.

Analytical Procedure

An Ethos UP with SK-15 high-pressure rotor was used to digest samples with multielement spikes at various concentration levels.

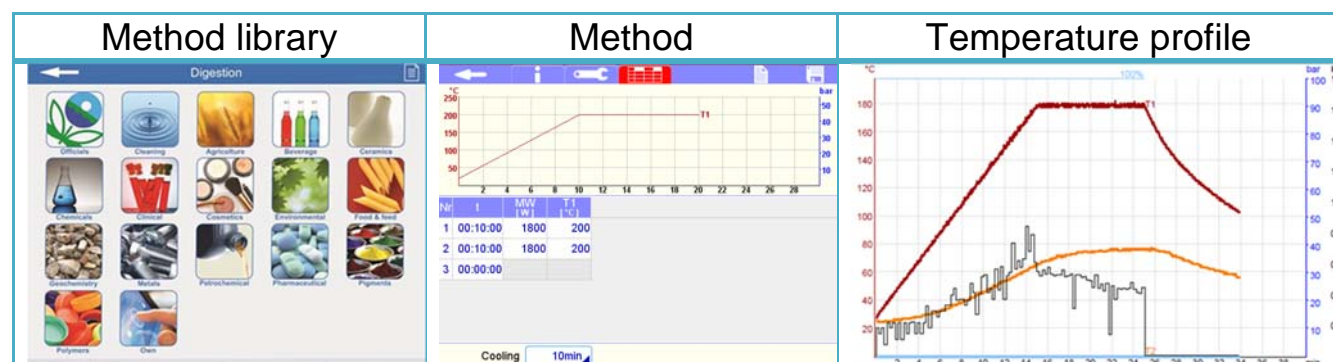
Two aliquots of each sample type were collected and digested in separate vessels. The test conditions are represented in the table below:

Sample Name	Sample weight	Spike Level	Reagents
Magnesium Stearate	1 g	25 ppb 50 ppb	10 mL of HNO ₃ 65%
Capsules	0.7 g	25 ppb 50 ppb	10 mL of HNO ₃ 65%
Dietary supplement	0.9 g	25 ppb 50 ppb	10 mL of HNO ₃ 65%

Samples were digested in three separate batches, one for each sample type.

The Ethos UP is equipped with pre-installed methods, spanning hundreds of applications. The EasyCONTROL software, in combination with direct and contactless temperature/pressure sensors, allows the operator full control and real-time monitoring of the digestion process.

The Ethos UP is provided with Milestone Connect, a unique application which allows the operator to remotely monitor and control the digestion process via PC, tablet or smartphone.



APPLICATION NOTE



ICP-OES Results

All results are expressed in $\mu\text{g}/\text{kg}$

		Sample without Multielement spike		Multielement* spike 25 ppb (**Hg is 50 ppb)		Multielement* spike 50 ppb (**Hg is 100ppb)	
		Average ($\mu\text{g}/\text{kg}$)	Average (%)	Average ($\mu\text{g}/\text{kg}$)	Average (%)	Average ($\mu\text{g}/\text{kg}$)	Average (%)
Mg stearate	As	9.63	-	36.3	107%	52.7	86%
	Hg	<5	-	47.5	95%	91.6	92%
	Pb	<5	-	21.8	87%	46.3	93%
	Cd	<5	-	23.6	94%	47.9	96%
Capsule	As	8.7	-	22.9	91%	52.2	104%
	Hg	0	-	46.0	92%	89.8	90%
	Pb	0	-	25.6	102%	45.6	91%
	Cd	0	-	23.7	95%	46.9	94%
Dietary supplement	As	11.04	-	24.9	100%	53.4	107%
	Hg	0	-	48.5	97%	91.0	91%
	Pb	0	-	23.7	95%	47.3	95%
	Cd	0	-	24.3	90%	47.5	95%

*Merck ICP Multi-element standard solution IV. 23 elements stabilized in Suprapur, HNO_3 6.5%

**Merck mercury ICP standard 10000 mg/L Hg Certipur, HNO_3 10%

The results have been obtained using Agilent ICP-OES (710 series)

Conclusion

Milestone's Ethos UP with SK-15 high-pressure rotor offers a wide array of benefits for trace metals analysis preparation with USP <232> and <233>.

The SK-15's superior temperature and pressure capabilities allow for complete digestion of even the most difficult samples. With vent-and-reseal technology, loss of volatiles is minimized, resulting in excellent recoveries and more accurate ICP analyses. Due to its higher sample capacity, the SK-15 rotor offers up to 90% higher throughput compared to other high-pressure rotors available on the market.

The data shown in this application note demonstrates that higher digestion quality is achieved at higher temperatures, making analysis by ICP-OES more accurate.

