Tech Note

Using Microwave Sample Prep to Determine Trace Metal Levels in Pharmaceutical Matrices

Digestion of Pharmaceutical Samples Using the Milestone Ethos UP

Summary

New USP chapters, <232> and <233>, for the determination of inorganic contaminants in pharmaceutical samples are due to be implemented in 2018. While samples that are soluble in aqueous and organic solvents may be analyzed directly, a large portion of samples will require digestion. In fact, digestion may be preferred for ICP-MS analysis, even if the sample is soluble in an organic solvent. Closed-vessel digestion is prescribed by USP and it is expected that microwave digestion will be the predominant sample preparation technique used. Microwave digestion can achieve high temperatures and pressures and offers many benefits when compared to traditional sample preparation techniques such as hot plate.

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Microwave Digestion of Pharmaceutical Samples

The Milestone Ethos UP microwave digestion system incorporates all of the benefits of closed vessel digestion – speed, data quality, ease-of-use - in a safe and compact bench-top system.

This technical note describes the digestion of magnesium stearate to determine levels of Mercury, Arsenic, Cadmium and Lead - the most toxic elements as outlined in the USP methods.

Magnesium stearate is commonly used in the pharmaceutical production process as a lubricant to prevent ingredients from sticking to manufacturing equipment.

Instrumentation

The ETHOS UP meets many of the requirements of today's pharmaceutical laboratory. It offers several unique benefits including:

- High throughput to increase productivity
- Flexibility to digest a variety of matrices
- Intuitive software
- Industry leading safety

The Ethos UP is constructed using stainless steel, features a built-in camera and can accommodate both high-pressure and high-throughput rotors.

Figure 1. The Milestone Ethos UP

The Ethos UP includes 300 built-in digestion methods, which virtually eliminates method development. Additionally, the UP features Milestone Connect, which enables remote system control, 24/7 technical support and access to a comprehensive library of content developed especially for the analytical lab.

SK-15 High Pressure Rotor

The SK-15 rotor is most suitable for pharmaceutical labs where a wide variety of matrices need to be digested. The rotor's high temperature (300°C) and pressure (100 bar) capabilities ensure a high quality digestion of even the most difficult and reactive samples.

The SK-15 is controlled using a direct temperature sensor that continuously measures the internal temperature during the run. This ensures complete and reproducible digestions. The SK-15 also features Milestone's patented "vent-and-reseal" technology for controlling and limiting, the internal pressure of each vessel.

A large selection of high purity quartz and TFM inserts are available for the SK-15 rotor to accommodate smaller sample amounts or minimize the dilution factor of the analytical solution.

Figure 2. The SK-15 High Pressure Rotor

Table 1. Digestion of Magnesium Stearate with Different Multielement Spike Levels

Vessel	Sample	Wt	Spike	Reagents
1	Magnesium Stearate	1 g	25 ppb	10 mL HNO_3 65%
2	Magnesium Stearate	1 g	50 ppb	10 mL HNO_3 65%
3	Magnesium Stearate	1 g	100 ppb	10 mL HNO_3 65%
4	Magnesium Stearate	1 g	500 ppb	10 mL HNO_3 65%
5	Magnesium Stearate	1 g	1,000 ppb	10 mL HNO_3 65%

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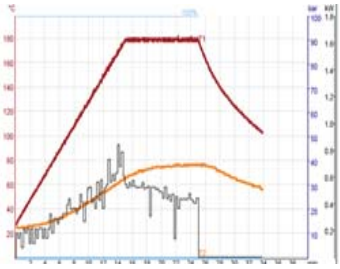
Analytical Procedure

Table 1 shows results of the digestion of magnesium stearate in the SK-15 rotor with different concentration levels of a multielement spike.

ICP-OES Results

Table 1 shows the results of magnesium stearate with 25 µg/Kg, 50 µg/Kg, 100 µg/Kg, 500 µg/Kg, 1000 µg/Kg spikes of multielement standard with Arsenic, Mercury, Cadmium and Lead.

The results were obtained using an Agilent ICP-OES (710 series). All results are expressed in µg/Kg.

Method	Temperature Profile
	

Conclusion

Milestone's Ethos UP is a good solution for laboratories looking to take advantage of the multiple benefits afforded by microwave sample preparation.

Due to its high temperature and pressure capabilities, the SK-15 rotor ensures a complete digestion of the sample matrix. This results in better ICP- MS data as shown by the complete recovery of all elements - including volatiles.

The results shown in this technical note demonstrate that a better digestion quality, achieved at higher temperatures (and pressure), results in higher quality ICP-OES data.

About Milestone

With over 50 patents and more than 18,000 instruments installed in laboratories around the world, Milestone has been widely recognized as the global leader in metals prep technology for the past 26 years. Committed to providing safe, reliable and flexible platforms to enhance your lab's productivity, customers worldwide look to Milestone for their metals digestion, organic extractions, mercury analysis and clean chemistry processing needs.

Table 2. Magnesium Stearate with spikes of multielement standard with As, Hg, Cd & Pb

Element	Initial	Concentration	Recovery	Concentration	Recovery	Concentration	Recovery	Concentration	Recovery	Concentration	Recovery
	0	25	-	50	-	100	-	500	-	1000	-
As	9.63	36.3	107%	52.7	86%	114	104%	560	110%	1097	109%
Hg	<5	23.8	95%	46	92%	95.2	95%	484	97%	972	97%
Cd	<5	23.6	94%	47.9	96%	94.6	95%	473	95%	940	94%
Pb	<5	21.8	87%	46.3	93%	88.3	88%	462	92%	916	92%

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