



DIGESTION OF PHARMACEUTICAL SAMPLES USING ETHOS UP

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

Introduction

New USP chapters <232> and <233> for the measurement of inorganic contaminants in pharmaceutical samples are due to be implemented in early 2015. While samples that are soluble in aqueous and organic solvents may be analyzed directly, a large proportion of samples will require digestion, and 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 offering greater digestion power than hot plate closed vessel digestion for example.



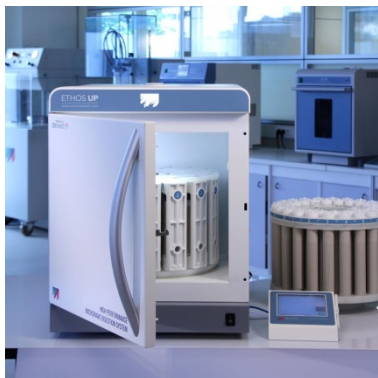
Milestone's Ethos UP, microwave digestion system, incorporates all of the benefits of closed vessel microwave digestion while making sample preparation fast, easy, effective, and the highest quality.

This application report evaluates the digestion quality of **Magnesium stearate, Capsules and dietary supplement** measuring the Mercury, Arsenic, Cadmium and Lead elements (most toxic element mentioned by the USP method) content.

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Instrumentations



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

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

The Milestone Ethos UP is a very flexible and high performing platform used for trace elements and routine analysis in pharmaceutical laboratories. The Ethos UP is available with multiple configurations, and most suitable one for pharmaceutical samples is the SK-15 high pressure.

The SK-15 work with the Milestone “vent-and-reseal” technology for controlling and limiting the internal pressure of each vessels.

SK-15 High Pressure rotor



The SK-15 perfectly matches the pharmaceutical lab needs to determine trace elements, thanks to its capability to digest large sample amount and its high temperature/pressure capabilities.

The 15 positions high pressure rotor is safely controlled via direct temperature sensor that constantly controls the digestion temperature during the run, ensuring perfect digestion of even the most difficult and reactive samples.



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Analytical Procedure

The SK-15 have been used to digest samples using multielement spike in different concentration level. The Sk-15 is a high pressure rotor, so it can be used for digestion of large sample amount.

Two aliquots from each sample type has been collected and digested in two different vessels. Here are the conditions used for the test:

Sample Name	Sample weight	Spike Level	Reagents
Magnesium Stearate	1 g	25 ppb	10 mL of HNO ₃ 65%
Capsules	0,7 g	50 ppb	10 mL of HNO ₃ 65%
Dietary supplement	0,9 g	250 ppb	10 mL of HNO ₃ 65%

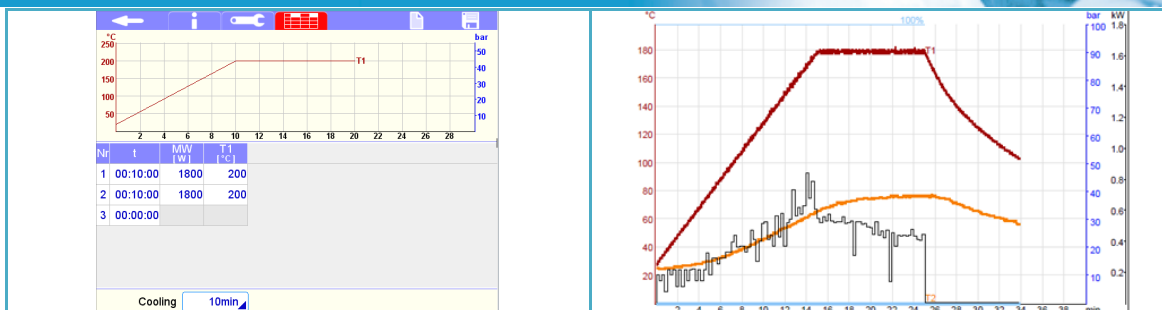
All samples have been digested in three separate batches; one for each sample type.

The Ethos UP is equipped with pre-installed libraries of methods with hundreds of applications. The EasyCONTROL software in combination with the direct and contactless temperature/pressure sensors allows the operator to fully control and monitor all the digestion process. The Ethos UP is provided with the Milestone Connect, the unique application that allows the operator to remotely monitor the digestion process, through any PC, tablets or smartphones.



Method	Temperature profile
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ICP-OES Results

All results are expressed in µg/Kg

		Sample without Multielement spike		Multielement* spike 25 ppb (**Hg is 50 ppb)		Multielement* spike 50 ppb (**Hg is 100ppb)	
		AVG µg/Kg	AVG %	AVG µg/Kg	AVG %	AVG µg/Kg	AVG %
Mg stearate	As	9,63	-	36,3	107%	52,7	86%
	Hg	<5	-	23,8	95%	46	92%
	Pb	<5	-	21,8	87%	46,3	93%
	Cd	<5	-	23,6	94%	47,9	96%
Capsule	As	8,7	-	22,85	91,40%	52,2	104%
	Hg	0	-	35,5	92,20%	78,6	90%
	Pb	0	-	25,55	102,20%	45,55	91%
	Cd	0	-	23,7	94,80%	46,9	94%
Dietary supplement	As	11,04	-	24,97	99,86%	53,42	107%
	Hg	0	-	41,4	97,00%	87,15	91%
	Pb	0	-	23,7	94,80%	47,3	95%
	Cd	0	-	24,25	90,00%	47,55	95%

*Merck ICP Multi-element standard solution IV. 23 elements stabilized in Suprapur, HNO3 6,5%

**Merck mercury ICP standard 10000 mg/L Hg Certipur, HNO3 10%

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

Conclusions

Milestone Ethos UP with SK-15 high-pressure rotor, offers multiple benefits for sample preparation for trace metals analysis with USP <232> and <233>.

Thanks to the elevated temperature and pressure performances, SK-15 rotor allow to get high digestion



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quality, making the analysis by ICP-MS more accurate; while the closed vessels technology guarantee a complete recovery for all elements including the volatiles.

Due to its higher sample capacity, the SK-15 rotor offers from 30 to 90% higher productivity compared to any high pressure rotor available in the market.

The data showed in this technical note demonstrates that the better digestion quality achieved at higher temperatures (and pressure) makes analysis by ICP-OES more accurate.

