

DIGESTION OF PHARMACEUTICAL SAMPLES USING MILESTONE

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.

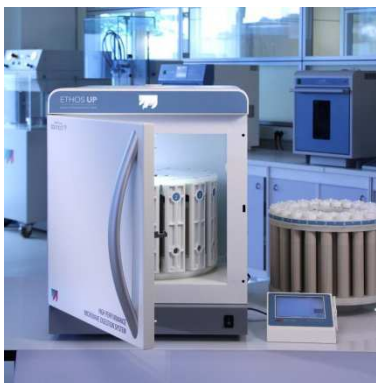
Milestone's Ethos UP, microwave digestion system, incorporates all of the benefits of closed vessel microwave digestion while making sample preparation fast, easy, effective, and the highest quality.

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

This material is a very common material used for tablets production, since it is used as lubricant during the to prevent that ingredients stick to manufacturing equipment.



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.

Analytical Procedure

The SK-15 have been used to digest Magnesium stearate 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.



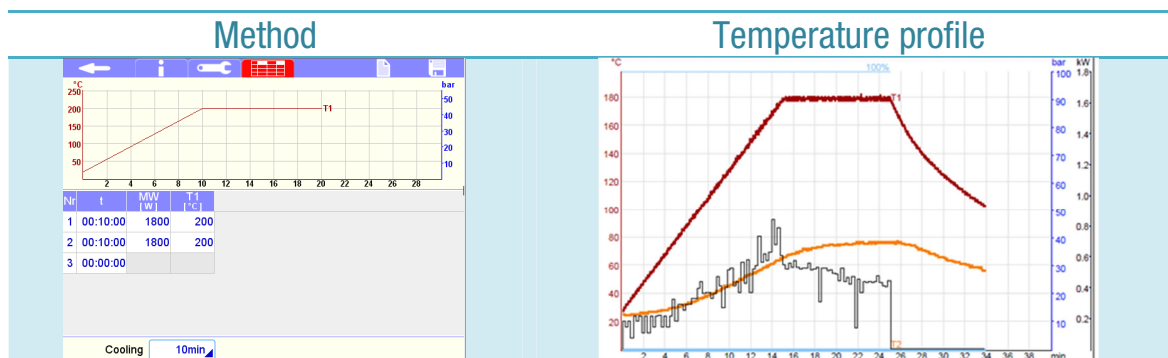
Here are the conditions used for the test:

Vessel number	Sample Name	Sample weight	Spike Level	Reagents
1	Magnesium Stearate	1 g	25 ppb	10 mL of HNO3 65%
2	Magnesium Stearate	1 g	50 ppb	10 mL of HNO3 65%
3	Magnesium Stearate	1 g	100 ppb	10 mL of HNO3 65%
4	Magnesium Stearate	1 g	500 ppb	10 mL of HNO3 65%
5	Magnesium Stearate	1 g	1000 ppb	10 mL of HNO3 65%

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.





ICP-OES Results

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.

All results are expressed in µg/Kg

	Recovery		Recovery		Recovery		Recovery		Recovery		
*Multielement Spike µg/Kg	0	25	50	Rec%	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 HNO₃ 6,5%

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 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.