



SAMPLE PREPARATION OF PHARMACEUTICAL SAMPLES FOR TRACE METAL ANALYSIS

Ensuring high-quality and productivity in elemental analysis of pharmaceutical samples using Milestone ETHOS UP

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.





EXPERIMENTAL

In this technical note, a recovery study on spiked Avicel PH-101, Magnesium stearate, Capsules and Dietary materials have been performed in order to prove the efficacy of EHTOS UP in the sample preparation for metal analysis.

INSTRUMENT

The ETHOS UP meets the requirements of modern analytical labs. It offers several unique benefits including:

- Ultimate Ease of use and Control
- Unrivaled performance and productivity
- Expertise and know-how
- Superior safety and reliability

The ETHOS UP is a flexible and high performing platform used for elemental analysis and routine determinations in many applications. It's construction of stainless steel coated with five PTFE layers and accommodates both high-pressure and high-throughput rotors.



Figure 1 – Milestone's ETHOS UP

easyTEMP

The easyTEMP contactless sensor directly controls the temperature of all samples and solutions, providing accurate temperature feedback to ensure complete digestion in all vessels and high safety. The superior temperature measurement of the easyTEMP allows the processing of mixed batch samples cutting down the labor time and increasing the overall throughput.

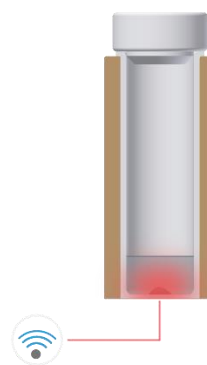


Figure 2 – EasyTEMP, contactless direct temperature sensor.

This technology combines the fast and accurate reading of an in-situ temperature sensor with the flexibility of an infrared sensor. The ETHOS UP software provides digestion history traceability and temperature measurement for every sample; the temperature diagram and profiles are displayed real-time, and then can be saved on the ETHOS UP terminal.

SK-15 HIGH PRESSURE ROTOR

The SK-15 rotor perfectly matches the needs of a modern analytical lab to determine trace elements, thanks to its capability for digesting large sample amounts at high temperature (up to 300 °C) and pressure (up to 100 bar).





Figure 3 – SK15 easyTEMP High Pressure Rotor

The 15-position rotor is controlled by a contactless direct temperature sensor that controls the internal temperature of all vessels throughout all digestion cycle. This ensures complete and reproducible digestions of even the most difficult and reactive samples. The SK-15 also features Milestone's patented "vent-and-reseal" technology for controlling the internal pressure of each vessel.

USER INTERFACE

The ETHOS UP comes with a dedicated touch screen terminal and the easyCONTROL software which incorporates our expertise and know-how in microwave sample preparation. The ETHOS UP user-interface fully control all the digestion parameters, provides complete documentation and expedite the

overall digestion procedure. The terminal is equipped with multiple USB and Ethernet ports for interfacing the instrument to external devices, and to the laboratory network. The ETHOS UP controller is user-friendly, icon-driven, Multilanguage and CFR-21 Part 11 compliant. To find the method which best suits your application simply select Included with the ETHOS UP is a unique web-based application: Milestone Connect. This app allows you to become a part of the Milestone community and gain exclusive access to a robust library of information: lists of parts, technical notes, user manuals, video tutorials, continuously updated application notes and all relevant scientific articles.



Figure 4 – easyCONTROL built-in library

ANALYTICAL PROCEDURE

ETHOS UP – SK 15 easyTEMP

SAMPLE	SAMPLE AMOUNT	ACID MIXTURE
Avicel PH-101 (Cellulose microcrystalline)	0.5 g	4 mL of HNO ₃ 65%, 1 mL of H ₂ O ₂ 30%
Magnesium Stearate	0.5 g	10 mL of HNO ₃ 65%
Capsules	0.7 g	4 mL of HNO ₃ 65%, 1 mL of H ₂ O ₂ 30%
Dietary supplement	0.9 g	4 mL of HNO ₃ 65%, 1 mL of H ₂ O ₂ 30%

Table 1 - Sample amount and acid mixture used for the microwave digestion run.



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STEP	TIME	T2	POWER
1	00:20:00	210 °C	1800 W
2	00:15:00	210 °C	1800 W

Table 2 – SK 15 microwave program used for digestion of samples

- Final dilution: 50 mL with deionized water

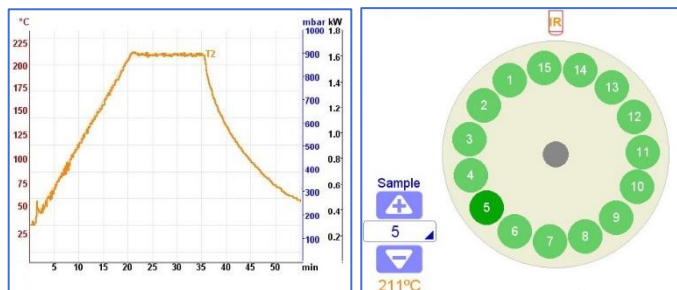


Figure 5 – SK15 Microwave Run Report and Multiple temperature traceability

QUANTIFICATION

ICP-OES Instrumental Parameters: RF power (W): 1300; Plasma flow (L/min): 15.0; Auxiliary Flow (L/min): 1.5; Nebulizer Flow (L/min): 0.75; Replicate read time (s): 10; Instrument stabilization delay (s): 15; Sample Uptake Delay (s): 30; Pump Rate (rpm): 15; Rinse Time (s): 10; Replicates: 3.

RESULTS AND DISCUSSION

The performance of the Milestone's Ethos UP equipped with SK-15 easyTEMP rotor was evaluated

through a recovery study on samples of interest for the pharma industry. All samples were fortified with a spike solution (Elemental Impurities according to ICH Q3D parenteral, Standard 1, ICP standard. Sigma-Aldrich code 89118-100ML) containing As, Cd, Co, Pb, Hg, Ni, Se, Ag, Tl and V (see spike concentration in Table 3). The sample were digested with Milestone's Ethos UP and subsequently analyzed via ICP-OES.

	As	Cd	Co	Pb	Hg ^a	Ni	Se	Ag	Tl	V
Spike value (mg/L)	15	2	5	5	3	20	80	10	8	10
Avicel PH-101										
Recovery % (n=3)	97.3	90.1	92.7	95.6	98.2	101.3	102.4	91.8	89.2	98.9
RSD (%)	0.6	1.8	0.8	2.5	1.3	1.6	0.4	1.7	2.4	2.6
Magnesium Stearate										
Recovery % (n=3)	107.2	94.2	93.6	97.6	95.3	98.4	103.8	97.5	91.4	97.3
RSD (%)	1.0	0.6	1.8	0.4	0.9	1.3	0.8	1.6	2.1	1.6
Capsules										
Recovery % (n=3)	91.1	92.3	95.3	102.3	97.6	93.4	104.3	96.2	92.2	98.3
RSD (%)	1.4	1.4	2.0	1.4	0.3	1.1	2.4	1.5	1.9	0.5
Dietary Supplement										
Recovery % (n=3)	100.2	95.4	94.3	95.2	97.5	96.7	101.6	93.4	92.3	101.2
RSD (%)	0.6	1.6	0.9	1.3	1.5	1.2	2.1	1.9	1.7	1.4

Table 3- Data of the recovery study on spiked samples of interest for Pharma.

^a Analyzed with ICP cold vapor generator module.



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The analytical results are shown in Table 3 with good recoveries of all elements and RSDs below 3%. This demonstrates the robustness and reproducibility of microwave digestion using the Ethos UP equipped with SK-15 easyTEMP technology.

CONCLUSIONS

The data shown in this technical note demonstrates full recovery of the element spiked in the samples. Pharmaceutical samples have been completely digested even in large sample amounts and in a mixed batch samples run. The digestion process has been accurately controlled by the easyTEMP sensor, ensuring same digestion quality and reliable results. In addition to full analyte recovery, microwave digestion using Millstone ETHOS UP provides the highest level of reproducibility, great ease of use and high productivity to be compliant with the new USP requirements.

