



NEW PERFORMANCE FOR HIGH VOLUME PHARMACEUTICAL LABORATORIES

Enabling high throughput in elemental analysis of several pharmaceutical matrices using the Milestone ETHOS UP with MAXI 24 HP

INTRODUCTION

New USP chapters <232> and <233> for the measurement of inorganic contaminants in pharmaceutical samples have been implemented. 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. Microwave digestion achieves high temperatures and pressures and offers many benefits when compared to traditional sample preparation techniques such as hot plate.

Microwave closed vessels is a widely established technology in several industries, as it provides full recovery of all target elements, even volatile elements, with high quality digestion in full safety.

Milestone's ETHOS UP equipped with the MAXI-24 High Performance (HP) rotor incorporates all of the benefits of closed vessel microwave digestion while making sample preparation fast, easy, effective, and of the highest quality.

This innovative solution perfectly integrates with the powerful ETHOS UP, matching both performance and throughput requirements of pharmaceutical elemental analysis.



| EXPERIMENTAL

In this industry report, a recovery study on spiked Avicel PH-101, magnesium stearate, ibuprofen and salicylic acid has been performed to prove the efficacy of the ETHOS UP with MAXI-24 HP for sample preparation and consequent metal analysis.

INSTRUMENT

The ETHOS UP is the most advanced microwave sample preparation equipment, it meets the requirements of modern analytical labs.



Figure 1 – Milestone's ETHOS UP

The ETHOS UP used in this study was equipped with MAXI-24 HP rotor controlled via Milestone's easyTEMP contactless temperature. The superior temperature measurement of easyTEMP allows the processing of different samples of similar reactivity, thus reducing labor time and increasing overall throughput.

MAXI-24 HP ROTOR

The latest Milestone's development is the MAXI-24 HP, which combines performance

and throughput within a single rotor-based platform. It completely innovates the rotor-base solutions providing high throughput without sacrificing the performance. Thanks to its 24 positions, it is the first high pressure and throughput rotor available in the market. The completely new design of its vessels allows to achieve conditions never seen for high throughput rotors. Thicker high purity PTFE-TFM vessels and caps, along with rugged PEEK shields are key ingredients to handle the conditions required to completely digest these samples.



Figure 2 – MAXI-24 HP Rotor

ANALYTICAL PROCEDURE

SAMPLE	SAMPLE AMOUNT	ACID MIXTURE
Avicel PH-101 (Cellulose microcrystalline)	0.5 g	5 mL of HNO ₃ (65%), 1 mL of H ₂ O ₂ (30%)
Magnesium Stearate	0.5 g	5 mL of HNO ₃ (65%), 1 mL of H ₂ O ₂ (30%)
Ibuprofen	0.5 g	5 mL of HNO ₃ (65%), 1 mL of H ₂ O ₂ (30%)
Salicylic acid	0.5 g	5 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.



All samples were weighted into the MAXI-24 HP vessel, approximately 0.5 g (as reported in table 1), then they were fortified with 100 μ L of a multi-elemental standard solution (As/Cd/Pb/Ag/ Co/Cu/Ni/Se/Tl/V). For the spiked final concentrations, please, refer to table 3.

STEP	TIME	T2	POWER
1	00:10:00	160 °C	1800 W
2	00:15:00	210 °C	1800 W
3	00:10:00	210°C	1800 W

Table 2 – MAXI-24 HP microwave program

After microwave digestion, the samples were diluted to 50 mL with DI water and then, analyzed in ICP-OES. Parallel procedure was performed on unspiked samples in order to calculate the recovery rate in relation to the spiked levels.

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 ETHOS UP equipped with MAXI-24 HP 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 samples were digested with Milestone's Ethos UP and subsequently analyzed via ICP-OES.

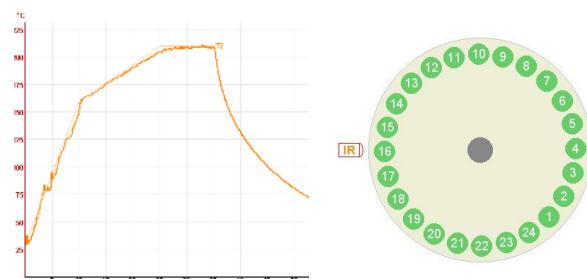


Figure 3 – MAXI-24 HP Microwave Run Report and Multiple temperature traceability

Figure 3 shown the temperature profile of the digestion as well as the multiple temperature visualization and recording for all the samples digested.

INDUSTRY REPORT ETHOS UP – MAXI 24 HP | PHARMACEUTICAL



	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)	103.7	92.5	94.3	93.1	99.6	101.1	110.9	92.5	91.7	103.6
RSD (%)	0.7	1.9	1.2	2.5	1.8	2.6	2.4	1.4	2.1	2.9
Magnesium Stearate										
Recovery % (n=3)	103.5	95.9	92.7	109.8	94.0	99.4	108.7	99.5	91.6	106.0
RSD (%)	1.5	2.1	1.3	1.1	1.8	1.5	2.3	2.4	2.1	1.2
Ibuprofen										
Recovery % (n=3)	113.4	98.7	95.4	105.6	94.7	97.8	107.1	108.4	94.3	102.4
RSD (%)	0.9	1.5	0.8	2.2	2.1	1.7	1.4	1.8	2.1	1.2
Salicylic acid										
Recovery % (n=3)	106.5	93.6	94.1	105.7	97.9	97.1	110.9	96.9	97.0	106.8
RSD (%)	1.2	0.9	1.4	1.7	2.5	2.1	1.4	1.1	1.0	1.6

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

The analytical results were 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 MAXI-24 HP easyTEMP technology.

CONCLUSION

The data shown in this industry report demonstrates full recovery of the elements spiked in the samples. The ETHOS UP with MAXI-24 was successfully applied in digesting samples, such as those from the pharmaceutical industry, even in large sample amounts.

Milestone ETHOS UP and MAXI-24 HP rotor provide the highest level of reproducibility, great ease of use and high productivity in alignment with the new USP

requirements. In addition, the Milestone ETHOS UP with easyTEMP control and easyCONTROL software, provides the highest level of reproducibility and traceability in perfect alignment with GMP regulations.

ABOUT MILESTONE

At Milestone we help chemists by providing the most innovative technology for metals analysis, direct mercury analysis and the application of microwave technology to extraction, ashing and synthesis. Since 1988 Milestone has helped chemists in their work to enhance food, pharmaceutical and consumer product safety, and to improve our world by controlling pollutants in the environment.



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