



An alternative and rapid method for measurement of inorganic contaminants in pharmaceutical samples

| INTRODUCTION

The USP chapter <281> describes the methodology for measurement of inorganic contaminants in pharmaceutical samples, where the adopted technique is the Sulfated Ashing.

This method consists in wetting the samples with few drops (1mL) of concentrated sulphuric acid at 98% prior the ashing step at $600\pm50^{\circ}\text{C}$.

The reason for doing sulphated ash is to prevent volatilization of some important elements to be determined. When phosphorus is absent, barium, calcium, magnesium, sodium and potassium are converted to their sulphates. Tin and zinc are converted to their oxides.

Determination of such elements is important since some minerals are essential to a healthy diet (e.g., calcium, phosphorous, potassium and sodium), whereas others can be toxic (e.g., lead, mercury, cadmium and aluminum).

The conventional method requires to evaporate the H_2SO_4 98% acid using a hotplate or flame under a fume-hood. This operation is very dangerous for the operator since he has to manage very hot crucibles and he could be exposed to the highly toxic sulphuric acid fumes.

These fumes are also very corrosive and can easily damage all instruments and tools placed under the fume hood and the hood itself.



In addition, by the nature of this procedure it leads to poor reproducibility.

Milestone PYRO is an advanced sulphated ashing system, that allows to run this particular application in only one step, thus assuring operators' safety.

This industry report has the intent to show the performances of PYRO microwave sulphate ashing system on two different pharmaceutical samples.

EXPERIMENTAL

INSTRUMENT



Picture 1 - Milestone PYRO Microwave ashing system

The new Milestone PYRO is an advanced microwave muffle furnace, suitable for sulfated ashing application.

It is equipped with a full stainless-steel door and the cavity has a volume in excess of 70 liters, thus allowing the use of a large muffle which in turn enhances the sample throughput.

The PYRO is equipped with two 950 Watt magnetrons for a total of 1900 Watt making it the most powerful microwave muffle furnace system available in the market. The system additionally employs a rotating diffuser that evenly distributes the

microwaves throughout the cavity, assuring a uniform temperature improving the reproducibility.



Picture 2 Milestone PYRO Sulfated Ashing muffle system

PYRO sulfated ashing muffle, enables the analyst to add sulfuric acid to the samples and directly place crucibles into the microwave muffle furnace, without a preliminary charring step. Tedious handling of samples and operator exposure to acid fumes are totally eliminated. Sulfuric acid fumes released from crucibles are continuously exhausted passing through a quartz tube and an air-cooled quartz collection vessel outside the unit.

Fumes are finally contained and neutralized in a dedicated acid scrubber module.

ANALYTICAL PROCEDURE

We have weighed accurately 1 g to 2 g of the substance in four porcelain crucibles (see details in Table 1).

The porcelain crucibles were initially preconditioned at constant weight (other types of crucibles can be used as silica, platinum or quartz).

Samples were then moistened with a small amount (usually 1-2 mL) of sulfuric acid. The samples must be completely wet by sulphuric acid as shown in Picture 3 (second crucible).



Crucible were placed into PYRO microwave ashing unit and ashed with the microwave program described in Table 2.

Duplicates	Sample	Weight (g)	Type of Crucible	H ₂ SO ₄ 98% Volume
1	Nifuroxazide	2.0057	Porcelain	2 mL
2	Nifuroxazide	2.0247	Porcelain	2 mL
3	Nifuroxazide	2.0012	Porcelain	2 mL
1	Ibuprofen	1.0071	Porcelain	1 mL
2	Ibuprofen	1.0290	Porcelain	1 mL
3	Ibuprofen	1.0020	Porcelain	1 mL

Table 1 – Details on type sample amount, crucibles and volume of conc. H₂SO₄ 98% used for the test.

Step	Time	T1	Power	Scrubber
1 (Charring)	00:10:00	250°C	1000 W	On
2 (Charring)	00:10:00	250°C	1000 W	On
3 (Ashing)	00:20:00	600°C	1800 W	Off
4 (Ashing)	00:30:00	600°C	1800 W	Off

Table 2 – PYRO microwave ashing program

RESULTS AND DISCUSSION



Picture 3- Samples during the steps of sulphate ashing run

The samples were completely ashed, obtaining a white residue of inorganic material. Crucibles were weighted and percentage of residue was then recalculated.

Sample	Crucible (g)	Crucible+Residue (g)	Residue %
Nifuroxazide (1)	53.2356	53.2394	0.189
Nifuroxazide (2)	58.6647	58.6685	0.187
Nifuroxazide (3)	53.0127	53.0164	0.185
Ibuprofen (1)	48.0675	48.0685	0.099
Ibuprofen (2)	44.1191	44.1199	0.078
Ibuprofen (3)	46.7442	46.7451	0.090

Table 3- Obtained results, % of residues

CONCLUSION

Milestone PYRO microwave ashing system offers the big advantage to run all samples in only one step ensuring full of operations and great performance.

Due to its muffle capacity and faster heating, the sample processing throughput is higher than conventional electrical muffle system.

The data shown in this technical note demonstrates that the ashing of samples in a PYRO is reproducible thanks to the great temperature homogeneity across all the muffle. The ability to remove and neutralize the H₂SO₄ fumes and reach high temperature in short time make the Pyro a great tool to perform sulfated ashing in compliance with the USP <281>.

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.