

Sulfated Ashing for Pharmaceutical Applications



Introduction

Pharmaceutical corporations are tasked with testing their products extensively, prior to distribution. Testing is performed on raw materials, excipients, and during the quality control process for the finished product. Traditional techniques require significant user interaction and are subject to error. The Phoenix BLACK™ sulfated ashing option provides a safe, automated, and reliable alternative and meets all muffle furnace requirements for most global pharmacopeias, including those for the United States, Britain, Japan, and Europe.

Traditional Methods

Traditional techniques require Bunsen burners, heat lamps, hot plates, and muffle furnaces continuously maintained at high temperature. This equipment poses significant safety risks, as users are directly exposed to hot surfaces and open flames. The risk of experimental error is also high, as weight must be taken, transferred manually, and calculated. Other furnace systems exist, but temperature uniformity, temperature measurement, and exposure to hot surfaces continue to be a concern. The Phoenix BLACK minimizes risk and maximizes lab efficiency by automating the sulfated ash process.

Phoenix BLACK Technology

The Phoenix BLACK is a muffle furnace that meets all microwave and standard muffle furnace requirements listed in ASTM, USP (<281> ROI & <733> LOI), AOAC, FDA, ISO, DIN, ASTM D5630-94, and ASTM D1506-94b. The system is easily programmable, contains a library of preprogrammed methods, and can ash up to 15 samples at a time. The continuous silicon carbide heating element is encased in a quartz fiber furnace, which maintains temperature uniformity throughout the cavity. Because the heating element is in the side of the furnace walls, it will not damage metallic crucibles, which can be used in the Phoenix BLACK. The Phoenix BLACK is compatible with all crucible types, including quartz, platinum, and ceramic.

All temperature measurements are performed using NIST-traceable thermocouples. The exterior of the furnace is cool enough to touch, even when the inside is at temperature. In order to access the interior of the furnace, the furnace door is placed in a holder that prevents the user from being exposed to the hot door surface. An optical sensor monitors the presence of the interior furnace door and will activate safety locks to ensure the cavity door is held open until the furnace door is put back in place. Upon method completion, active ventilation rapidly cools the furnace.

All sulfated ashing steps can be performed in the Phoenix BLACK with the sulfated ashing option, eliminating the need for additional equipment and minimizing operator input. Acid can be added to the sample in the crucible and placed directly into the Phoenix BLACK. A lower temperature sulfating/ashing step with active vapor scrubbing is automatically completed, prior to the high-temperature dry ashing of the organic sample.

The system can be programmed with a pause step to allow the sulfated crucible to be removed and weighed, prior to the dry ashing step. The Phoenix BLACK sulfated ashing option neutralizes toxic acid vapor through a series of scrubbers for a more environmentally sound, laboratory-friendly solution with no emission of hazardous fumes. The system also helps the laboratory comply with ISO 14000 Environmental Management requirements to eliminate greenhouse gases.

The Phoenix BLACK workstation allows quantification for document control and automatically determines the % ROI, % LOI or % Ash. Once generated, sample information cannot be modified, aiding in 21 CFR Part 11 compliance. All weighing and method information is included in the data file, as well as the final result, user-entered sample ID, and a date/time stamp indicating when the sample was ashed. All methods are stored automatically and the system provides the security of a password lock to reduce the possibility of erroneous method modification. Data is easily exported to a LIMS system for even easier data management.

Results

The Phoenix BLACK complies with all requirements included in both USP <733> and <281>. To demonstrate the accuracy and precision of the Phoenix BLACK, several different pharmaceutical compounds were ashed for trace metal analysis. Results are show below in **Table 1**.

Table 1: Trace Metal Analysis Using Phoenix BLACK with Sulfated Ashing Option

Sample	Conventional Muffle Furnace			Phoenix BLACK with Sulfated Ashing Option		
	Temperature (°C)	Time (Min)	ROI (%)	Temperature (°C)	Time (Min)	ROI (%)
Mycostatin	800	60	3.5	800	40	3.09
Amoxicillin Trihydrate (Antibacterial)	800	540	0.1-0.2	800	30	0.12
Nicotinamide (Feed Grade)	800	60	1.10	800	10	1.08
Dextromethorphan	800	60	<0.1	800	30	0.04

The Phoenix BLACK results closely match the results of the conventional muffle furnace. All of the tests were complete in significantly less time than the traditional muffle furnace. It should be noted that the time for the conventional muffle furnace does not include additional operator actions, such as using a hot plate or Bunsen burner, which may require an additional 30 minutes of operator time, prior to insertion of the sample into the muffle furnace. In most laboratories, this step requires constant attention, as the technician cannot leave an open flame. The Phoenix BLACK sulfated ashing option automates the sulfating/ashing step with sulfuric acid, reducing the amount of operator attention and creating a safer laboratory environment.

Conclusion

The Phoenix BLACK meets the requirements of USP <281> and <733>, as well as ASTM, ISO, and other standards. The system provides a simple, automated method of analysis with a high degree of accuracy and minimal operator input. The safety and automated nature of the system make it very operator-friendly and contribute to lab efficiency.

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