

Short communication

Efficiency improvement for sulfated ash determination by usage of a microwave muffle furnace

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Abstract

The usefulness of microwave muffle furnaces for increasing the efficiency of sulfated ash determination through automation was investigated. Substances critical in their behavior were selected as model substances for this purpose: megestrol acetate and a phthalazine derivative as substances with high foaming indices and azelaic acid as a substance with a high spatter index. The selection of an optimal temperature sequence in conjunction with quartz crucibles and/or with a spatter guard made of quartz filter paper made it possible to handle even these critical substances. The analysis results were comparable and reproducible in terms of classical pharmacopeia methodology.

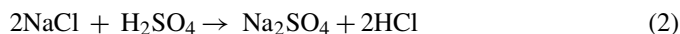
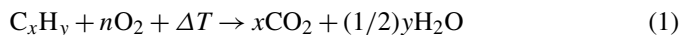
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1. Introduction

Volatile compounds arise when organic compounds are incinerated, while any inorganic compounds present would remain as residues. Sulfated ash determination, a method of analyzing inorganic contaminations, is based upon this process. The procedure is described in the pharmacopoeia as *Residue on Ignition* or *Sulfated Ash* [1,2]. The nonvolatile portions are referred to as sulfated ash, which remains behind when a substance is ignited to which concentrated sulfuric acid has been added.

Unlike the case with simple incineration (Eq. (1)), the volatilization of alkali halogenides (NaCl, KCl, etc.) is avoided when the sulfated ash method is applied because the addition of sulfuric acid transforms these substances into low volatile alkali sulfates (Eq. (2)). Thanks to its oxidative and dehydrating power, the concentrated sulfuric acid makes it easier for organic substances to be broken down during the process.



Depending on the composition, this can lead to inter-element disruptions, e.g. through the formation of phosphates in the

presence of phosphorus, or to decompositions at higher temperatures, such as the transformation of zinc sulfate into zinc oxide, and thus to inconsistent results. More detailed information concerning these types of disruptions can be found by Nadkarni et al. [3].

The method described in the pharmacopoeia is very intensive in terms of time and laboratory capacitance. Concentrated sulfuric acid is added after the substance has been weighed into a corresponding crucible and then carefully heated at low temperatures until the substance becomes carbonized. This carbonization is carried out through the use of a Bunsen burner or by means of parallelization for increasing throughput with the aid of a preincineration bench, which allows the heat to be regulated electrically. Concentrated sulfuric acid should be added once again after carbonization and additional heating should continue to be applied until white sulfur dioxide fumes are no longer generated. After this preincineration, the contents of the crucible is ignited in the furnace at $600 \pm 50^\circ\text{C}$ until the residue has been reduced to ash. The percentage of sulfated ash is determined after cooling by weighing the residue. Even with the preincineration bench, the preincineration procedure can take up to 4 h, depending on the behavior of the substance to be analyzed. Our most critical substance, a phthalazine derivative, behaves in such an unpredictable manner that a staff member needs to readjust the temperature continuously to ensure that the content of the crucible does not foam over (cf. Fig. 1 on the left). Requiring as it

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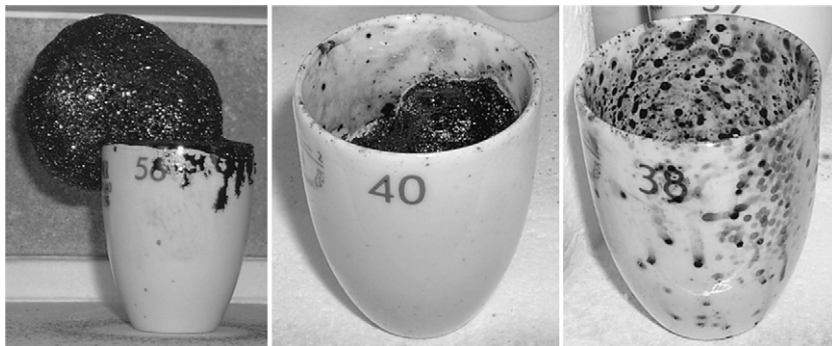


Fig. 1. Critical behavior (foaming over and/or spattering out) of the phthalazine derivative (left), megestrol acetate (center) and azelaic acid (right) during sulfated ash determination.

does up to 4 h, the preincineration of this substance has become our most intensive procedure in everyday laboratory work in terms of time and capacitance. In view of the fact that the sulfated ash test is used as a standard parameter in investigations leading up to the release of active ingredients, it represents an area of opportunity for increasing efficiency through automation.

2. Experimental

Microwave muffle furnaces offer opportunities for possible automation. With this in mind, the Phönix SAS (CEM GmbH, Kamp-Lintfort, Germany) microwave furnace was used for these investigations. The term “microwave furnace” implies that the samples to be incinerated are activated by microwave energy, but this is not the case. The procedure used with this device is a furnace-in-a-furnace approach. A magnetron emits regulated amounts of microwave radiation. These suffuse a ceramic insulating subrack permeable with air and are absorbed in the actual heating chamber by a silicone carbide heating element located on the interior walls of the insulator. This in turn releases its energy to the samples in the form of heat radiation. As a result, platinum crucibles can also be used for sulfated ash assessment of substances containing fluorine. A thermocouple in the interior chamber measures the actual temperature and regulates the magnetron accordingly. Sulfuric acid fumes are suctioned off by a vacuum pump and neutralized in wash-bottles. The interior chamber is protected against acid vapors by a quartz plate [4].

The procedure is carried out by weighing the sample into a crucible (1 g) and then adding concentrated sulfuric acid (2 ml; 95–97%, p.A., Merck, Darmstadt, Germany). The crucible is then placed in the microwave furnace and the temperature program is started. Once the program has been completed, the residue is allowed to cool, after which it is weighed out.

Model substances were selected for testing the usability of microwave furnaces with critical substances that were regarded as particularly critical in everyday work: megestrol acetate (from in-house production) and the phthalazine derivative (also produced in-house) exhibit very high degrees of foaming, and azelaic acid (for synthesis, ca. 88%, Merck, Darmstadt, Germany) spatters (cf. Fig. 1). Lactose (lactose monohydrate for biochemical applications, Merck, Darmstadt, Germany) served

Table 1

Temperature program for incineration per microwave muffle furnace in accordance with [5]

Time (min)	Temperature (°C)
15	90
15	130
20	220
15	240
15	300
30	600

only as a comparison substance, because of its inconspicuousness.

3. Results and discussion

Sulfated ash assessment was first carried out in classical porcelain crucibles of 40 ml interior volume with a temperature program (cf. Table 1) that was drawn from relevant scientific publications [5].

The components phthalazine derivative, megestrol acetate and azelaic acid exhibited the same behavior as with the classical method, i.e. they foamed out of the crucible or spattered wildly. More precise investigations of the behavior of the substances revealed that megestrol acetate already begins to exhibit a high degree of foaming at approximately 100 °C. Azelaic acid, on the other hand, begins to spatter greatly at temperatures of around 200 °C, while a phthalazine derivative exhibits extreme foaming at temperatures around 400 °C, expanding to a volume of approximately 170 ml while doing so. In order to preclude the possibility of foaming over and/or spattering outward uncontrollably, it is important that the respective substances are not heated up too rapidly at the critical temperatures. In view of the fact however that the critical behavior of the substances is spread across a wide temperature range, a slow, linear temperature program was used as the optimum alternative in contrast to the temperature program to be found in Table 1: 40–500 °C in 3.5 h, hold for 1 min, afterwards to 600 °C in 8 min.

The temperature program alone was nonetheless not sufficient for achieving success. Further investigations showed that the crucibles used were the key to success. Standard porce-

lain crucibles with volumes of only around 40 ml are too small for critical substances. Quartz crucibles that are tall in shape, and thus saving space in the furnace, with volumes of 140 ml (i.d. = 60 mm, $h = 75$ mm; CEM GmbH, Kamp-Lintfort, Germany) proved to be the best crucibles for the substances under investigation. For cases involving substances with unknown behavior, one should look into the furnace at regular intervals during the first analysis in order to see whether the substance is spattering wildly or foaming over. The analysis of the foaming megestrol acetate and of the non-problematic lactose was able to be performed in the aforementioned quartz crucibles without further ado (cf. Fig. 2). For spattering substances, such as the azelaic acid, a round quartz filter paper (Ashing Pads, diameter 55 mm; CEM GmbH, Kamp-Lintfort, Germany) was laid on top to guard against spattering (cf. Fig. 2). This is neither destroyed by the sulfuric acid nor incinerated by the high temperatures, which is the reason it must be included in the tare weight beforehand.

A wider quartz crucible or quartz dish with 240 ml volume (i.d. = 95 mm, $h = 55$ mm; CEM GmbH, Kamp-Lintfort, Germany) was used with substances with unusually heavy foaming such as the phthalazine derivative (cf. Fig. 2). One can trace the behavior of the four model substances during preliminary incineration in microwave muffle furnaces following the addition of sulfuric acid in Fig. 2. The images document increments of approximately 100 °C, illustrating for the viewer the above statements regarding the critical temperatures of the different substances: megestrol acetate ~100 °C, azelaic acid ~200 °C, phthalazine derivative ~400 °C. It is clear that none of the substances escapes during incineration, thanks to the selection of the crucible form and/or the application of the spatter guard.

Products which both foam and spatter are well known in the food industry, and this behavior is usually to be traced back to the high fat, moisture or sugar content [6]. Determination of water content using the Karl Fischer method yielded water content levels that were too low, to provide an explanation for the extreme foaming and/or spattering: phthalazine derivative: 0.49%; megestrol acetate: <0.01%; azelaic acid: 0.07%. The non-critical comparison substance lactose monohydrate exhibited a comparatively large amount of water (5.2%), due to the water of crystallization.

The lubricating oil industry is also familiar with the problem of extreme foaming resulting from moisture content, and recommends the addition of 2-propanol to combat it [7]. This was tried with the sulfated ash determination of the phthalazine derivative. Two millilitres of 2-propanol ($\geq 99.9\%$, LiChrosolv, Merck, Darmstadt, Germany) were also added to the phthalazine derivative and concentrated sulfuric acid in a tall quartz dish (140 ml) and processed in accordance with the aforementioned temperature program. Vigorous reactions with spattering arose at temperatures between 100 and 200 °C, but the strong foaming anticipated at temperatures around 400 °C did not occur. This means that the addition of 2-propanol is an alternative to the use of wide quartz crucibles for substances that exhibit extreme foaming. A spatter guard consisting of quartz filter paper (Ashing Pads) will however need to be used. It must be borne in mind



Fig. 2. Tracking the incineration of megestrol acetate, phthalazine derivative, azelaic acid and lactose (from the left) in the microwave muffle furnace at different temperatures (from the top to the bottom): room temperature, 103, 209, 301, 402, 502 and 599 °C. Temperature program: 40–500 °C in 3.5 h (hold for 1 min), afterwards to 600 °C in 8 min.

when using 2-propanol instead of the wide quartz dish that this is a deviation from pharmacopoeia guidelines.

A comparative analysis of an organic substance containing silicone was carried out to test the correctness of the results. The substance was not critical in terms of foam over or spatter behavior. The two analysis results of sulfated ash determination, in accordance with the classical method ($8.18 \pm 0.13\%$, $n=4$) and the microwave method ($7.98 \pm 0.16\%$, $n=4$) yielded comparable and repeatable values. This means that a microwave muffle furnace can be utilized for sulfated ash determination in routine analytical procedures.

4. Conclusions

A microwave furnace functions like a programmable electrically heated muffle furnace, in light of the fact that microwave energy is converted into thermal energy and this acts upon the samples. As a result, platinum crucibles can also be used and performance is possible in accordance with previous testing regulations without the need for deviations. The advantage thereby lies in the automation, because up to nine samples can be processed in parallel in the quartz vessels selected and the manual preliminary incineration stage – which took up to 4 h, depending on substance behavior – can be omitted. Substances with critical behavior, e.g. those which foam over and/or spatter, can also be handled properly through the selection of appropriate crucibles

as flat dishes and/or spatter guards made of quartz filter paper. As a result, sulfated ash determination proceeds in a way that is more controlled, more automated and safer – since no contact with toxic and/or caustic waste gases and no hot surfaces occur – than that used in the classical method.

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