

Monitoring of the Drying Process by Direct Solid-Phase Microextraction

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Abstract: SPME is known as a rapid and convenient method for analyzing air-borne organic compounds in closed systems ('headspace SPME'). In this investigation we have applied this technique to the monitoring of the drying process of chemicals containing small amounts of organic solvents under specific conditions. Interesting results were found and some of them are presented and discussed in this paper.

Keywords: Drying · Pharmaceuticals · Solid-phase microextraction · Solvents · SPME

1. Introduction

The drying of solid materials (chemicals, foods, pharmaceuticals) is a major industrial unit operation. It consists of removing a liquid from the solid material up to an acceptably low value. For pharmaceutical products the limits are generally in the mg/kg or even in the µg/kg range. For the control of the process, it is necessary to continuously monitor the moisture content during the operation. This is usually done by sampling and off-line analysis in the laboratory, which is time consuming and unsuitable for the control of rapidly changing processes. On-line monitoring is obviously of greatest interest. In this paper we present some results obtained in our laboratories using headspace solid-phase microextraction (SPME) as a monitoring method in the drying of pharmaceuticals.

2. SPME

SPME is a simple, convenient, and sensitive analytical technique, which was developed at the University of Waterloo (Canada) by Pawliszyn [1][2]. It is a valuable technique for analyzing air-borne organic compounds. The method is a headspace sampling technique which concentrates volatile organic compounds (analytes) by adsorption onto a selective polymer-coated silica fiber prior to thermal desorption in the injection port of a gas chromatograph. It is especially suitable and straightforward when concentrations are constant over time *i.e.* for systems which are fully equilibrated. Quantitation in the absence of full equilibrium is much more complex because the kinetics of extraction are limited by the diffusion within the fiber coating and through a boundary layer. Some models have been developed recently [3].

3. Experimental Design and Conditions

The laboratory drying equipment used was a modified Büchi Rotavapor (Fig. 1) from which the cooling system had been removed in order to keep the headspace inside the apparatus as small as possible. The solid material to be dried was placed in the 250 ml rotating round-

bottom flask and the nitrogen flow was introduced through a Teflon tubing insert into the core of the solid. The temperature of the process was regulated with a thermostated water bath. Dry nitrogen from a tank was directed through a rotameter and the flow periodically checked for accuracy with a bubble flowmeter. Vacuum was produced by a water aspirator and maintained at the desired value by a pressure regulator.

The wet material used in this investigation was a pharmaceutical intermediate containing ~ 4% of isopropanol.

The process was monitored using a SPME fiber from Supelco with a 65 µm CW/DVD coating. The volatiles emitted were collected at different times by inserting the needle of a SPME fiber through a silicone rubber septum, located at the outlet of the equipment. The total amount of volatile analytes was measured by direct injection in a simplified gas chromatograph (TV 9000; Brechbühler AG) developed in our laboratories and operating without a separating column [4]. It consists of an injector for a wide-bore column linked to a standard FID detector by a short capillary of 30 cm length. The signal was interpreted using the integration program Chrom-Card (Fig. 2). The sampling time was 2 min and the injection time 1 min.

The drying experiments were carried out under following experimental condi-

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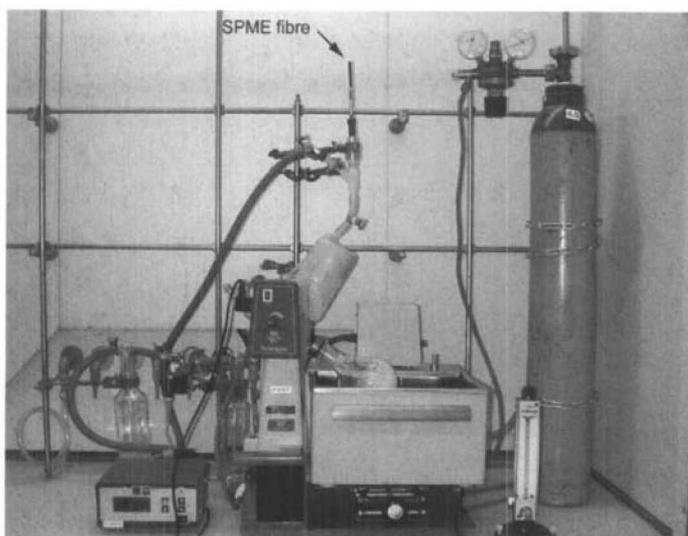


Fig. 1. Laboratory drying equipment

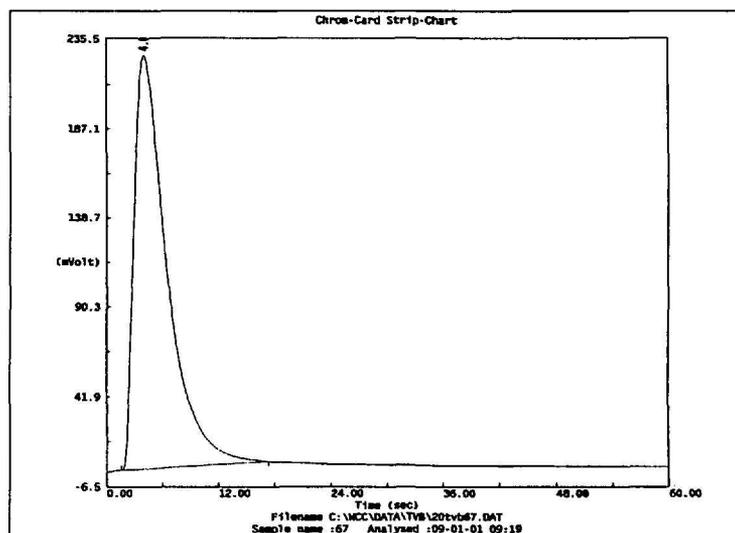


Fig. 2. Typical signal obtained by direct desorption of volatiles in the TV 9000

tions: temperature from 40 to 70 °C; pressure from 20 mbar to atmospheric pressure (960 mbar); nitrogen flow rate from 0 to 3200 ml/min (under experimental conditions).

4. General Procedure

The material to be dried was weighed (~60 g) and placed in the apparatus and the experimental conditions set up. After a stabilization time of ~1h, the experiment was started and SPME analyses were made at different times. Periodically, the dryer was opened and a solid sample (~1g) was withdrawn for analysis. After recording the weight of the residual solid (mass balance), the equipment was rapidly reset for further measurements. The analyses of solid samples were made using an internal headspace GC-procedure.

and the partition coefficients between the fiber and the gas phase, K_{fg} , depend on many parameters such as the type of analytes, fiber type and operating conditions (temperature and pressure). Knowing the proportionality constants and the amounts captured by the fiber, concentrations in the gas phase can be easily calculated. Unfortunately, very few proportionality constants have been published and general models to calculate them are not readily available. A viable practical approach to overcome this difficulty is to calibrate the fiber for the given analytes and to measure long enough to ensure complete equilibration.

In our study the analyte concentration changed constantly during the drying process, rapidly at the beginning and more slowly at the end. Fortunately, the equilibration time of the fiber for our solvent was fairly short (within minutes), so

that we could obtain reliable results without reaching full equilibrium by using consistent sampling time and keeping the operating parameters constant. For a sampling time of 2 min one can consider the measured concentrations as being 'quasi' steady-state concentrations, which simplifies calculations greatly. The reproducibility of the results was excellent for experiments carried out at atmospheric pressure but poor for the work carried out under reduced pressure. The latter is primarily due to the bad regulation of the pressure (stroke regulation).

Kinetics of Drying

Fig. 3 shows a typical drying plot. (60 °C; 960 mbar; 222 ml nitrogen/min) The drying process was modeled by using the general rate law $-dm/dt = km^\alpha$, where m is the amount of solvent present in the solid, k a drying constant, and α the

5. Results and Discussion

Thermodynamic Considerations

Adsorption of volatiles onto the SPME fiber has been shown to be dependent on the temperature, pressure, and gas circulation in the drying apparatus. The most efficient parameter in the drying process proved to be the gas circulation.

A fundamental property of SPME is that the analytes partition between the fiber coating and the gas and calculation of the concentrations always involves equilibrium relationships. At equilibrium, the concentration of the analytes in the fiber coating is directly related to the concentration in the gas phase:

$$K_{fg} = C_f / C_g \quad (1)$$

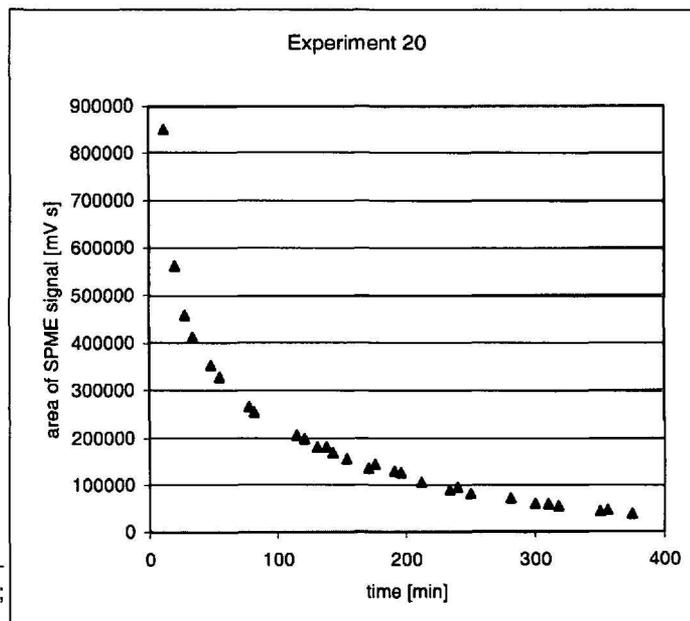


Fig. 3. Typical SPME monitoring (60 °C; 960 mbar; 222 ml nitrogen/min)

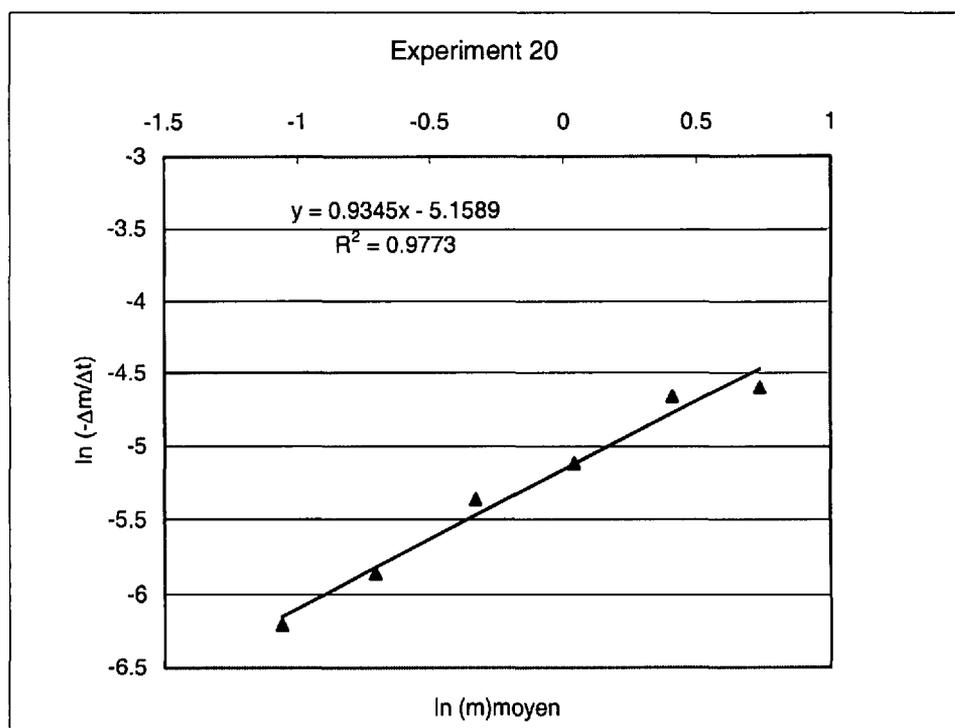


Fig. 4. First-order kinetics of the process

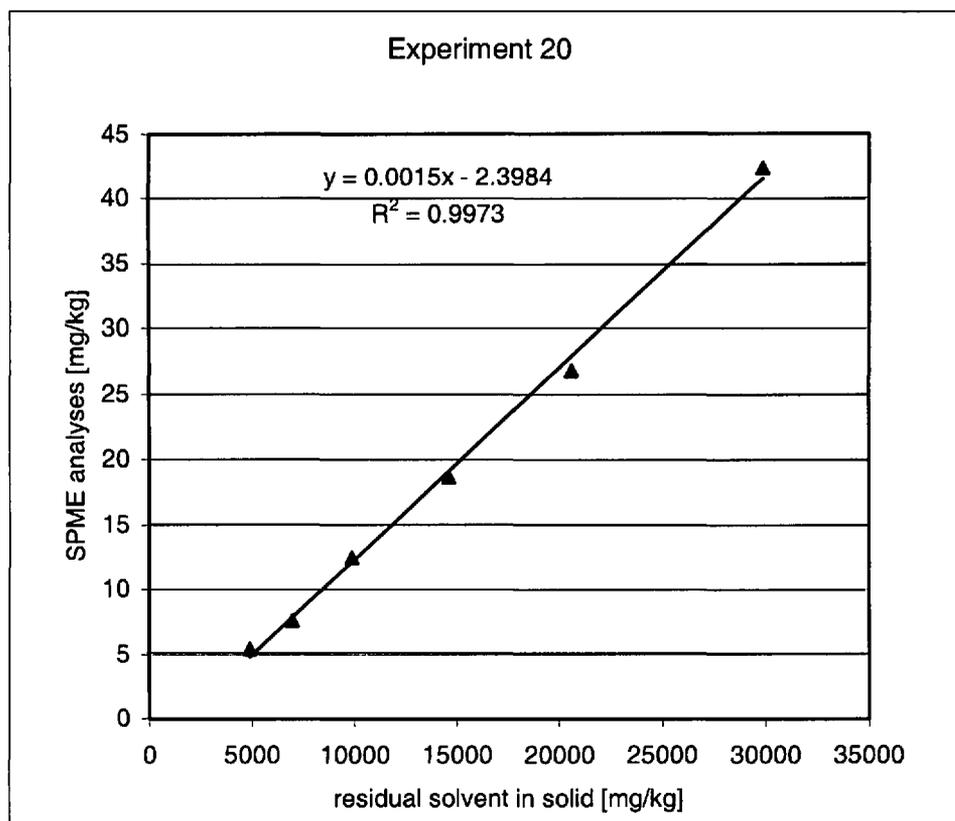


Fig. 5. Correlation between SPME and solid analyses

order of the process [-]. Values of α between 0.9 and 1.1 were found for all our experiments, which indicates that drying is a first-order process (Fig. 4).

Calibration of the SPME fiber

Response factors were determined by preparing samples of isopropanol volumetrically (0–5 μ l) in 22 ml vials with screw and PTFE septum and injecting them into the TV 9000 (three replications). Responses varied with the fiber type, the age of the fiber and the experimental conditions. Correlations were excellent.

On-line Monitoring of the Drying Process by SPME

By using appropriate calibration curves, it was possible to monitor with a time interval 5' at a frequency of 1 in 5' the amount of residual solvent in the solid at any time by direct SPME, without solid sampling (Fig. 5). Thus, the end-point of the drying process can be predicted with a good accuracy, which saves a great deal of time.

6. Conclusions

The on-line monitoring of the drying process by using direct headspace SPME has been investigated. An accurate prediction of the end-point of the process can be made, provided adequate calibration curves are available. We are extending our investigations to other operating conditions, especially to the work under reduced pressure, with and without gas circulation.

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- [1] A.C.L. Pawliszyn, *Anal. Chem.* **1990**, *62*, 2145–2148.
- [2] A.C.L. Pawliszyn, 'Solid-Phase Microextraction: Theory and Practice', Wiley-VCH, New-York, **1997**.
- [3] R.J. Bartelt, B.W. Zilkowski, *Anal. Chem.* **1999**, *71*, 92–101.
- [4] A. Béné, A. Fornage, J.-L. Luisier, P. Pichler, J.-C. Villettaz, *Sensor and Actuators B.* **2001**, *72*, 184–187.