

Monitoring the elimination of solvents from pharmaceutical powders by a SPME-direct method

J. Besse ^a, F. Bigou ^a, J. -L. Luisier ^{a,*}, R. Nzébo ^a, P. PICHLER ^b, R. Rossé ^a

^a Haute Ecole Valaisanne, HEVs, Route du Rawyl 47, CH-1950 SION, Switzerland

^b Brechbühler AG, CH-SCHLIEREN, Switzerland

* e-mail: jluc.luisier@hevs.ch

INTRODUCTION

We describe here an easy method for monitoring the “drying” pharmaceutical or chemical powder. In this method, the volatile compounds are trapped, at an outlet of the drying system, onto a SPME (solid phase micro extraction) fibre and then directly desorbed into the a simple apparatus (1) derived from a GC, without column separation. In the method we propose, the adsorbed solvents are measured as a single peak, which is directly proportional to the concentration of organic solvents of the head space (2). This methods have been successfully tested at a laboratory scale, under normal or reduced pressure as well as in an industrial dryer. As each measurement can be obtained within 4-5 minutes, the results obtained allow to follow the elimination of a solvent from a batch of pharmaceutical or chemical products. Peak area is proportional to the residual amount of solvent. Various analytical techniques like GC, GC-MS, HPLC (3) allow the detection and quantification of residual solvents in pharmaceutical powders, but all these methods are time consuming.

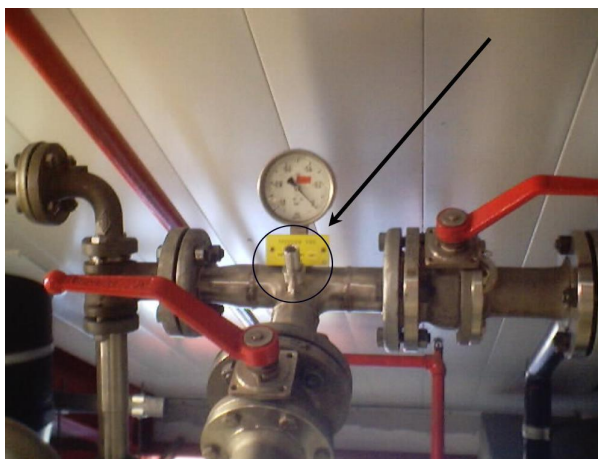


Fig. 1: Holder for a SPME on the Comber Dryer

RESULTS

A holder allowing sampling/extraction by the SPME fibre was implemented on the drying process unit, an ordinary laboratory rotovapor or an industrial dryer (Fig. 1, Comber dryer, 3000 L). In the first case, some instabilities of the resulting curve were due to instabilities in the pressure control of the rotovapor. Fig 2 shows the results of the monitoring of the elimination of isopropanol from three batches of a pharmaceutical product on the rotovapor drying unit. The results correlate very well with those obtained by standard methods like extraction and gaschromatography or by weight loss calculations with a R^2 of 0.996. Moreover, the regular curve allows to monitor the drying time and to control the reproducibility of the whole process and to predict the end of the drying process.

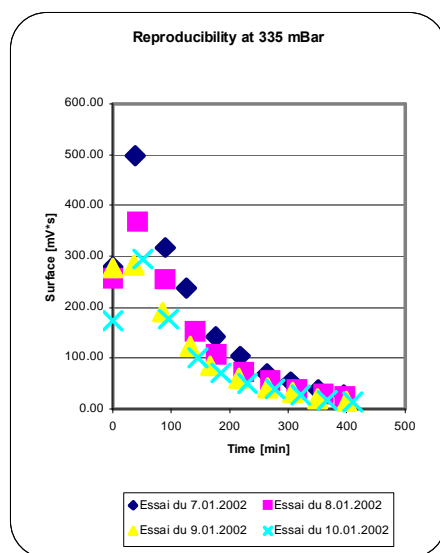


Fig.2. Reproducibility of the drying on a rotovapor

EXPERIMENTAL PART

Equipment: SPME fibre from Supelco, Bellefonte, PA (USA); TV9000 from Brechbühler AG, CH-Schlieren (Switzerland); Chromcard data integration software from FISIONS Instruments. Experimental conditions for the TV9000 : FID Detector; liner of internal diameter of 2 mm; injection temperature : 225°C; detection temperature : 300°C ; helium flow rate: 2 ml/min; hydrogen flow rate : 750 ml/min; air flow rate : 400 ml/min.

CONCLUSION

The method shows :

A simple – robust – easy to use method allowing the control of the drying process.

A reproducible signal - Not influenced by the presence of water.

No highly qualified personnel needed for instrumental operation.

The applications for such a device hold most promise in the areas of quality control and monitoring the efficiency of chemical and manufacturing processes.

References

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