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EDITORIAL

HPLC-MS and CE-MS, Finally Mature Techniques for Routine Analysis?

When I was asked to be a guest editor for CHIMIA and to prepare a special issue which describes the state of the art in the field of LC-MS, I accepted instantly since I thought it is a great idea to summarise the performance we can achieve nowadays. Soon it became clear that such a survey should contain a lot of different viewpoints and personal experiences of people using these techniques and developing them further. In a second step, I asked Dr. *Gerard Hopfgartner* from *Hoffmann-La Roche* to to be my co-editor and to assist me in selecting suitable authors. We agreed that the aim of such a summary would be to show today's possibilities, future perspectives, and unsolved problems. It was certainly not easy to find authors with the corresponding experience and background as well as time to write a contribution. Due to Dr. *Hopfgartner*'s continuous effort to find suitable candidates, we can finally present this issue.

Since it was not our intention to publish original papers dealing with highly specialised aspects, we asked the authors for a more personal review and summary of their work so far, as well as of their experiences. Here is the result, which we hope will give a sufficiently broad survey, although not all aspects could be covered. The reader will find descriptions of new technical solutions, such as ion-trap HPLC-MS, or of future perspectives of CE-MS as well as their applications, of possibilities to carry out structure elucidation and quantification, and finally of the advantages/disadvantages of the different ionisation techniques currently used.

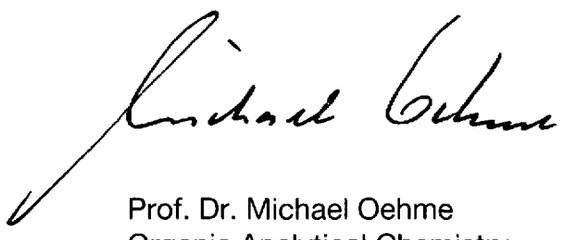
In many ways, the development of LC-MS during the past decade can be described by my own experience. My first contact with HPLC coupled to a mass spectrometer was around 1987, when people started to claim that HPLC-MS had become a mature and sensitive technique. Since we had reached the end point of GC-MS in terms of detection limits, selectivity, and application range in the fields of environmental and food analysis, it was very tempting to apply HPLC-MS to polar and/or thermolabile compounds such as biotoxins or photochemical reaction products. The particle-beam interface was considered to be the solution of the main problem at that time, namely how to transfer a total effluent of *ca.* 1 ml/min from a HPLC column to the mass spectrometer. In addition, it was stated that pure electron-ionisation mass spectra could be generated, thus making the structure elucidation of unknown compounds straight-forward. However, my disappointment was considerable, mainly due to completely unsatisfactory detection limits (around 150 ng were needed for an acceptable mass spectrum) and limitations

concerning volatility of the substance. An alternative ionisation technique, thermospray, was much more promising, but still one could not predict when and under what conditions a compound was ionisible, and structure elucidation of unknowns substances was hardly possible.

When electrospray and atmospheric-pressure ionisation techniques showed up at the beginning of the 1990s, at least the transfer of eluent flows around 1 ml/min into the MS was solved. However, those who were hoping that HPLC-MS would have detection limits similar to GC-MS, as well as its ease to identify unknown substances, were disappointed once more. For quadrupole systems, around 50 ng of a low-molecular compound were needed to record a full mass spectrum which contained at best a few fragments, beside the protonated or deprotonated molecular ion or ion adducts. Really, not very much material for a structure elucidation. MS/MS generated a few more fragments, but still, in most cases, not enough information was available for the identification of a completely unknown structure.

Suddenly, things started to happen when ion traps entered the HPLC-MS market. Detection limits in the full-scan mode were lowered by nearly two orders of magnitude, and the consecutive on-line generation of multiple daughter-ion mass spectra allowed to gather structure-relevant information. When we received the very first commercial instrument in our group in 1995, it soon became clear that we had a tool which started to get comparable with GC-MS. Interestingly, the same experiences as in the good old days of GC-MS were made. Not the MS, but the separation system was frequently the reason for troubles caused by, *e.g.*, adsorption problems on the column, column bleeding, contaminants from seals, or insufficient solvent qualities. But finally, we had a tool which allowed to obtain a lot of structure information from 1 ng with detection limits in the low pg range. Yes, this was a real breakthrough though quite a number of problems still have to be solved, such as avoidance of adsorption and high background at these concentrations. In conclusion, a mature technique which requires a skilled operator.

What about capillary electrophoresis and electrochromatography coupled to MS? Well, here we are still at the stage of exploring their possibilities as this issue shows. Major problems are, furthermore, a robust interface and sufficiently low detection limits. However, I am certain that we will see a similar progress in the near future as for HPLC-MS.



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The Editorial Board of CHIMIA would like to express its warmest thanks to the coordinating guest editor Prof. *Michael Oehme* (as well as to his co-editor Dr. *Gerard Hopfgartner*) acknowledging the interesting selection of authors and topics as well as the efficient realization of the present special issue on 'Hyphenated Techniques'.