

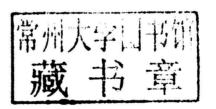
# MODERN SAMPLE PREPARATION FOR CHROMATOGRAPHY

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### Preface

In the last 10 to 15 years, considerable progress has been made in chromatography, in particular by the introduction of new separation media, higher pressure instruments for HPLC (UPLC), as well as by the introduction of more sensitive detectors with developments in tandem mass spectrometry for both LC (LC/MS/MS) and GC (GC/MS/MS). This progress required further development and changes in sample preparation for chromatography, which have been achieved by the introduction of new techniques and the introduction of new materials with better performance in sample preparation practice. The capturing of this progress in a new book dedicated to sample preparation for chromatography was one of the main goals of the present material. More recently, in sample preparation for chromatography there is the tendency to use simpler techniques than in the past, the analysis depending more on the performance of the chromatographic equipment and less on processing of the sample. The idea of "minimal" sample preparation appears more and more attractive, since sample preparation is typically labor intensive and requires welltrained operators. The concept of minimal sample preparation puts pressure on developing methods that are simpler and more efficient. Some ways to achieve this goal are discussed in this book. An additional objective of the book is to present sample preparation for chromatography as a coherent subject and to include the description of the new developments as a logical progress in the field. This approach

was taken in a previous book published by Elsevier in 2002 by the authors of present book and having the title Sample Preparation in Chromatography. The present book can be considered an update of the older book, with most of the material rewritten in a simpler and shorter manner and with a significant reduction of the description of derivatization procedures for various classes of molecules. The new book is focused on true sample preparation procedures and does not include descriptions of techniques that are basically stand-alone analytical methods, such as pyrolysis-GC/MS, bidimensional chromatography, or other hyphenated chromatotechniques. These stand-alone analytical procedures are well described in dedicated monographs and cannot be seen just as sample preparations. A problem related to a book on sample preparation for chromatography is the extent to which specific applications are described. Virtually every analytical method includes a sample preparation step, and an enormous number of applications of sample preparations are reported in the literature. The details necessary for applying sample preparation steps can be easily obtained from the original source, and their inclusion in a book was considered of little usefulness, as well as impossible to capture comprehensively. For this reason, only a few examples of applications used for illustrating different procedures were included in the book. The book is intended to be addressed to chemists of a wide range of levels of specialization, from both industry and academic sectors. It is **xii** Preface

intended to enhance the understanding of principles and techniques used in sample preparation for chromatography that can help in obtaining reliable results in chemical analyses and in making the correct decision related to the studied system.

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#### PARTI

# GENERAL CONCEPTS IN SAMPLE PREPARATION



# 1

# Preliminaries to Sample Preparation

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#### 1.1 COLLECTION OF INFORMATION AND PLANNING FOR A CHROMATOGRAPHIC ANALYSIS

#### **General Comments**

Chemical and/or physical modification of a sample to make it amenable for a chemical analysis or to improve the performance of analysis is indicated as *sample preparation*. The modification is necessary because it is common that the chemical analysis is not possible or it is not convenient without a preliminary processing of the sample. Samples can be considered as made from two distinct parts, the *analytes* and the *matrix*. The analytes are the molecular species of interest in the sample, and the matrix is the rest of the sample components. Sample preparation can be

performed for sample dissolution, matrix modification and/or simplification, analytes concentration, preliminary separation of the analytes from the sample, chemical changes of the analytes. All these operations are performed before the core analysis with the purpose to improve the analysis results.

The steps in a chemical analysis can be summarized as follows: information collection → planning → sample collection → sample preparation → core analysis → data processing → results interpretation. As shown, the chemical analysis designed to characterize (identify, quantitate, etc.) the analytes typically involves some steps related to information and some to operations. The core analysis considered in this book is chromatography.

#### Chromatographic Core Analysis

Chromatography comprises several techniques used for the separation of different molecular species from a mixture. The chromatographic separations are performed for both laboratory and industrial applications. In the laboratory, chromatography can be applied for analytical purposes or for other applications (e.g., preparative). In analytical chromatography the separation is coupled with a detection capability for the separated components. Some chromatographic techniques have a very high separation power and can be coupled with exceptionally high sensitive detectors. High performance liquid chromatography (HPLC), for example, allows the separation and quantitation of a wide variety of compounds even in very complex mixtures such as biological or other natural samples. Gas chromatography (GC), in particular when coupled with mass spectrometric detection (GC/MS), is used for the analysis of volatile compounds allowing both quantitation and compound identification even in samples with many components. In addition, both HPLC and GC techniques can be applied on very small amounts of sample. All these qualities made chromatography the most utilized procedure of chemical analysis. For this reason, an enormous body of information is available regarding chromatographic methods of analysis, including dedicated scientific journals, books, Website articles. The details of chromatographic separation and measurement are important for the sample preparation step, since sample preparation must be designed to make the sample amenable for that specific method of analysis. For this reason, the description of the analytical method includes sample preparation as an intrinsic part of the procedure.

It is common that the sample injected in a chromatographic instrument has already been subject to specific modifications (sample preparation) that are necessary to have the analytes amenable for the chromatographic analysis. This processing transforms the initial *raw sample* into a *processed sample* (see e.g., Ref. 1). After a sample preparation step, the *processed sample* is used for the core chromatographic procedure of analysis. The transformation of the *raw sample* into the *processed sample* is the subject of this book.

# Collection of Information Regarding the Analysis

The collection of information for a chemical analysis should include (1) the purpose of analysis, (2) the nature of material to be analyzed, (3) sampling and sample characteristics, (4) the analytes to be measured, (5) methods of analysis (possibilities for sample preparation and core analytical methods available for the requested analysis), (6) data processing, (7) available instrumentation, materials, and expertise in the laboratory, (8) available funding and other potential restrictions, (9) relation with results from previous work, results from other laboratories or databases, and (10) certainty of the information about the sample, the method of analysis, and other resources. The sources of information

include (1) the provider of the sample(s)/collector of the sample(s), (2) the recipient of the results (possibly the same as the sample provider), (3) public knowledge related to the sample and analysis (literature, web information, etc.), and (4) private (and personal) knowledge on the analysis. The step of information collection for a chromatographic analysis does not differ in principle from that for a general analysis, with the exception that the analytical method selection is restricted to a chromatographic one. The steps during information collection are not necessarily taken in a specific sequence, and in most cases the iteration of the process is necessary for bringing an uniform understanding. The correlation between different pieces of information is very important. Some of the collected information can be certain, but some can be vague or uncertain. This aspect qualifying the information must always be taken into consideration during the planning of the analysis. Several comments on each step regarding information collection are further made:

1. The information regarding the purpose of the analysis is very important. The analysis should be geared toward answering specific questions, even if the analysis is only exploratory or the goal of performing the analysis is vague. From the purpose of analysis, it must be known whether qualitative, quantitative, or both types of results are expected from the analysis, or if special types of analysis such as that of enantiomers or of compounds structure are projected. The list of analytes (single or multiple component analysis) or class of analytes that must be analyzed (if known), the required precision of the results (in particular for quantitative analysis), the further use of the results, and the rapidity with which the results must be delivered must be known before starting an analysis. Also, it must be known if the whole sample

should be analyzed or only a specific part (surface, soluble component, selected points, etc.). The information on the purpose of analysis also helps to decide whether a specific protocol must be followed during the analysis or that no regulations are imposed. Some analyses are required to be nondestructive, and in certain cases the analysis is done in conjunction with preparative purposes, which also should be known. A wide range of requests can be made for an analysis, and samples must be analyzed for numerous reasons. In industrial environments such purposes may include official or legal requirements, assessing the quality of raw materials, process control or troubleshooting, assuring the quality of finished products, research, reverse engineering, or development purposes. Samples are frequently analyzed for health-related purposes (e.g., medical analyses, analysis of pharmaceuticals, analysis of metabolites), for evaluating environmental issues, for forensic purposes, for exploratory reasons, and for fundamental research. Depending on the analysis reason, specific decisions are made about the analytical process.

2. The information regarding the type of sample should tell if it is of a known type or a new type. The physical state of the sample (homogeneous, nonhomogeneous, solid, liquid, gas) is also important. Details about the nature of the sample matrix (organic or inorganic material, biological, environmental, composite, etc.) must be obtained. The knowledge about the matrix composition (and about the analytes) will be important for deciding if a new analytical method is needed or if one already available can be used or adapted. To this information should be added the knowledge about the amount of sample available (large quantity, small quantity, readily available, unique, etc.), the value of the sample, the origin of the

- sample, sample thermal stability and perishability, safety concerns about the sample. Also, the number of samples to be analyzed at one point or in an extended period of time must be known. This will help to decide if a routine analysis will be necessary or a unique or limited time analysis should be used.
- 3. Information about the sampling process is also very useful, in particular indicating the sample homogeneity, the age of the sample, potential contamination. In some cases the sample must be returned to the provider after a small amount has been used for analysis and this should also be known. Knowledge regarding other analyses already performed on the sample is always important, and occasionally it is useful to have information about other analyses that are planned to be performed later on the sample. In case that very little information is available about the sample, preliminary analyses should be sometimes performed. This preliminary analysis can be qualitative or semiquantitative. For example, a GC/MS analysis (if possible) may provide valuable qualitative information for an unknown sample.
- 4. The information about the analytes to be measured is another important component in planning an analysis. This includes the nature of the analytes or at least the class of the analytes (inorganic, organic, functional groups in organic compounds, ionic character, etc.). If this information is missing, it must be known at least if the analytes are small molecules or polymeric ones. In case of small analyte molecules, data regarding volatility, solubility, and reactivity are very useful. For macromolecules, a general characterization is typically necessary. Other data regarding the analytes are helpful, such as information on the estimated level of analytes in the sample (trace, medium levels, major constituent). The aspect regarding the

- level of analytes is very important in deciding about the required sensitivity of the analytical method as well as the sample enrichment approach to be used.
- 5. The collection of information on methods of analysis is a very important step. The method of analysis can be considered as divided into two different steps, the sample preparation and the core analytical procedure. However, it is common that the information on an analytical method includes together the details about an appropriate sample preparation, the core chromatographic separation, and the measurement procedure. When sample and the analytes are of a known type, it is common that a good method of analysis is available. The scientific literature (printed or on the web) contains an enormous number of analytical methods. Separate sample preparation procedures, core analytical separations, as well as measurements are also available in the literature. In many cases, the sample preparation is adjusted to match up with the analytical chromatographic separation and measurement, but it is not uncommon that the same sample preparation can be used for more than one type of analysis. In some cases, a reported analytical method can be directly applied to a certain analysis. However, it is common that a direct application without any change is not possible. In this case, one or more reported analytical methods should be compared and a new technique can be developed. A third possibility exists, when no such analysis as the one of interest is known, and an entirely new method should be developed. In this case, the information about similar methods is still very useful. The selection or development of an analytical method must take into account, besides the nature of the analytes and the matrix of the sample a number of other