Drugs and Poisons in Humans
A Handbook of Practical Analysis
It was with great pleasure that I accepted the invitation to write the foreword for *Drugs and Poisons in Humans. A Handbook of Practical Analysis*. Dr. Osamu Suzuki and Dr. Mikio Yashiki, two outstanding Japanese scientists, first published the Handbook in Japanese in 2002. Specialists throughout Japan contributed analytical methods for a wide variety of therapeutic and illicit drugs, pesticides, and natural toxins and alkaloids. In fact, rarely has such a wide spectrum of analytes and metabolites been addressed within a single reference manual.

At the beginning of the book, general topics are addressed, including instructions on handling biological materials, measurement of drugs in alternative specimens, and guidance on resolving analytical problems that may occur. There are discussions of extraction modalities and detection methodologies and how to select these appropriately based on the physiochemical characteristics of the drug. Analysis of specific classes of drugs and relevant metabolites are covered in subsequent chapters. Clinical, analytical and forensic toxicology and clinical chemistry laboratories will find the volume informative and useful. Toxicologists are often faced with developing methods for new drugs and metabolites with little information available in the literature. This book provides a great starting point for method development providing procedures that have been utilized in real life situations. In addition, toxicologists developing new methodologies may use this volume as a guide to selecting the most appropriate instrumentation to handle the breadth of their analytical workload.

One of the most valuable aspects of the Handbook is the inclusion of specific case studies. Useful also are the discussions on suggested analyte concentration ranges and troubleshooting tips. The 2002 version of the Handbook in Japanese was judged to be highly valuable and led to the production of an English version. This Handbook also has been updated to include additional methods and procedures for this edition.

Despite the value of these methodologies, it is essential for laboratorians to validate fully a method within their own laboratory. Differences in instrumentation, sample size, extraction procedures (such as different solid-phase extraction columns) and experience level of personnel may vary markedly between laboratories. Therefore, these methods provide help and guidance in initiating a new analysis, but do not take the place of independently determining limits of detection, quantification and linearity, and the selectivity and precision of the assay in their own hands. Internal standardization is always the preferred approach, although use of external standard addition may be necessary with difficult matrices, such as decomposed postmortem specimens. Quality assurance and quality control procedures are essential components of accurate and reliable methods and should be included in the analysis of each batch of specimens. Quality control samples should span the linear range of the assay. The issue of method validation cannot be emphasized too strongly and is necessary for the accurate application of these diverse analytical methods.
Dr. Suzuki and Dr. Watanabe have gathered an extensive array of methods for the measurement of xenobiotics and metabolites in biological matrices. *Drugs and Poisons in Humans. A Handbook of Practical Analysis* will be a well-used reference for toxicology laboratorians and will help guide assay development.

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The readers of this book will immediately realize that all authors are Japanese scientists; this is the English translation of a book which was published in Japanese by Jiho, Inc., Tokyo in 2002. Upon translation, the Editors added five new chapters to the previous 67 chapters in view of international occurrences of poisoning by drugs and poisons.

The most important aim of this book is to provide the most reliable and reproducible methods for analysis of drugs and poisons; therefore, the newest methods and ones requiring skills have not been adopted. Each chapter has been written by at least one expert currently engaged in the quantitative analysis of each toxin. This book is arranged so precisely that any fresh analytical chemist can start analytical experiments on a drug or a poison in a crude biological matrix, even if the analyst has no experience of analyzing the compound. Special care has been given to clarify the origins (manufacturers) or synthetic methods for chemicals to be used in reproducing the experiments, and also to present detailed procedures for the extraction of a drug or a poison from complicated matrices such as whole blood, tissues and urine.

Compounds causing cases of poisoning will increase and vary according to events in the world; the technology of analytical instruments is also advancing very rapidly. The Editors do not claim that this book covers all compounds to be analyzed and are well aware of the limitations of the book. The Editors hope that this book will be revised according to feedback received in the near future; some groups of drugs and poisons will then be added in a later edition.

The Editors also hope that this book will be widely distributed in the world and be useful for many analysts affiliated to forensic, environmental, clinical and doping control institutions.

The Editors wish to thank the following people for helping to make the present publication of this book possible: Dr. T. Mager and Mr. A. Spencer, Springer-Verlag, Heidelberg, for undertaking the laborious work of the publication; Messrs. T. Araki, D. Kobayashi and S. Hattori, Jiho, Inc., Tokyo, for kindly encouraging us to translate the original Japanese version; Mr. and Mrs. Kouichi Watanabe, the parents of one of the Editors, for typing extensive pages of manuscripts for the translation.

Osamu Suzuki
Kanako Watanabe
Editors
Notes on the use of this book

Contents

This book is composed of 9 chapters of general nature and 63 chapters of specific toxins. In the latter chapters, compounds with high poisoning frequency have been chosen; detailed procedures of analyses have been presented for each compound or each group. The methods mentioned are relatively new and easily reproducible in every chemical laboratory equipped with the standard analytical instruments. In this book, preliminary tests such as color and immunological reactions are almost omitted; most of them are chromatographic ones.

Each chapter on specific toxin is composed of: 1 Introduction; 2 Reagents and their preparation; 3 Instrumental conditions; 4 Procedure; 5 Assessment of the method; 6 Poisoning cases, toxic and fated concentrations; 7 Notes; and 8 References.

Especially, protocols for experimental procedure are headed by small letters of Roman numerals.

For notes, small alphabets are shown on the right shoulder of a corresponding word in the text. For references, Arabic numerals in brackets are shown in the text.

Symbols, units and expressions

Length: $10^{-9}$ m has been expressed as nm (not mµ); volume: $10^{-6}$ m³ expressed as mL (not cc); concentration: mol in 1 L volume expressed as M (not mol/L); NMR shift: δ values (not γ values); fraction: for example g/mL (not g mL⁻¹).

In GC analysis, when the initial oven temperature is 50 °C with 1-min hold, followed by its elevation at 5 °C/min up to 150 °C; after 5-min hold at the latter temperature, it is again elevated at 20 °C/min up to 280 °C. These steps of the procedure are simply described as follows.

50 °C (1 min) → 5 °C/min → 150 °C (5 min) → 20 °C/min → 280 °C.
Abbreviations

There are a number of abbreviated words being commonly used in the field of analytical toxicology. The following abbreviated words can be used in the text of this book without explanation.

CI: chemical ionization
CID: collision-induced dissociation
EI: electron impact ionization
FID: flame ionization detector
GC: gas chromatography or its instrument
GC/MS: gas chromatography/mass spectrometry or its instrument
GC/MS/MS: gas chromatography/tandem mass spectrometry or its instrument
HPLC: high-performance liquid chromatography or its instrument
IS: internal standard
LC: liquid chromatography = HPLC or its instrument
LC/MS: liquid chromatography/mass spectrometry or its instrument
LC/MS/MS: liquid chromatography/tandem mass spectrometry or its instrument
NPD: nitrogen-phosphorus detector
SIM: selected ion monitoring
TIC: total ion chromatogram or total ion current
TLC: thin-layer chromatography
UV: ultraviolet (detection)
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