

## Book Review

### Clarke's 'Isolation and Identification of Drugs' (2nd edition)

Senior consulting editor: A. C. Moffat

Reviewed by

I A Blair

Director, Mass Spectrometry Laboratory, Department of Pharmacology, School of Medicine, Vanderbilt University, Nashville, Tennessee 37232, USA

Clarke's 'Isolation and Identification of Drugs' has become an invaluable reference work for many scientists in the fields of pharmacy, pharmacology and toxicology. The first edition was published in two volumes that appeared in 1969 and 1975. It is timely that a second edition has now become available. This remarkable book has been thoroughly revised to include drugs that have come on the market since the first edition and in addition, most of the original material has been up-dated. The real strength of the first edition came from the enormous amount of information that it contained, coupled with a presentation that allowed the material to be readily accessed. Fortunately, the original format has been maintained and the second edition is as easy to use as the first. There are monographs on 300 drugs that were not included in the first edition. Part 1 of the book provides an overview of analytical methods. There are 18 chapters in this section which is an increase of 6 over the first edition. New chapters include hospital toxicology and drug abuse, therapeutic drug monitoring, drug abuse in sport, analysis of metals and anions, analysis of pesticides and high pressure liquid chromatography. The chapter on paper chromatography has been omitted from the new edition. The inclusion of these extra chapters, coupled with the increased coverage of drugs has necessitated a change in size although the page length is similar to the first edition.

Part 1 of the book attempts to provide in 300 pages a complete overview of analytical techniques that are used in drug analysis. Some of the topics in this section are a little dated and could probably have been pruned thus making the book's size perhaps more manageable. The first chapter in this part (Widdop) deals with Hospital Toxicology and Drug Abuse Screening. An excellent and comprehensive overview of the subject is presented. Sections are included on how to deal with samples from suspected overdose, poisoning, and substance abuse cases. Full directions are provided on how to sample blood, urine and stomach fluids together with the potential advantages of analysing each particular fluid. A suggested work-up and extraction procedure is provided, together with methods for making rapid preliminary identification of suspected ingested substances.

The second chapter (Jackson) provides an overview of Forensic Toxicology. It covers some of the ground presented in the first chapter but focusses more on the legal implications that ensue after finding dangerous xenobiotics in biological fluids obtained from human subjects. Analytical questions that are addressed include how to determine which poison has been administered and how to quantify the amount ingested. The analytical requirements to answer such questions properly are enormous and no single method has general applicability. This article provides a logical approach to solving such problems and it can be viewed as an extension of the first chapter. The two subsequent chapters on Metals and Anions (Yeoman) and Pesticides (Fysh) seem a little out of place in a text entitled 'The Isolation and Identification of Drugs' and could well have been omitted to reduce the size of this rather lengthy volume. But the articles themselves are not without merit and scientists in clinical toxicology will undoubtedly find them useful.

The fifth chapter discusses Drug Abuse in Sport (Moss and Cowan). A reasonable overview of the drugs

1986 ISBN 085369 166 5: pp 1248 + index (48pp). UK: Pharmaceutical Press, London SE1 7JN (£88 inc); USA: Rittenhouse Book Distributors, Inc., 511 Feheley Drive, King of Prussia, Pennsylvania 19406; Canada: McAinsh & Co. Ltd, 2670 Old Leslie Street, Willowdale, Ontario M2K 2X5; Australia: The Australian Pharmaceutical Publishing Co. Ltd, 35 Walsh Street, West Melbourne 3003; New Zealand: Pharmaceutical Society of New Zealand, Pharmacy House, 124 Dixon Street, P.O. Box 11640, Wellington 1; Japan: Maruzen Co. Ltd, 3-10 Nihonbashi 2-chome, Chuo-ku, Tokyo 103.

involved is presented, although the article is slanted towards the expertise of the authors. A wealth of data, particularly from the anabolic steroid literature has been omitted. In their defence, the authors have drawn on a number of recent examples to illustrate the principles involved in the analysis of banned drugs. With this general background it should be relatively easy for the interested reader to find particular examples in the literature.

The chapter on Therapeutic Drug Monitoring (Marks) presents a thorough and logical account of the rationale for carrying out such determinations. A selected list is provided of those drugs whose plasma concentrations should be monitored in patients undergoing therapy. This information is presented in tabular form together with literature references. It should prove useful for researchers in clinical pharmacology laboratories. Further chapters on Samples and Sampling (Toseland) and Quality Control in Clinical Analysis (Burnett and Williams) amplify and extend many of the comments made in earlier chapters. The importance of choosing appropriate samples and in ensuring quality control of the data is stressed. An omission from the otherwise excellent chapter on quality control is any mention of the 'good laboratory practices' programme that many of us are involved with.

The ninth chapter in Part 1 is devoted to a discussion of Colour Tests (Stevens). This chapter represents the first of a series of topics on analytical methodology. It will provide an invaluable source for investigators working in settings where drug analysis is carried out. Laboratory copies will probably have to be protected from marauding organic chemists searching for new ways to spray thin layer plates. The reagents are grouped in alphabetical order and are extremely easy to access. Extensive instructions are provided for the preparation of the individual reagents together with literature references. Details are also provided so that investigators can decide which is the most appropriate colour test for a particular drug class. The next chapter on Immunoassays (Stewart) is written in a different style and offers a very basic view of the topic, together with elementary instructions on the use of radioimmunoassay, enzyme immunoassay, fluoroimmunoassay and luminescence assays. The limited number of examples and lack of modern literature references are a little disappointing for a text intended as a reference work.

The chapter on Thin-layer Chromatography (Moffat) provides a basic overview of the subject together with an encyclopaedic collection of solvent systems. A comprehensive guide to the recent literature is provided and all the references have been up-dated from the earlier edition. There is one serious omission in the article. The ready availability of pre-coated plates has almost made their preparation in the analytical laboratory redundant. Pre-coated channel plates allow up to four analyses per 5 cm × 20 cm plate with little chance of cross-contamination of the sample. Furthermore, the

use of plates with pre-concentration zones ensures uniform Rf data. Finally, the use of these plates spares the laboratory personnel from the iniquities of fine dust particles in the atmosphere that seem to be endemic where thin-layer plates are made. It is difficult to see why a discussion on the use of these plates was omitted from such an otherwise well written account.

The twelfth chapter on Gas Chromatography (Leach and Ramsey) concentrates mainly on the use of packed column technology. Most modern analytical laboratories have converted to the use of capillary columns now that bonded phase fused silica columns are readily available. These columns overcome all the criticisms that the authors level at capillary column chromatography. The ability to re-generate the columns by washing with suitable organic solvents also helps to balance the initial cost outlay. The extensive information that the authors have provided on retention indices means that the article will still prove to be extremely useful. This chapter also includes key chromatographic data for the monographs on the individual drugs in Part 2. The next chapter, on High Pressure Liquid Chromatography (Gill), has some unexpected omissions. There is no discussion of microbore columns and no reference to the use of chiral bonded columns. However, in general, this is an excellent section devoted to providing recent examples of drug analysis from the literature and is a welcome and useful addition to the book. The chapter on Ultraviolet and Visible Spectrophotometry (Fell) has been extended to include some basic principles and examples of fluorescence. This makes the article a cohesive source of information, providing both basic theory and some recent examples. The next chapter on Infra-red Spectrophotometry (Chapman) is a basic introduction to the subject. The section on Fourier transform infra-red could have been dealt with in greater detail in view of the great potential of the technique when combined with gas chromatography. Otherwise, the chapter is a very good source for the literature on infra-red spectrophotometry of drugs.

The sixteenth chapter (Ardrey) is on the use of Mass Spectrometry in the identification and analysis of drugs. The discussion is somewhat dated and serves to provide a relatively superficial introduction to the subject. Fast atom bombardment mass spectrometry has provided a significant advance in our ability to carry out the preliminary structural analysis of metabolites derived from drugs and other xenobiotics. It cannot simply be dismissed as a technique that is not used! Furthermore, there is not a single reference to the use of fused silica capillary columns for combined gas chromatography-mass spectrometry. This technique represents as much a revolution to the analytical laboratory as does fast atom bombardment to structural analysis. The chapter on Nuclear Magnetic Resonance Spectroscopy (Carr) also has some omissions. There are no references to the use of high field instruments or to modern techniques that are used in structural analysis. The chapter does provide

a reasonable introduction to the field but could have been substantially improved by the use of more recent examples. The final chapter (Tilstone and Stead) attempts the impossible task of discussing Pharmacokinetics and Metabolism in 29 pages. The authors have set out to do this by largely ignoring the exciting advances in pharmacogenetics that have been made over the last five years. They have written a very general introduction that provides information to supplement the data in the monograph section. It would have probably taken a review almost as long as Clarke's book to do these topics justice, so perhaps the authors have done as well as could be expected within space constraints.

The real strength of Clarke's book lies in Part 2 where all the Analytical and Toxicology Data are collated. Monographs have been written on over 1300 drugs and related substances. Each compound is accompanied by both structural and empirical formulae and a superb index allows extremely easy access. Many of the drug entries include actual infra-red and ultraviolet spectra together with major peaks from their mass spectra. Other relevant physical properties that are reported include pKa, melting points and solubility. In addition, a catalogue is provided of colour tests, retention indices, Rf values and methods of analysis by both gas chromatography and high pressure liquid chromatography. This information will be invaluable for devising new assays and for identifying unknown compounds from biological fluids. The extensive documentation should also be extremely useful for devising new analytical approaches to substances with similar structures to those described

in the monographs. Further information is provided on disposition, therapeutic concentrations and toxic plasma concentrations. The pharmacokinetic parameters include volumes of distribution and plasma half-life. Each of the entries is referenced to allow the original article to be accessed and references to nearly 2500 articles are presented within the text. This is a unique piece of work that will hopefully continue to be up-dated as new drugs appear, and as our understanding of biotransformations improve. In particular, it will be important in the future to present information on the most active enantiomer of a racemic drug and to provide pharmacokinetic parameters for that enantiomer.

Parts 3 and 4 of the book comprise indexes for Parts 1 and 2. Data such as melting points and mass spectra are collected and presented in a logical way. These Parts will be useful in identifying unknown drugs. An additional short section is provided on reagents that are used in the analytical methods section.

Overall, Clarke's 'Isolation and Identification of Drugs' is an impressive piece of work. It will be an essential text for all scientists working in the areas of drug design, drug metabolism, clinical biochemistry and toxicology. There are some weaknesses in the individual chapters on analytical methodology but that is perhaps to be expected in a treatise of such enormous breadth and in which available space is a limiting factor. This second edition with its extensive revision is a considerable improvement on the first edition and will be an important text for many years to come. It should be available in all departments where drugs are prescribed, synthesized or analysed.