hormonal and enzymatic control, like fibroblast growth factor or cytokines, with their interaction with the blood–brain barrier, glucocorticoids, oestrogens and metalloproteinases. The authors of Section 4 mainly address those readers who are interested in in vitro studies of the blood–brain barrier. Modes of endothelial cell isolation, coculture with astrocytes, and the influence of serum in culture media are discussed, and examples are shown of how the function of the blood–brain barrier can be studied in silico in order to predict the permeability of drugs and drug candidates.

Section 5, the first section of the second volume, turns towards drug delivery to the brain. It starts with a discussion of p-glycoprotein, the export protein in the luminal membrane of the endothelial cells, which is a key player for the barrier function. P-glycoprotein recognizes an exceptionally broad variety of substrates and transports them back into blood circulation, thus hampering effective treatment of many CNS-related diseases. The development of redox-controlled prodrugs or the use of cytotic pathways are some of the ways to bypass the export pump and to overcome the barrier.

In Section 6, the dynamics of cerebral blood flow and oxygen are described as well as possibilities of displaying metabolic functions with imaging techniques. The final section discusses various pathological conditions of the brain, like inflammation, stroke, parasitic infection, and diabetes. The main text ends with a description of the blood–retina barrier. Embryologically, this barrier can be regarded as part of the central nervous system, and its blood vessels share many characteristics with those of the brain. In contrast to brain capillaries, the vessels of the retina can be studied in situ, and therefore, they may be used as an easily accessible model of the blood–brain barrier. The book closes with a comprehensive subject index.

It took 13 years from the famous book about the molecular biology of the blood–brain barrier by William Pardridge to the publication of the present book by Dermietzel and colleagues, and the result is very convincing. The book can easily be read by experts and laymen, facilitated by the many coloured illustrations. It has only some minor weaknesses. Considering the complexity of the subject, it becomes obvious that not every aspect can be discussed in the same detail, but, beside p-glycoprotein, there are other important transport proteins located in the blood–brain barrier that could have been included in the discussion. In addition, the Choroid Plexus, an important blood–CNS barrier, would also have been worth more than just some passing mentions. In view of the many authors, it is also not surprising that one or two aspects are pointed out twice or that not all illustrations are made in the same style.

Despite these small limitations, the authors have succeeded in making a great leap forward towards a better understanding of the structure and function of cerebral microvessels. Hopefully the book will find a broad readership and become a benchmark for blood–brain barrier textbooks.

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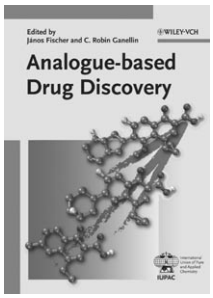
Analogue-based Drug Discovery

Edited by *IUPAC*, *Janos Fischer* and *C. Robin Ganellin*.

Wiley-VCH, Weinheim 2006. XXXI + 575 pp., hardcover € 155.00.—ISBN 3-527-31257-9

The similarity principle is an important strategy in medicinal chemistry. It states that similar compounds have similar biological activity. Thus, a biologically active compound provides a good starting point for finding new compounds with better pharmacological properties. The similarity principle can be successfully used in early drug design as soon as the first ligands are known. On the other hand, drugs on the market provide a wealth of information about pharmacokinetic parameters, adverse effects, etc., that can direct the development of optimised drugs. The latter scenario is addressed in the book "Analogue-based Drug Discovery".



For this purpose, the editors distinguish between *pioneer drugs* and *analogues*. Analogues, in this context, have a relationship to an existing drug. The term analogue is not only used for compounds with structural similarity, but also for compounds with a similar pharmacological activity, so-called pharmacological analogues, such as nifedipine and verapamil, which are structurally unrelated, though both block L-type calcium channels.

The book contains three main parts. Part I covers a brief definition of analogue-based drug design and explains general strategies for using analogues in drug discovery. Examples are chemical modifications frequently used in medicinal chemistry (homologisation, cyclisation, etc.) and the use of privileged fragments. Several examples of the application of the strategy are given.

Part II forms the main part of the book and gives many historic case studies of analogue-based drug discovery. The examples are taken from different therapeutic areas such as anti-infectives, anticancer agents, and anti-hypertensives and cover a broad range of chemical classes.

Part III contains a tabular overview of a collection of drug analogues for different targets and therapeutic indications, nicely illustrating the structural relationships of many compounds.

The different chapters are mostly well written with only few minor errors. The index is sufficiently detailed for drugs to be found quickly in the relevant chapters. Unfortunately, the chemical structures are not consistently drawn.

Important general aspects of analogue-based drug discovery are discussed in the first part of the book (e.g. homologous variations, SOSA approach, chemogenomics). This part is rather short, and a broader introduction to the field would have been valuable. For example, the successful use of modern

computational techniques in analogue finding or optimisation is almost completely neglected.

The second part of the book, which gives a plethora of case studies from very different therapeutic areas and target families, is the most valuable part. It can serve as a rich source of examples in analogue-based drug design. Examples are given for structural analogues as well as for pharmacological analogues. Different aspects of analogue-based drug design are covered by examples. For instance, the chapters on opiates or corticosteroids show the use of natural products as starting points for analogue-based drug design. A detailed history of this strategy is outlined for beta-blockers, while other examples illustrate that in vivo observations can initiate the development of new drugs, such as the discovery of cisplatin and drospirenone. Analogue optimisation under constraints of pH stability and pharmacodynamics is exemplified by proton-pump inhibitors.

Some contributions focus on the pharmacological aspects of the different compounds discussed instead of clearly emphasising the strategy that was finally successful. Lessons learnt from the case studies could have been given more clearly.

Overall the book is of interest for medicinal chemists who already have a sound knowledge of aspects of analogue-based drug design.

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DOI: 10.1002/cmdc.200600146

Neurobiology of DOPA as a Neurotransmitter

Edited by *Yoshimi Misu* and *Yoshio Goshima.*

CRC Press, Boca Raton 2006. 384 pp., hardcover $ 140.00.—ISBN 0-415-33291-5

The book *Neurobiology of DOPA as a Neurotransmitter*, edited by Yoshimi Misu and Yoshio Goshima, focuses on the neurobiological aspects of L-3,4-dihydroxyphenylalanine (DOPA), a non-proteinogenic amino acid. Most scientists as well as some in the general public recognize this amino acid as crucial in the treatment of neurological disorders, particularly Parkinson's disease. In this respect, DOPA was long thought to serve only as a neurologically inert precursor, which is enzymatically transformed to dopamine (dihydroxyphenylethylamine). Dopamine itself was regarded as a preeminent neurotransmitter, and a large part of research in the field of neurobiology concentrated on this neuroactive substance. The role of DOPA itself has only recently come to the focus of attention, and the present book presents a timely overview of the different aspects of this amino acid in neurotransmission.

The scientific concepts, perspectives, and studies are presented in 22 chapters, each written by one or several experts in their field. These chapters are grouped into five parts, describing the history (part I), biosynthesis and metabolism (part II), release (part III), pharmacology (part IV) and neurotoxicology (part V) of DOPA in all its aspects.

In the first part, an excellent historical overview of DOPA is given by a pioneer in the discovery of the role of dopamine and DOPA in the treatment of Parkinson's disease, Oleh Hornykiewicz (Medical University of Vienna). The chapter describes the developments starting with the first synthesis in 1911 by Funk, the discovery of DOPA decarboxylase, and the suggestion of the biosynthetic metabolism (L-Tyr→DOPA→dopamine→noradrenaline→adrenaline) to the discovery of the role of dopamine/DOPA for effective treatments of Parkinson's disease starting in the late 1950s. Most significantly, the shift of the recognition of DOPA from an 'inert precursor' to a neurologically active substance in its own right is carefully laid down.

This paradigm change is then carefully taken up by two pioneers in the field, the editors Yoshimi Misu and Yoshio Goshima. In the following chapters they describe the early evidence of DOPA as a neurotransmitter candidate and the uptake of DOPA in the CNS. Three chapters carefully detail the various aspects of the release of DOPA and the experimental characterization of these processes. The major part of the book deals with the pharmacology of DOPA; 10 chapters describe various aspects such as DOPA recognition, physiological responses, behavioral and modulatory effects, and the role of DOPA in relation to other neurotransmitters.

Clearly, a book written by over 40 leading experts sometimes suffers from overlap between chapters and from detailed descriptions of fractions of the vast research on DOPA. The editors did structure the book in a logical and comprehensive way, and the overlap is thus minimized. Some chapters are written in a cutting-edge-research descriptive style, and others reflect critical and fundamental findings on the complex biology of DOPA.This comprehensive overview of the recent developments of DOPA as a neurotransmitter is a must-read for every neuroscientist working on endogenous neurotransmitters. In particular, the chapters on pharmacology and neurotoxicology are written by experts for experts. In addition, the introductory chapters provide an overview regarding the neurobiology of DOPA and thus provide interesting aspects to any researcher working on this amino acid. As DOPA is involved in many other different biological functions such as melanogenesis, as an intermediate for many other biologically active molecules, and also as a key amino acid in mussel adhesive proteins, scientists from such different fields as natural products chemistry, biochemistry, and even materials science will find it an interesting read.

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