



# Progress in Drug Research

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## Foreword by the Editor

This 59th volume of the series *Progress in Drug Research* contains seven reviews which all highlight latest insight and discoveries in drug research and applications. Recently, polyamine metabolism and function attracted considerable interest in connection with the pathology of brain damage, cancer and other diseases. As a consequence, inhibition of monoamine oxidase became an important target in drug research and development. Nikolaus Seiler, a pioneer in this field of research, and his colleagues, provide – in the first article – an account of properties, applications and therapeutic potentials of polyamine oxidase inactivators, thus indicating a way for new therapies and for improving known ones.

The recent, renewed interest in the mechanism of action of ribavirin results from its synergetic enhancement of interferon therapy and the need to develop more efficacious agents for the treatment of hepatitis C virus infection. In the second article, Zhi Hong and Craig E. Cameron describe the mechanism of action of ribavirin and propose new strategies for development of nucleoside analogs that may replace ribavirin in the future.

In the next review, Jie Hong Hu and Charles Krieger summarise the numerous studies to elucidate why there is selective involvement of motor neurons in amyotrophic lateral sclerosis. Recent observations have demonstrated altered activities and protein levels of diverse kinases in the brain and spinal cord of transgenic mice, and the authors undertake to demonstrate the role of protein kinases and protein phosphatases as well as the molecular organization of protein phosphorylation networks. A better insight in these processes is crucial to determine the mechanisms of selective motor neuron death and, thus, the involvement of motor neurons in amyotrophic lateral sclerosis.

The transport of dopamine across the neuronal membrane to concentrate the neurotransmitter inside the cell is catalyzed by the dopamine transporter. The recent advances in knowledge of the transmembrane spanning protein have led to more insight into its mechanism and pharmacology: James O. Schenk's review focuses on the kinetics of transporters and kinetic measurements and provides an overview of the multisubstrate mechanism of dopamine transporter and its pharmacology especially with regard to amphetamine, cocaine and methylphenidate. In the next article, Laszlo

Prokai provides first an overview of the extrahypothalamic and receptor distribution, and of the neurophysiological, neuropharmacological and neurochemical effects of the thyrotropin-releasing hormone, and proceeds then to a thorough discussion of the efforts devoted to enhance therapeutically beneficial central nervous system effects *via* structural modifications of the endogenous peptide. In the context of developing agents to treat maladies affecting the brain and the spinal cord, thyrotropin-releasing hormone served as a molecular lead and the author can report successful development of several centrally active analogues.

In the sixth article, David F. Horrobin presents a novel category of psychotropic drugs: neuroactive lipids as exemplified by ethyl eicosapentaenoate. It was found that neuroactive lipids represent an entirely new class of psychotropic agents and ethyl eicosapentaenoate is the first example in this group undergoing extensive clinical investigation. Placebo-controlled studies have demonstrated that it is effective in depression, in the treatment-unresponsive schizophrenia and in tardive dyskinesia.

The last article deals with estrogen-dependent disorders. Subrabhat Ray and his colleagues outline the manifold problems in designing a tissue-selective estrogen for use as a pharmaceutical in estrogen-dependent disorders and highlight the current status of estrogen receptors.

All these seven review articles contain extensive bibliographies, thus enabling the interested reader and the active researcher to have easy access to the original literature. The various indices facilitate the use of these monographs and also help to use PDR as an encyclopedic source of information in the complex and fast growing field of drug research.

The series *Progress in Drug Research* was founded in 1958/59. In the 43 years of its existence, drug research has undergone drastic changes, but the original purpose of these monographs remains unchanged: dissemination of information on trends and developments, discussion of crucial points and creation of new prospects on future drug design. The Editor is anxious to maintain the high standard of PDR and is grateful to the authors for their willingness to undertake the hard work of writing comprehensive review articles for the benefit of all involved with drug research. It is these authors' high qualification and experience on which the success of these monographs is based.

In ending this foreword, I would like to thank the authors for their contributions, the members of the Board of Advisers for their active help and

advice and the reviewers for their constructive criticism which is important for improving these monographs. Last but not least, I am greatly indebted to Birkhäuser Publishers and in particular to Beatrice Menz and Gabriele Fer-töszögi, Editorial Department Biosciences, for their active participation with editing and producing this new volume. Hans-Peter Ebnetter, Bernd Luchner, Eduard Mazenauer and Gregor Messmer as well as the typesetters, Sylvia and Micha Lotrovsky, have contributed their vast experience and intimate knowl-edge to the production of this book. My sincere thanks are due for their cre-ative efforts and also for their personal engagement and for the rewarding, harmonious cooperation.

My very special thanks go to Mr. Hans-Peter Thür, Birkhäuser Publishing CEO. For the many decades of our close cooperation, Mr. Thür gave PDR and its Editor his full support and never ceased to give impulses which go far beyond his function as CEO. I would like to acknowledge that some of the most valuable articles have been the result of Mr. Thür's suggestion, and it is also due to his encouragement the I continue, after 43 years, still with great enthusiasm with the editorship of this series of monographs.

Basel, August 2002

Dr. E. Jucker