Monoamine Oxidase and Its Selective Inhibitors

Modern Problems of Pharmacopsychiatry

Vol. 19

Series Editors

S. Karger Basel Mnchen Paris London New York Sydney

Satellite Symposium of the International Brain Research Organization,
Mannheim, March 29-30, 1982

Monoamine Oxidase and Its Selective Inhibitors

Volume Editors
H. Beckmann, Mannheim; P. Riederer, Wien

109 figures and 89 tables, 1983

S. Karger Basel Mnchen Paris London New York Sydney

Modern Problems of Pharmacopsychiatry

National Library of Medicine, Cataloging In Publication
Monoamine Oxidase and Its Selective Inhibitors satellite symposium of the International Brain Research Organization,
Mannheim, March 29-30, 1982
(Modern problems of pharmacopsychiatry, v 19)
1 Monoamine OXldase - congresses 2 Monoamme OXidase Inhibitors - congresses I Beckmann, H. (Helmut)
II Riederer, P (Peter) III International Bram Research Organization IV Senes
WI MOL68Pv 19(QV77.5M7505 1982)
ISBN 3-8055-3595-3

Drug Dosage
The authors and the publisher have exerted every effort to ensure that drug selection and dosage
set forth in
this text are in accord with current recommendations and practice at the time of publication.
However, in view
of ongoing research, changes in government regulations, and the constant flow of information
relating to drug
therapy and drug reactions, the reader is urged to check the package insert for each drug for any
change in indications
and dosage and for added warnings and precautions. This is particularly important when the
recommended
agent is a new and/or infrequently employed drug.

All rights reserved.
No part of this publication may be translated into other languages, reproduced or utilized in any
form or by any
means, electronic or mechanical, including photocopying, recording, microcopying, or by any
information storage
and retrieval system, without permission in writing from the publisher.

Copyright 1983 by S Karger AG, P.O. Box, CH-4009 Basel (Switzerland)
Printed in Switzerland by gdz (Genossenschaftsdruckerei Zurich)
ISBN 3-8055-3595-3

Contents

Preface ........................................................................................................ IX
List of Abbreviations .................................................................................. X

Basic Aspects of MAO and Its Selective Inhibitors

Sourkes. T.L. (Montreal, Que.): Monoamine Oxidase: Synthesis, Metabolism and
Function .................................................................................................... 1
in the Selective Inhibition of Monoamine Oxidase ..................................... 15
Buech. O.; Feiner. A.E. (Basel): Characterization of a New, Short-Acting
and Specific Inhibitor of Type A Monoamine Oxidase ............................ 31
in Healthy Volunteers by COP 11305 A, a New Specific Inhibitor of
MAO-A .................................................................................................... 53
Inhibition for Antidepressant Therapy .................................................. 63
Kawai. S.; Nakano. T. (Gifu); Nagatsu. T. (Yokohama): A New Assay of
Monoamine Oxidase Activity for Selective Substrates and Inhibitors ........... 75
Strolin Benedetti. M.; Dostert. P.; Guffroy. e. (Rueil-Malmaison); Tipton. K.F. (Dublin): Partial or Total Protection from Long-Acting Monoamine Oxidase Inhibitors (MAOIs) by New Short-Acting MAOIs of Type A MD780515 and Type B MD780236 ....................................... 82

Contents VI

Selective and Nonselective MAO Inhibitors in Therapy

Birkmayer, W. (Vienna); Knoll, J. (Budapest); Riederer. P. (Vienna); Youdim, M.B.H. (Haifa): (-)-Deprenyl Leads to Prolongation of L-Dopa Efficacy in Parkinson's Disease ....................................................... 170
Yu, P.H.; Hertz, L. (Saskatoon, Sask.): Studies of the Type A and Type B Monoamine Oxidase: A New Approach to Their Development and Subcellular Localization ................................................................. 177
Van de Merwe, T.J.; Pare, C.M.B.; Glover, V.; Sandler. M. (London): Tranylcypromine Isomers in Depressed Outpatients: Effects on Depression, Monoamine Oxidase Inhibition and Tyramine Pressor Response .................. 189
Greeff, K.; Denes. B.; Tawfik. H. (Dusseldorf): Cardiovascular Effects of (+)- and (-)-Tranylcypromine Compared to Other Monoamine Oxidase Inhibitors. 220
Effects in vitro and in vivo of the Antidepressant Ro 11-1163, a Specific and Short-Acting MAO-A Inhibitor ................................................................. 231

MAO in Psychiatric Research
Oreland. L.; Arai. Y.; Stenstrm, A. (Umea); Fowler. C.J. (Sdertiilje): Monoamine Oxidase Activity and Localisation in the Brain and the Activity in Relation to Psychiatric Disorders .............................................. 246
Reynolds. G.P. (Cambridge); Riederer. P. (Vienna): Assessment of MAO Inhibitors Using Postmortem Human Brain Tissue: Biochemical and Therapeutic Implications ........................................ 255
Agarwal, D.P. (Hamburg); Philippu, G.; Milech. U. (Wurzburg); Goedde, H. W. (Hamburg); Schrappe, O. (Wurzburg): Platelet Monoamine Oxidase Activity in Alcoholics ........................................ 260
Buchsbaum. M.S.: Coursey, R.D. (College Park, Md.): Biological High-Risk Paradigm and Platelet MAO Activity in Community Samples ................... 278

Contents VII

Murphy, D.L.; Cohen, R.M.; Siever, L.J.; Roy, B.; Karoum, F.; Wyatt, R.J.; Garrick, N.A.; Linnoila, M. (Bethesda, Md.): Clinical and Laboratory Studies with Selective Monoamin-Oxidase-Inhibiting Drugs. Implications for Hypothesized Neurotransmitter Changes Associated with Depression and Antidepressant Drug Effects ........................................ 287
Propping, P.; Friedl, W. (Heidelberg): Platelet MAO Activity and High Risk for Psychopathology in a German Population ................................. 304
Gattaz, W.F. (Mannheim): Platelet MAO Activity in Major Psychoses .......... 315
Hoisboer, F.; Benkert, O. (Mainz); Demisch, L. (Frankfurt): Changes in MAO Activity during Estrogen Treatment of Females with Exogenous Depression. 321
Fühndrich, E.; Muller-Oerlinghausen, B. (Berlin): MAO Activity in Platelets before and after Sleep Deprivation as Predictor for Antidepressive Drug Response ........................................ 327
Sourkes, T.L. (Montreal, Que.): Discussion of Symposium, and Proposals for Further Work ................................................................. 337
Birkmayer, W. (Vienna): Outline .......................................................... 341
Subject Index ........................................................................... 343
Author Index ...................................................................... 351

Preface

The great interest in MAO inhibitors awakened by introducing
them into the treatment of depression (G.E. Crane, N. Kline), Parkinson's
disease (W. Birkmayer), as well as the possible implications of
MAO for schizophrenia (D.L. Murphy, R.J. Wyatt) has been overshadowed
by these drugs' serious side effects. In fact, in the late sixties and
the early seventies, MAO research was rather rare. Joseph Knoll
worked on the pharmacology of (-)deprenyl; Johnston developed the
concept of the MAO-A and MAO-B subtypes, and Merton Sandler's
group described multiple forms of MAO in the human brain. Again, it
took some years before a fortunate constellation consisting of Joseph
Knoll ? Moussa Youdim ? Peter Riederer ? Walther Birkmayer led to
the first clinical application of (-)-deprenyl for Parkinson's disease.
Confirmation of this trial by several research groups, and the discovery
of dopamine to be an excellent B-substrate in man (Merton Sandler),
stimulated research into MAO once again. A number of new compounds
have been tested for their possible clinical application, and the
'dernier cri' are selective, reversible inhibitors. The new approaches
have led to an increasing frequency of MAO symposia during the past
years. Why then another such meeting? We are of the opinion that theoretical
progress in MAO research must have a clinical correlate, and we
expect a stimulating dialogue between clinicians who have experience
with these new drugs and research workers who are veterans in the
field.
We thank our host, Prof. Dr. Dr. H. Hfner, for holding this symposium
in the Zentralinstitut fr Seelische Gesundheit, Mannheim. We
are also very grateful to Mrs. I. Treudler and Rahm-Pharma for the excellent
organization of this international meeting.

Helmut Beckmann,
Peter Riederer

List of Abbreviations

AMP Adenosine monophosphate
ATP Adenosine triphosphate
BSA Bovine serum albumin
COMT Catechol-O-methyltransferase
CRAO Clorgyline-resistant amine
oxidase
CSF Cerebrospinal fluid
DA Dopamine
DA-S04 Dopamine-3-0-sulfate
DOPAC 3,4-dihydroxyphenylacetic
acid
DST Dexamethasone suppression test
ECD Electron-capture detector
EPQ Eysenck Personality Questionnaire
FAD Flavin adenine dinucleotide
FMN Flavin mononucleotide
FPI Freiburger Personlichkeitsinventar
GOT Glutamic oxaloacetic transaminase
GPT Glutamic pyruvic transaminase
-GT -Glutamyl transpeptidase
HDRS Hamilton depression rating scale
5-HIAA 5-Hydroxyindoleacetic acid
HPLC High-pressure liquid chromatography
S-HT S-Hydroxytryptamine = serotonin
L-S-HTP L-S-Hydroxytryptophan(e)
HVA Homovanillic acid
MAO Monoamine oxidase
MAO! Monoamine oxidase inhibitor
MEK Methyl ethyl ketone
MHPG 3-Methoxy,4-hydroxyphenyl glycol
MMPI Minnesota Multiphasic Personality Inventory
MOPEC-S04 3-Methoxy,4-hydroxyphenyletheneglycol sulfate
NA Noradrenaline
NE Norepinephrine
PB Blood pressure
PE Phenylephrine
PEA Phenylethylamine
PFBOA Pentafluorobenzylamine hydrochloride
PRP Platelet-rich plasma
RDC Research Diagnostic Criteria
SEM Standard error
TCP Tranylcypromine
TRY L-Tryptophan (ε)
TY Tyramine