Basic and Clinical Toxicology of Mustard Compounds

Mahdi Balali-Mood • Mohammad Abdollahi Editors

Basic and Clinical Toxicology of Mustard Compounds



Editors
Mahdi Balali-Mood
Medical Toxicology Research Centre
Mashhad University of Medical Sciences
Mashhad
Iran

Mohammad Abdollahi Department of Toxicology & Pharmacology Tehran University of Medical Sciences Tehran Iran

ISBN 978-3-319-23873-9 DOI 10.1007/978-3-319-23874-6 ISBN 978-3-319-23874-6 (eBook)

Springer Cham Heidelberg New York Dordrecht London © Springer International Publishing Switzerland 2015

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made.

Printed on acid-free paper

Springer International Publishing AG Switzerland is part of Springer Science+Business Media (www. springer.com)

Preface

Later on the use of chemical warfare agents (CWA) during World War I, all the nations knew the extent of the tragedy and became against CWA. In spite of the Geneva Protocol in 1925 and further chemical weapon conventions and conferences in the last century, CWA including sulfur mustard (SM) and the nerve agents were unfortunately used in the Iraq-Iran conflict (1983–1988) by the Iraqi time regime and in the terrorist attack in Matsomoto and Tokyo metro of Japan (1994–1995).

SM was first synthesized by a Belgian chemist, Cesar Mansuète Despretz in 1822; then a German chemist, Victor Meyer, completely described the chemical structure of SM in 1886. It was first used during World War I in 1917. Nitrogen mustard (NM) was initially synthesized as a CWA after World War I, but has never been used as a chemical weapon. It is used as an anticancer medicine. Lack of scientific knowledge on mustard compounds (MC) in medicine and the science of toxicology have made a heavy mess of confusion among some health professionals and scientists on the differentiation between NM and SM. The problems of NM administration and its toxic effects in patients who take this chemical as an antineoplastic agent and also malpractice on the clinical management of patients who were exposed to SM during the chemical wars or in occupational settings have lead us to form this book.

There have been some little books with narrow separate subjects on NM and SM, but a comprehensive book on Basic and Clinical Toxicology of MC as a reference for pharmacologists, toxicologists, and health professionals who deal with different facets of these compounds has been missing.

The main objective of this book is to provide scientific information and practical guide on MC for the scientists and health professionals who are involved in educational activity, research, and medical care of the patients. The regulatory authorities in different departments of Labor, environment, industries, military, and health as well as the international governing bodies such as the UN, WHO, ILO, Red Cross, and OPCW or the national authorities of CW conventions and military toxicologists shall also use this book.

The first editor of this book has been in charge of the Medical Toxicology Centre (the referral center for CWA victims during the Iraq-Iran war) of Mashhad University

vi Preface

of Medical Sciences since 1982. All the exposed chemical warfare victims, mainly SM poisoning cases who were transferred to Mashhad have been under his medical attention. He has likewise been involved in instruction and research in medical aspects of the CWA, mainly SM exposure at the national and international stages, giving plenary lectures at the world conferences of toxicology and published over 60 articles, book chapters, monographs, and books in this area. The second editor of this book is also an internationally known scientist with lots of studies, publications, and citations in the field of toxicology and pharmacology. Both editors have had collaborations with different international organizations including WHO and OPCW dealing with toxicological issues. The selected authors of the chapters are highly experienced experts in the fields and have done their great efforts for the best writing and revising the chapters under the supervision of the editors.

This volume holds 15 chapters from chemistry, history of employment, basic pharmacology and toxicology to clinical, military, occupational, and environmental aspects of MC. The national and international concerns on the use of MC as CWA have also been considered. The concluding chapter written by the editors summarizes the whole book content and provides expert opinion of the editors. We hope that all students, researchers, regulators, military, security, and health professionals who are involved in the area of toxicology specially CWA will benefit from this book.

Understanding and kind supports of our families who encouraged us to work hard at home on this book project are highly appreciated. We are of course very grateful to the authors of the chapters for their hard work during writing and making several revisions. We would also wish to thank the Springer publisher specially Ms Manika Power (right away moved out of Springer) and Ms Rosie Daniel, who kindly cooperated with this book project.

We would welcome any comments and feedback from the experts in the field to help us improve the future editions.

Mahdi Balali-Mood, MD, PhD Medical Toxicology Research Centre, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Mohammad Abdollahi, Pharm D, PhD
Department of Toxicology and Pharmacology,
Faculty of Pharmacy and Pharmaceutical Sciences Research Center,
Tehran University of Medical Sciences, Tehran, Iran

Editor Biography



Mahdi Balali-Mood was awarded BSc 1st class Hon of chemistry in 1963 and then MD in 1970 from Tehran University. After his medical military service and training in internal medicine/clinical toxicology, he was appointed as an assistant professor in clinical toxicology and head of his newly established Poisoning Treatment Center (PTC) of Mashhad University in 1974. Mahdi was awarded a scholarship from the Ministry of Science of Iran and did his PhD in Clinical Pharmacology & Toxicology at Edinburgh University Medical School in 1978–1981. He was then working as a lecturer in this department until winter 1982, when decided to return to Mashhad to advance his established PTC, as the chemical war gas attack of Iraqi army against Iranian troops was his main concern.

Mahdi was promoted to associate professor and full professor of Medicine and Clinical Toxicology, Mashhad University Medical Sciences (MUMS) in 1984 and 1988, respectively.

He has served as a Clinical Toxicology Adviser to the International Programme on Chemical Safety (IPCS) and the World Health Organization (WHO), 1989 to date. He has also been a member of the IPCS Programme Advisory Committee since 2000.

Prof. Balali-Mood was a founding member and the first President of Iranian Society of Toxicology and was also elected twice as the President of Irantox between

viii Editor Biography

1989 and 2001. He has been a member of the Iranian Academy of Medical Sciences since its establishment in 1990.

Mahdi with collaboration of the other internationally recognized medical toxicologists founded the Asia-Pacific Association of Medical Toxicology (1989) and served as the first Vice-President and then as the President for 8 years (1994–2001). He was elected as a Permanent Member of the Academy of Sciences for Developing World (TWAS) in 1997. He was a member of Scientific Advisory Board of the Organization for Prohibition of Chemical Weapons (OPCW) 2004–2011.

His other achievements include co-founder and Director, Medical Toxicology Research Centre, Faculty of Medicine, Mashhad University of Medical Sciences, 1988 to date; Editor-in-Chief, *Scientific Journal of Birjand University of Medical Sciences*, 2002 to date; and Associate Editor and editorial board member of many national and international medical journals.

His research areas are Clinical Toxicology of Chemical Warfare Agents, Organophosphorous Pesticide Poisonings, Heavy Metals, Drug Abuse/Overdosage, Epidemiology of Poisonings, Occupational and Environmental Toxicology, and Natural Toxins including snake and spider bites.

Prof. Balali-Mood was awarded several national and international prizes on Teaching, Research, and Medical Care including the prizes in medical care of chemical war veterans and research from the Presidents of IR Iran in 2003 and 2011, respectively. He supervised more than 100 theses for MSc, PhD, PharmD, MD, and specialities in clinical medicine, mostly on CWA. Mahdi is the author/editor of 29 books/monographs/chapters and 147 articles and 289 short papers and abstracts. His recent books on *Basic and Clinical Toxicology of Organophosphorus Compounds* and on *Biological Toxins and Bioterrorism* were published by Springer in 2014 and 2015, respectively.

Editor Biography ix



Mohammad Abdollahi (MA) acquired a PharmD in 1988 from the University of Tehran and then finished a PhD in Toxicology and Pharmacology in 1994 from the Tehran University of Medical Sciences in 2001. MA completed his postdoctoral training in Mechanistic Toxicology in the School of Pharmacy of the University of Toronto. In the interim, he contributed in a key meta-analysis study in the School of Medicine, University of Toronto. MA has obtained the honor of full professorship of Tehran University of Medical Sciences (TUMS) since the second half of 2002. He has chaired the Department of Toxicology and Pharmacology at the Faculty of Pharmacy, TUMS since 2005. So far, MA has contributed in authoring more than 650 papers in prestigious journals and authoring 48 book chapters and editing 11 books. MA has been listed among top scientists of ESI/ISI and OIC Member States. According to Google Scholar, current H-index, total citations, and i10 index of MA are 64, \$\geq 15,500\$, and 340, respectively. Total citations of MA in the books are more than 1000. MA is the Editor-in-Chief of two TUMS prestigious journals published by Springer BMC and Elsevier. MA has cooperated with some key international organizations such as OPCW (Organization for Prohibition of Chemical Weapons) as a Scientific Advisory Board in the Netherlands (since 2012), WHO (World Health Organization) as a Member of Guideline Developing Group for Prevention of Lead Poisoning in Switzerland (since 2011), COPE (Committee on Publication Ethics) as a Council Member in the UK (since 2013), World Library of Toxicology as the Country Correspondent (since 2008), IAS (Islamic-World Academy of Sciences) as a Fellow (since 2007), International Society of Pharmacoeconomics and Outcomes Research (ISPOR) Iran Chapter as a Founder/Board of Directors (since 2013), and Asian Council of Science Editors as the Board of Directors (since 2014). In addition to more than ten prestigious national awards, MA has received the prominent award of IAS-COMSTECH in 2005 in the field of Pharmacology & Toxicology. The main research interests of MA are Mechanistic and Environmental Toxicology, Evidence-Based Medicine, and Pharmacology. MA's contribution to this field is attested by an extensive array of citations in papers and books. MA has uncovered the critical mechanistic connections between the toxicity of chemicals and the etiology of human diseases.

Contents

1	Chemistry of Mustard Compounds	1
2	History of Use and Epidemiology of Mustard Compounds Leila Etemad, Mohammad Moshiri, and Mahdi Balali-Mood	29
3	Basic Pharmacology and Toxicology	49
4	Clinical Pharmacology and Toxicology of Mustard Compounds Adel Ghorani-Azam and Mahdi Balali-Mood	63
5	Delayed Complications and Long-Term Effects of SM Poisonings: Experience of Iran-Iraq War Emadodin Darchini-Maragheh, Peter G. Blain, and Mahdi Balali-Mood	101
6	Upper Respiratory Complications of Sulfur Mustard (SM) Poisoning	135
7	Lower Airway Complications of Sulfur Mustard Exposure Mostafa Ghanei and Amin Saburi	171
8	Dermatologic Aspects of Sulfur Mustard Exposure	213
9	Ocular Injury by Mustard Gas; Early and Late Complications Nasser Shoeibi, Mojtaba Abrishami, and Alireza Eslampoor	253
10	Immunological and Hematological Complications of Sulfur Mustard Poisoning	273

xii Contents

11	Psychiatric Complications of Sulfur Mustard (SM) Poisoning Mohammad Reza Fayyazi Bordbar, Farhad Faridhosseini, and Ali Saghebi	291
12	Genotoxicity, Teratogenicity and Mutagenicity of Sulfur Mustard Poisoning Effat Behravan and Mitra Asgharian Rezaee	317
13	Verification of SM Exposure in Biological Samples	349
14	Occupational and Environmental Mustard Exposure, Prevention and Chemical Weapons Convention Slavica Vucinic, Branka Djurovic, and Biljana Antonijevic	359
15	Summary and Conclusion	389
Ind	ex	401

Contributors

Mohammad Abdollahi, PharmD, PhD Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran

Mojtaba Abrishami, MD Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Sciences, Tehran, Iran

Biljana Antonijevic Faculty of Pharmacy, University of Belgrade, Belgrade, Serbia

Morteza Mazloum Farsi Baf Faculty of Medicine, Mashhad Branch, Islamic Azad University, Mashhad, Iran

Mahdi Balali-Mood Medical Toxicology Research Centre, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Beeta Balali-Mood MoodBioPharm, London, UK

Effat Behravan Medical Toxicology Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Peter G. Blain Medical Toxicology Centre, Newcastle University, Newcastle, UK

Mohammad Reza Fayyazi Bordbar Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Emadodin Darchini-Maragheh Medical Toxicology Research centre, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Branka Djurovic Institute of Occupational Medicine, Military Medical Academy, Medical Faculty/University of Defense, Belgrade, Serbia

Alireza Eslampoor, MD, FICO Eye Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

xiv Contributors

Leila Etemad Pharmaceutical Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Farhad Faridhosseini Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Mostafa Ghanei Chemical Injuries Research Center & Faculty of Medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

Adel Ghorani-Azam Faculty of Medicine, Medical Toxicology Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran

Pouran Layegh Dermatology Department, Cutaneous Leishmaniasis Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Ghaem Hospital, Mashhad, Iran

Mahmoud Mahmoudi Department of Immunology and Allergy, Immunology Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Masoud Maleki Dermatology Department, Cutaneous Leishmaniasis Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Emam Reza Hospital, Mashhad, Iran

Mohammad Moshiri Pharmacodynamy and Toxicology Department, Faculty of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran

Health Insurance Research Office, Mashhad Branch, Health Insurance Research Office, Armed Forces Insurance Organization of Islamic Republic of Iran (Mashhad Branch), Tehran, Iran

Sara Mostafalou, PharmD, PhD School of Pharmacy, Ardabil University of Medical Sciences, Ardabil, Iran

Mitra Asgharian Rezaee Department of Toxicology and Pharmacology, Faculty of Pharmacy, Kerman University of Medical Sciences, Kerman, Iran

Bamdad Riahi-Zanjani Medical Toxicology Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Amin Saburi Chemical Injuries Research Center & Faculty of medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

Mahmood Sadeghi Medical Toxicology Research Center, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Ali Saghebi Department of Psychiatry, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Nasser Shoeibi, MD Eye Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Contributors xv

Dirk Steinritz Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany

Horst Thiermann Bundeswehr Institute of Pharmacology and Toxicology, Munich, Germany

Slavica Vucinic National Poison Control Centre, Military Medical Academy/ Medical Faculty, University of Defense, Belgrade, Serbia

Ramin Zojaji Mashhad Branch, Otorhinolaryngology Department, Islamic Azad University, Mashhad, Iran

Arya Teaching Medical Hospital ENT Department, Islamic Azad Medical University, Mashhad, Iran