SAPONINS USED IN TRADITIONAL AND MODERN MEDICINE

ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY

Editorial Board:

NATHAN BACK, *State University of New York at Buffalo*

IRUN R. COHEN, *The Weizmann Institute of Science*

DAVID KRITCHEVSKY, *Wistar Institute*

ABEL LAJTHA, *N. S. Kline Institute for Psychiatric Research*

RODOLFO PAOLETTI, *University of Milan*

Recent Volumes in this Series

Volume 400A

EICOSANOIDS AND OTHER BIOACTIVE LIPIDS IN CANCER, INFLAMMATION,
AND RADIATION INJURY, Part A

Edited by Kenneth V. Honn, Santosh Nigam, and Lawrence J. Marnett

Volume 400B

EICOSANOIDS AND OTHER BIOACTIVE LIPIDS IN CANCER, INFLAMMATION,
AND RADIATION INJURY, Part B

Edited by Kenneth V. Honn, Santosh Nigam, and Lawrence J. Marnett

Volume 401

DIETARY PHYTOCHEMICALS IN CANCER PREVENTION AND TREATMENT

Edited under the auspices of the American Institute for Cancer Research

Volume 402

AIDS, DRUGS OF ABUSE, AND THE NEUROIMMUNE AXIS

Edited by Herman Friedman, Toby K. Eisenstein, John Madden, and Burt M. Sharp

Volume 403

TAURINE 2: Basic and Clinical Aspects

Edited by Ryan J. Huxtable, Junichi Azuma, Kinya Kuriyama, and Masao Nakagawa

Volume 404

SAPONINS USED IN TRADITIONAL AND MODERN MEDICINE

Edited by George R. Waller and Kazuo Yamasaki

Volume 405

SAPONINS USED IN FOOD AND AGRICULTURE

Edited by George R. Waller and Kazuo Yamasaki

Volume 406

MECHANISMS OF LYMPHOCYTE ACTIVATION AND IMMUNE REGULATION VI:
Cell Cycle and Programmed Cell Death in the Immune System

Edited by Sudhir Gupta and J. John Cohen

Volume 407

EICOSANOIDS AND OTHER BIOACTIVE LIPIDS IN CANCER, INFLAMMATION,
AND RADIATION INJURY, Volume 2

Edited by Kenneth V. Honn, Lawrence J. Marnett, Santosh Nigam, Robert L. Jones,
and Patrick Y-K. Wong

Volume 408

TOWARD ANTI-ADHESION THERAPY FOR MICROBIAL DISEASES

Edited by Itzhak Kahane and Itzhak Ofek

A Continuation Order Plan is available for this series. A continuation order will bring delivery of each new volume immediately upon publication. Volumes are billed only upon actual shipment. For further information please contact the publisher.

SAPONINS USED IN TRADITIONAL AND MODERN MEDICINE

Edited by

George R. Waller

Oklahoma State University
Stillwater, Oklahoma

and

Kazuo Yamasaki

Hiroshima University
Hiroshima, Japan

SPRINGER SCIENCE+BUSINESS MEDIA, LLC

Library of Congress Cataloging in Publication Data

Saponins used in traditional and modern medicine / edited by George R. Waller, Kazuo Yamasaki.

p. cm.—(Advances in experimental medicine and biology; v. 404)

“Proceedings of an American Chemical Society Symposium on Saponins: Chemistry and Biological Activity, held August 20–24, 1995, in Chicago, Illinois”—T.p. verso.

Includes bibliographical references and index.

ISBN 978-1-4899-1369-2

ISBN 978-1-4899-1367-8 (eBook)

DOI 10.1007/978-1-4899-1367-8

1. Saponins—Therapeutic use—Congresses. I. Waller, George R. II. Yamasaki, Kazuo. III. American Chemical Society Symposium on Saponins: Chemistry and Biological Activity (1995: Chicago, Ill.) IV. Series.

[DNLM: 1. Saponins—therapeutic use—congresses. 2. Saponins—chemistry—congresses. W1AD559 v. 404 1996

RM666.S195S27 1996

615'.32—dc20

DNLM/DLC

for Library of Congress

96-29021

CIP

Proceedings of the 210th National Meeting of the American Chemical Society Symposium on Saponins: Chemistry and Biological Activity, held August 20 – 24, 1995, in Chicago, Illinois

ISBN 978-1-4899-1369-2

© 1996 Springer Science+Business Media New York

Originally published by Plenum Press, New York in 1996

Softcover reprint of the hardcover 1st edition 1996

10 9 8 7 6 5 4 3 2 1

All rights reserved

No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, electronic, mechanical, photocopying, microfilming, recording, or otherwise, without written permission from the Publisher

To Otis C. Dermer
Scientific Editor *par excellence*

PREFACE

The extraordinary technological advances made in saponin research in recent years that have been created and developed by the scientific establishments throughout the world are exciting, and they present intellectually challenging problems which are becoming more solvable using modern techniques. How many of us could have imagined a decade ago what has been accomplished in the chemical, biological, agricultural, and pharmaceutical laboratories that are being done routinely today. Advanced techniques in NMR spectroscopy, mass spectrometry, x-ray crystallography, use of enzymes, various chromatographic procedures, and new bioassays have been developed; the advances in these areas have been truly phenomenal. On the other hand we have not progressed nearly so much in natural products, particularly in saponin research, in adopting molecular biology in our scientific endeavors. It is our hope that finding a saponin that can inhibit a disease or plant traits (e.g. resistance to a virus, microorganism, or insects) can be isolated to a specific gene and this will become routine during the 21st century. The advances made in this book in our understanding of traditional and modern medicine are outstanding. We must be alert and learn to contribute to the knowledge of medicine and molecular biology with natural products, and particularly saponins.

Chemists, biochemists, and biologists from more than 25 countries presented their work at a 5-day symposium organized by the American Chemical Society (ACS), Division of Agricultural & Food Chemistry at the 210th Meeting during August in Chicago. Saponins have not been the subject of an ACS symposium before, and scientists in this field have not had an opportunity to consult with each other [at this level] and to develop plans for future work.

Saponins are a class of natural products which are structurally constructed of aglycones (triterpene or steroidal) and sugars (pentose(s), hexose(s), and/or uronic acid(s)). An appropriate hydrolysis of saponins yield sugars and the aglycone; however, hydrolysis does not necessarily produce the genuine aglycone. Saponins are biological detergents because of glycosylation of the hydrophobic aglycone, and when agitated in water form a soapy lather which gives rise to the name of the group of compounds. This unique ability to cause foaming has been used by mankind throughout the centuries for making cleaning solutions, and indeed it can act as an aid in identification of plant extracts. Triterpenoid, steroid, and steroid alkaloid glycosides are widely spread throughout the plant kingdom, and several have been found in marine animals. Some saponins have cardiac activity, hemolytic activity, activity as fish poisons, cholesterol-reducing ability, bitterness, ability to act as sweeteners, and cosmetics activity, and can also serve as allelochemicals; these are behaviors found in certain saponins rather than in all members of this chemical family. From the biological viewpoint saponins have a diverse group of properties, some deleterious but many beneficial. Their use in plant drugs, folk medicines, etc. has generated great interest in the chemical characterization of these molecules. This has been evident in the Orient (particularly Japan), where the literature on the isolation, purification, separation, structural elucidation, and biological activity of saponins attests to the skill of natural-products biochemists and chemists. It seems that the advantage of saponins to the plant producing them is that they function as protecting agents, growth regulators, and allelochemicals.

Interactions between participants during this meeting helped develop cooperative relationships, and promotes continued assistance of research and development on saponins

among scientists from over the world. Such research on saponins is now revealing a large array of plants from which to choose, while only a few have been studied at this time. In the future, cell culture techniques will allow the isolation and characterization of individual saponins as well as the enzymes catalyzing their production. The industrial demand for saponins is increasing and, with more attention being given to this field, it offers a renewable resource that provides a stable raw material with a practical and dependable supply.

The book is divided into three sections: commercial utilization and biosynthesis, inhibition of diseases of mankind, and antifungal and hemolytic activities. Inhibition of diseases of mankind can be broken down into the treatment of anti-cancer, molluscicidal, cardioactive, and hypercholesterolemic diseases, immunological adjuvant systems, and a host of traditional medical diseases. It was difficult to separate the traditional medicines from the modern medicines since the two are so closely intertwined. Attention is called to the appendixes which contain useful information on the saponin disease network and NMR and MS data bases. The partial reports of this symposium were published by *Chem. & Eng. News*, September 11, **73**, 28-35 (1995) and August 28, **73**, 8-9 (1995) are recommended for reading, although they are not included in this book.

Although this book cannot give a complete account of the meeting, we hope that it will serve as the starting point to help guide the research of others. We especially thank those who contributed chapters but did not attend the symposium. We are pleased that saponin research and development as well as its commercial products will now be the subject of ongoing international meetings.

We acknowledge with sincere appreciation financial support for this symposium from the following organizations/companies: International Science Foundation, Japan Society of Industrial Machinery Manufacturers, Kikkoman Co. Ltd., Maruzen Pharmaceutical Co. Ltd., NPS Pharmaceuticals, Inc., Shimadzu Scientific Instruments, Inc., The Soros Foundation, and the United States Tobacco Company.

George R. Waller
Kazuo Yamasaki

¹The next international meeting will be sponsored by the Phytochemical Society of Europe in Pulawy, Poland in 1999.

CONTENTS

COMMERCIAL UTILIZATION AND BIOSYNTHESIS

Commercial Utilization of Plant-Derived Saponins: An Overview of Medicinal, Pharmaceutical, and Industrial Applications Manuel F. Balandrin	1
Steroid Glycosides from Suspension Cultures of <i>Dioscorea deltoidea</i> Cells and Their Biological Activity Inessa S. Vasil'eva and Valentina A. Paseshnichenko	15
Glycosidases That Convert Natural Glycosides to Bioactive Compounds Chung Ki Sung, Geun Hyung Kang, Sang Sun Yoon, Ik-Soo Lee, Dong Hyun Kim, Ushiro Sankawa, and Yutaka Ebizuka	23
Purification and Properties of UDP-Glucose: Diosgenin/Tigogenin Glucosyltransferase from <i>Solanum melongena</i> Leaves Cezary Paczkowski and Zdzislaw A. Wojciechowski	37
Evidence for Separate Udp-Glucose: Spirostanol and Udp-Glucose: Solasodine Glucosyltransferases in <i>Solanum melongena</i> Cezary Paczkowski, Molgorzata Kalinowska, Roland Woldanski, and Zdzislaw A. Wojciechowski	47
Purification and Characterization of a B-Glucosidase which Converts Furostanol Glycosides to Spirostanol Glycosides from <i>Costus speciosus</i> Kentaro Inoue and Yutaka Ebizuka	57
Enzymatic Glycosylation of Tomatidine in Tomato Plants Jan Zimowski	71

Specificity of Elementary Composition of Plants in Synthesizing Saponins M.J. Lovkova, S.M. Sokolova, S.M. Ponomareva, and G.N. Busuk, and O.V. Shelepova	81
---	----

INHIBITION OF DISEASES OF MANKIND

Anti-Tumor-Promoting Activities of Triterpenoid Glycosides. Cancer Prevention by Saponins Takao Konoshima	87
Steroidal Saponins from the Liliaceae Plants and Their Biological Activities Yoshihiro Mimaki and Yutaka Sashida	101
Modified Steroidal Glycosides with Potential Biological Activity D. Iurea, C.V. Uglea, P.K. Kintia	111
Search for Molluscicidal and Antifungal Saponins from Tropical Plants K. Hostettmann, A Marston, M. Maillard, and J.L. Wolfender	117
New Saponins from Vietnamese Ginseng: Highlights on Biogenesis of Dammarane Triterpenoids Nguyen Minh Duc, Ryoji Kasai, Kazuhiro Ohtani, Aiko Ito, Kazuo Yamasaki, Nguyen Thoi Nham, and Osamu Tanaka	129
Investigations of Molluscicidal Saponins from the Endod Plant <i>Phytolacca dodecandra</i> Susanne T. Thiilborg, Claus Cornett, and Else Lemmich	151
Structure/Function Studies on Qs-21, a Unique Immunological Adjuvant from <i>Quillaja saponaria</i> Charlotte Read Kensil, Sean Soltysik, Deborah A. Wheeler, and Jia-Yan Wu	165
Saponins with Antifilarial Activity from <i>Acacia auriculiformis</i> Shashi B. Mahato	173
Molecular Structures of Saponins from <i>Quillaja saponaria</i> Molina Dirk C. van Setten and Gerrit van de Werken	185
Effect of Some Saponins on Glucose Transport System Kazuo Yamasaki	195

Inhibitory Effect of Oleanene-Type Triterpene Oligoglycosides on Ethanol Absorption: The Structure-Activity Relationships Masayuki Yoshikawa and Johji Yamahara.....	207
Search for an Endogenous Mammalian Cardiotonic Factor Koji Nakanishi, Nina Berova, Lee-Chiang Lo, Ning Zhao, James H. Ludens, Adrienne A. Tymiak, Bethanne Warrack, and Garner T. Haupt, Jr.....	219
Bioactive Triterpenoid and Steroid Saponins from Medicinal Plants in Southwest China Chong-Ren Yang and Xing-Cong Li	225
The pH-Dependent Channels Formed by Cauloside C Galina N. Likhatskaya, Dmitry L. Aminin, Irina G. Agafonova, Sergey N. Gnedei, Elena B. Shentsova, Lybov I. Strigina, and Michail M. Anisimov	239
Steroidal Glycosides from <i>Petunia hybrida</i> L. Seeds and Their Biological Activity S.A. Shvets, P.K. Kintia, and M.A. Naibi	251
Bioactive Saponins from Solanaceous and Leguminous Plants Toshihiro Nohara, Shoji Yahara, and Junei Kinjo	263
Steroidal Glycoalkaloids: Nature and Consequences of Bioactivity James G. Roddick	277
Saponins from the Compositae Plants: Structures of the Saponins from <i>Aster scaber</i> Thunb Tsuneatsu Nagao, Ryuichiro Tanaka, and Hikaru Okabe.....	297
Chemistry and Biological Activity of Steroid Saponins from Moldovian Plants P.K. Kintia	309
Steroid and Triterpenoid Oligoglycosides of Marine Origin L. Minale, M. Iorizzi, E. Palagiano, and R. Riccio	335
New Cardioactive Steroid Saponins and Other Glycosides from Mexican <i>Tribulus cistoides</i> Hans Achenbach, Harald Hübner, and Melchior Reiter	357
Studies on Bioactive Saponins from Chinese Medicinal Plants Rensheng Xu, Weimin Zhao, Junping Xu, Baoping Shao, and Guowei Qin	371

Structural and Antimalarial Studies of Saponins from <i>Nauclea diderrichii</i> Bark Maroufath Lamidi, Evelyne Ollivier, Monique Gasquet, Robert Faure, Lucienne Nzé-Ekekang, and Guy Balansard	383
New Biologically Active Steroidal and Triterpenoid Glycosides from Medicinal Plants R. Aquino, F. De Simone, N. De Tommasi, S. Piacente, and C. Pizza	401
Biological Activity of Saponins from Two <i>Dracaena</i> Species C.O. Okunji, M.M. Iwu, J.E. Jackson, and J.D. Tally	415
Phyto-Pharmacology of Saponins from <i>Symphytum officinale</i> L. Khalid Aftab, Fehmeena Shaheen, Faryal Vali Mohammad, Mushtaq Noorwala, and Viqar Uddin Ahmad	429
Metabolites of Nuatigenin ((22S,25S)22,25-Epoxy-3 β ,26-Dihydroxy-Furost-5-Ene) Accumulate in the Bile of Rabbits Fed Oats Jan St. Pyrek, Suresht K. Aggarwal, Perry Barboza, Jack P. Goodman, and Pei-Ying Yang.....	443
Acylated Saponins from <i>Crocoshia</i> Plants Yoshihisa Asada and Tsutomu Furuya	459
Medical Activities of <i>Aesculus hippocastaneum</i> (Horse-Chestnut) Saponins E. Dworschák, M. Antal, L. Biró, A. Regöly-Mérei, K. Nagy, J. Szépvölgyi, O. Gaál, and G. Biró	471
A Chemical Study of the Steroidal Glycosides from <i>Atropa belladonna</i> Seeds S.A. Shvets, N.V. Lattserdis, and P.K. Kintia	475
Triterpene Saponins from Plants of the Flora of Turkey Ihsan Calis and Otto Sticher	485
Triterpene Glycosides of <i>Sophora japonica</i> L. Seeds L.A. Gorbacheva, V.I. Grishkovets, G.A. Drozd, and V.Ya. Chirva	501
Antiviral Activity of Tomatoside from <i>Lycopersicon esculentum</i> Mill K. Spinu, V. Vorozhbit, T. Grushko, P. Kintia, P. Skoferts, V. Vutkaryov, and V. Bologa	505

ANTIFUNGAL AND HEMOLYTIC ACTIVITIES

19 New Steroidal Saponins from <i>Allium</i> Plants: Isolation, Structural Elucidation, and Effect on Blood Coagulability Jun-peng Peng and Xin-sheng Yao	511
Fungitoxic Activity of Saponins: Practical Use and Fundamental Principles Katalin Gruiz	527
Saponins as Antimycotic Agents: Glycosides of Medicagenic Acid Uri Zehavi and Itzhack Polacheck	535
Saponin Detoxification by Plant Pathogenic Fungi Anne E. Osbourn, Paul Bowyer, and Michael J. Daniels	547
Hemolytic Activity of Triterpene Glycosides from the Dendrochirotida Order Holothurian Vladimir I. Kalinin, Nina G. Prokofieva, Galina N. Likhatskaya, Elena B. Schentsova, Irina G. Agafonova, Sergey A. Avilov, and Olga A. Drozdova	557
Antifungal and Hemolytic Activity of Aerial Parts of Alfalfa (<i>Medicago</i>) Species in Relation to Saponin Composition M. Juryzsta and G.R. Waller	565

APPENDIX

Saponin Network for Mass Spectrometry and Nuclear Magnetic Resonance Spectrometry	575
Contributors	579

INDEXES

Latin Name Index	587
Subject Index	593