Biochemistry of Selenium

BIOCHEMISTRY OF THE ELEMENTS

Series Editor: Earl Frieden

*Florida State University
Tallahassee, Florida*

Volume 1 **BIOCHEMISTRY OF NONHEME IRON**
Anatoly Bezkorovainy

Volume 2 **BIOCHEMISTRY OF SELENIUM**
Raymond J. Shamberger

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.

Biochemistry of Selenium

Raymond J. Shamberger

*The Cleveland Clinic Foundation
Cleveland, Ohio*

PLENUM PRESS • NEW YORK AND LONDON

Library of Congress Cataloging in Publication Data

Shamberger, Raymond J., 1934–
Biochemistry of selenium.

(Biochemistry of the elements, v. 2)

Bibliography: p.

Includes index.

1. Selenium—Physiological effect. 2. Selenium—Metabolism. I. Title. II. Series.

[DNLM: 1. Selenium. QU 130 B6144 1980 v. 2]

QP535.S5S45 1983

574.19/214

82-22316

ISBN-13: 978-1-4684-4315-8 e-ISBN-13: 978-1-4684-4313-4

DOI: 10.1007/ 978-1-4684-4313-4

© 1983 Plenum Press, New York
Softcover reprint of the hardcover 1st edition 1983
A Division of Plenum Publishing Corporation
233 Spring Street, New York, N.Y. 10013

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

Preface

In recent years many exciting research results have indicated that selenium, depending on its concentration, can influence mammalian metabolism. It has been estimated that in selenium-deficient areas, selenium or selenium-vitamin E combinations added to animal feed can prevent annual losses to beef and dairy cattle and sheep valued at 545 million dollars and poultry and swine losses valued at 82 million dollars.

Some animal diseases that can be prevented by a selenium-supplemented diet include liver necrosis, nutritional muscular dystrophy, exudative diathesis, pancreatic degeneration, mulberry heart disease, infertility, growth impairment, periodontal disease, and encephalomalacia. Selenium intake levels are dependent on the plant or animal feed concentrations, which, in turn, are dependent on the pH of the soil and the types of rocks from which the soils are derived.

At normal metabolic levels selenium possesses an antioxidant effect manifested through glutathione peroxidase, and selenium also has an effect on cytochrome P-450 and heme metabolism. Comparisons are made between metabolism of selenium and sulfur in plants, animals, and humans. At greater selenium intake levels acute poisoning occurs when high-selenium-content (10,000 ppm Se) plants are consumed in large quantities. The toxic reactions were first manifested in cavalry horses near Fort Randall, Nebraska, in the 1860s.

Selenium has been found to be a potent anticarcinogen for a variety of chemically-induced cancers, and some inverse relationships between selenium occurrence and human cancer mortality have been demonstrated. The anticarcinogenicity of selenium holds much promise in regard to finding the body's anticancer mechanism. If this mechanism is elucidated, perhaps cancer control can be achieved. The potential of selenium may even surpass that of interferon. In addition, selenium has been shown to prevent Keshan disease, a severe myocardiopathy which occurs in young Chinese children. Inverse epidemiological relationships have also been observed between coronary heart disease and environmental selenium.

Much evidence indicates that selenium or selenium–vitamin E combinations counteract the toxic effects of mercury, methylmercury, cadmium, lead, silver, thallium, and arsenic in animals. Selenium–vitamin E combinations may offer a workable antidote to metal toxicity in humans exposed to these environmental hazards.

The forms of naturally occurring selenium are classified according to whether they are of low or high molecular weight. The synthetic forms of selenium along with their chemotherapeutic effects are also outlined. Because the levels of selenium are important in tissues, numerous non-destructive as well as destructive methods of selenium analyses are outlined.

In order to reduce the cost of the textbook, lists of several references were reduced to the most recent reference. The author wishes to thank Kathryn Risko, Phyllis Pittman, and Helen Brewster for their excellent typing, and Barbara DeWitt, Cindy Kopf, Ann McHugh, and Andrea Yartin for their careful help in proofreading.

Contents

1. Forms of Selenium

1.1 Low Molecular-Weight Compounds	1
1.1.1 Selenocysteine	1
1.1.2 Selenocystine	2
1.1.3 Selenohomocystine	2
1.1.4 Se-methylselenocysteine	3
1.1.5 Selenocystathionine	3
1.1.6 Selenomethionine	4
1.1.7 Se-methylselenomethionine	5
1.1.8 Dimethyl Selenide	6
1.1.9 Dimethyl Diselenide	6
1.1.10 Trimethyl Selenonium	6
1.1.11 Elemental Selenium	7
1.1.12 Selenotaurine	7
1.1.13 Selenocoenzyme A	7
1.1.14 Other Compounds	7
1.2 Macromolecular Forms of Selenium	8
1.2.1 Formate Dehydrogenase	8
1.2.2 Glycine Reductase	11
1.2.3 Nicotinic Acid Hydroxylase	15
1.2.4 Xanthine Hydrogenase	16
1.2.5 Thiolase	16
1.2.6 Glutathione Peroxidase	17
1.2.7 Miscellaneous Selenoproteins	23
1.2.8 Seleno-tRNA's	24
<i>References</i>	25

2. Selenium Deficiency Diseases in Animals

2.1 Introduction	31
2.2 Dietary Liver Necrosis and Factor 3	32
2.2.1 Discovery	32

2.2.2 Pathology	36
2.2.3 Biochemical Defect	37
2.2.4 Hepatosis Dietetica	38
2.3 Nutritional Muscular Dystrophy	38
2.3.1 Pathology	38
2.3.2 Prevention of NMD	40
2.4 Exudative Diathesis	44
2.5 Pancreatic Degeneration	45
2.6 Mulberry Heart Disease	46
2.7 Reproductive Problems	47
2.8 Myopathy of the Gizzard	49
2.9 Growth	50
2.10 Selenium—Responsive Unthriftiness of Sheep and Cattle	51
2.11 Periodontal Disease of Ewes	52
2.12 Encephalomalacia	52
<i>References</i>	54

3. Metabolism of Selenium

3.1 Absorption	59
3.2 Placental Transfer	65
3.3 Mechanism of the Antioxidant Action of Selenium	65
3.4 Effect of Paraquat	69
3.5 Effect on Cytochrome P-450	70
3.6 Selenium and Hepatic Heme Metabolism	71
<i>References</i>	72

4. Comparative Metabolism and Biochemistry of Selenium and Sulphur

4.1 Introduction	77
4.2 Comparative Metabolism of Selenium and Sulphur	78
4.2.1 Microorganisms	78
4.2.2 Plants	86
4.2.3 Animals	95
4.3 Comparative Biochemistry of Selenium and Sulphur	106
4.3.1 Selenopersulfide as an Electron Transfer Catalyst	106
4.3.2 Iron–Sulphur Proteins	110
4.3.3 Sulphur Salts and Selenium Toxicity in Animals	111
4.3.4 Other Selenium–Sulphur Interactions	114
<i>References</i>	116

5. Biological Interactions of Selenium with Other Substances

5.1	Cadmium	125
5.1.1	Pathological Effects	125
5.1.2	Cadmium–Zinc Interactions	127
5.1.3	Cadmium–Selenium Interactions	129
5.1.4	Effect on Drug Response	134
5.2	Arsenic	135
5.3	Copper	140
5.4	Silver	142
5.5	Cobalt	144
5.6	Manganese	146
5.7	Lead	147
5.8	Mercury	149
5.8.1	Inorganic and Organic Mercury	149
5.8.2	Tissue Distribution	151
5.8.3	Properties of the Mercury–Selenium Complex	152
5.8.4	Teratogenicity	152
5.9	Thallium	154
5.10	Tellurium	154
5.11	Vanadium	155
5.12	Bismuth	155
5.13	Other Substances	156
	<i>References</i>	157

6. Environmental Occurrence of Selenium

6.1	Geochemistry of Selenium	167
6.2	Soil Selenium	170
6.3	Uptake and Concentration of Trace Elements in the Roots, Stems, and Leaves of Plants	171
6.4	Forage Selenium	174
6.5	Selenium in Water	175
6.6	Selenium in Food	175
6.7	Intakes and Recommended Daily Allowance in Humans	180
6.8	Regulations in Regard to Animal Diets	180
	<i>References</i>	181

7. Toxicity of Selenium

7.1	Introduction	185
7.1.1	Acute Toxicity	186
7.1.2	Blind Staggers	188

7.1.3	Alkalai Disease	188
7.1.4	Toxicity in Rabbits	189
7.1.5	Toxicity in Hamsters	190
7.1.6	Toxicity in Sheep	190
7.1.7	Toxicity in Rats	191
7.1.8	Effect of Diet on Toxicity	192
7.1.9	Biochemical Lesions	195
7.1.10	LD ₅₀ of Various Selenium Compounds	197
7.2	Industrial Medical Aspects	201
7.2.1	Occupational Hazards	201
7.2.2	Permissible Limits for Selenium Exposure	202
7.2.3	Toxicity in Humans	202
	<i>References</i>	204

8. Selenium in Health and Disease

8.1	Selenium and Cancer	207
8.1.1	Skin Cancer	207
8.1.2	Liver Cancer	209
8.1.3	Colon Cancer	212
8.1.4	Breast Cancer	214
8.1.5	Tracheal Cancer	222
8.1.6	Chemotherapeutic Effect of Selenium	222
8.1.7	Epidemiological Relationship	225
8.1.8	Selenium Blood Levels in Cancer Patients	227
8.1.9	Selenium as a Carcinogen	229
8.2	Selenium and Mutagenesis	232
8.2.1	Antimutagenicity	232
8.2.2	Mutagenicity	235
8.3	Selenium and Immunity	239
8.3.1	Effect of Selenium on Humoral Immunity	239
8.3.2	Cell-Mediated Immunity	241
8.3.3	Nonspecific Immune Effects of Selenium	242
8.4	Selenium and Dental Caries	243
8.5	The Anti-Inflammatory Properties of Selenium	246
8.6	Selenium and Heart Disease	247
8.6.1	Animals	247
8.6.2	Humans	250
8.7	Selenium and Aging	254
8.8	Cystic Fibrosis	255
8.9	Multiple Sclerosis	256
8.10	Cataracts	256
8.11	Other Diseases	257

8.12 Radioselenium as a Diagnostic Agent	258
<i>References</i>	259
 9. Synthetic Forms of Selenium and Their Chemotherapeutic Uses	
9.1 Anti-Infective Agents	273
9.1.1 Antibacterial	273
9.1.2 Antiviral	276
9.2 Antifungal Agents	277
9.3 Antiparasitic Agents	279
9.4 Compounds Affecting the Central Nervous System	280
9.4.1 Hypnotics	280
9.4.2 Analgesics and Local Anesthetics	281
9.4.3 Tranquilizing Drugs	282
9.5 Compounds that Affect the Autonomic Nervous System	284
9.6 Compounds that Affect the Circulatory System	287
9.7 Anti-Inflammatory Compounds	287
9.8 Antihistamines	288
9.9 Anticancer Agents	289
9.10 Antiradiation Agents	294
9.11 Steroids	297
9.12 Selenocoenzyme A	299
9.13 Selenium-Containing Carbohydrates	300
9.14 Seleno–Amino Acids	301
<i>References</i>	304
 10. Analytical Methods of Selenium Determination	
10.1 Introduction	311
10.2 Sample Preparation and Storage	311
10.3 Destructive Analysis	312
10.3.1 Ashing	313
10.3.2 Closed-System Combustion	313
10.3.3 Wet Digestion	313
10.3.4 Measurement of Selenium	314
10.4 Nondestructive Analysis	321
10.4.1 Neutron Activation Analysis	321
10.4.2 X-Ray Fluorescence Analysis	322
10.4.3 Proton-Induced X-Ray Emission	323
<i>References</i>	323
 INDEX	 329