



Polyphenols: Mechanisms of Action in Human Health and Disease

Second Edition

Volume 1

Edited by
Ronald Ross Watson
Victor R. Preedy
Sherma Zibadi



POLYPHENOLS: MECHANISMS OF ACTION IN
HUMAN HEALTH AND DISEASE

This page intentionally left blank

POLYPHENOLS: MECHANISMS OF ACTION IN HUMAN HEALTH AND DISEASE

SECOND EDITION

Volume 1

Edited By

RONALD ROSS WATSON

VICTOR R. PREEDY

SHERMA ZIBADI



ACADEMIC PRESS

An imprint of Elsevier

Academic Press is an imprint of Elsevier
125 London Wall, London EC2Y 5AS, United Kingdom
525 B Street, Suite 1650, San Diego, CA 92101, United States
50 Hampshire Street, 5th Floor, Cambridge, MA 02139, United States
The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, United Kingdom

© 2018 Elsevier Inc. All rights reserved.

No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording, or any information storage and retrieval system, without permission in writing from the publisher. Details on how to seek permission, further information about the Publisher's permissions policies and our arrangements with organizations such as the Copyright Clearance Center and the Copyright Licensing Agency, can be found at our website: www.elsevier.com/permissions.

This book and the individual contributions contained in it are protected under copyright by the Publisher (other than as may be noted herein).

Notices

Knowledge and best practice in this field are constantly changing. As new research and experience broaden our understanding, changes in research methods, professional practices, or medical treatment may become necessary.

Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds, or experiments described herein. In using such information or methods they should be mindful of their own safety and the safety of others, including parties for whom they have a professional responsibility.

To the fullest extent of the law, neither the Publisher nor the authors, contributors, or editors, assume any liability for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions, or ideas contained in the material herein.

Library of Congress Cataloging-in-Publication Data

A catalog record for this book is available from the Library of Congress

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library

ISBN 978-0-12-813006-3

For information on all Academic Press publications visit our website at <https://www.elsevier.com/books-and-journals>



Acquisition Editor: Tari Broderick
Editorial Project Manager: Pat Gonzalez
Production Project Manager: Punithavathy Govindaradjane
Cover Designer: Mark Rogers

Typeset by SPi Global, India

Contents

Contributors	xi	3 Styles	20
Preface	xv	4 Ingredients	21
Acknowledgments	xvii	5 Health Benefits of Beer Polyphenols: Xanthohumol	23
		6 Summary	29
		References	30
		Glossary	32
I			
OVERVIEW OF POLYPHENOLS AND HEALTH			
1. Polyphenols in the Prevention of Acute Pancreatitis in Preclinical Systems of Study: A Revisit	3	4. Polyphenolic Flavonoids and Metalloprotease Inhibition: Applications to Health and Disease	33
ELROY SALDANHA, SURESH RAO, MOHAMMED ADNAN, MICHAEL L.J. PAIS, TARESH SHEKAR NAIK, RITESH D'CUNHA, RESHMINA D'SOUZA, MANJESHWAR SHRINATH BALIGA		DEJAN AGIĆ, MARIJA ABRAMIĆ, VESNA RASTIJA, ROSEMARY VUKOVIĆ	
1 Introduction	3	1 Introduction	33
2 Curcumin	4	2 Matrix Metalloproteinases	34
3 Resveratrol	5	3 Angiotensin-Converting Enzyme	36
4 Quercetin	5	4 Conclusion	38
5 Genistein	6	References	38
6 Ellagic Acid	6	5. Biological and Pharmacological Effects of Polyphenolic Compounds From <i>Ecklonia cava</i>	41
7 Cinnamtannin B-1	6	AKIKO KOJIMA-YUASA	
8 Green Tea Polyphenols	6	1 Introduction	41
9 Conclusions and Future Directions	6	2 Biological and Pharmacological Effects of Phlorotannins From <i>E. cava</i>	41
References	7	3 Protective Effect Against Ethanol-Induced Liver Injury	47
Further Reading	7	4 AMPK in the Protective Effects of Phlorotannins	49
	8	5 Conclusion	50
	9	References	50
2. Polyphenols as Supplements in Foods and Beverages: Recent Discoveries and Health Benefits, an Update	11	6. <i>Clerodendrum volubile</i> : Phenolics and Applications to Health	53
ANDRÉA PITTELLI BOIAGO GOLLÜCKE, ROGÉRIO CORREA PERES, DANIEL ARAKI RIBEIRO, ODAIR AGUIAR		OCHUKO L. ERUKAINURE, OLAKUNLE SANI, MD. SHAHIDUL ISLAM	
1 Polyphenols and Supplementation	11	1 Introduction	53
2 New Insights on Polyphenol Metabolism and Action	12	2 Phenolics and Health	53
3 Benefits of Polyphenol's Consumption: Experimental Data	13	3 Phytochemistry of <i>Clerodendrum volubile</i>	54
4 Antimicrobial Activity of Polyphenols	14	4 Biological Activities of <i>Clerodendrum volubile</i>	57
5 Noxious Activities Induced by Polyphenols: An Intriguing Issue	14	5 Proposed Mechanism of Action of <i>C. volubile</i>	65
6 Concluding Remarks and Future Challenges	15	6 Conclusion	65
References	16	Acknowledgments	66
	16	References	66
3. Xanthohumol and the Medicinal Benefits of Beer	19	7. <i>Eryngium campestre</i> L.: Polyphenolic and Flavonoid Compounds; Applications to Health and Disease	69
SUSAN M. ELROD		BOUZIDI SOUMIA	
1 Introduction	19	1 Introduction	69
2 History of Beer and Brewing	19	2 About the Plant	70
	19	3 Distribution	70

4 Traditional Uses	70	3 Moving Toward Integrative Prevention and Care: The Link Between Nutrition and Mental Health	120
5 Phytochemistry	72	4 Citrus Polyphenols and Flavonoids	121
6 Biological and Pharmacological Activities	74	5 Citrus Polyphenols in Mental Disorders	123
7 Conclusion	77	6 Conclusions and Future Directions	128
References	77	References	129
8. Antioxidant Activity of Anthocyanins in Common Legume Grains	81	II	
WINDA CHRISTINA HARLEN, IGNASIUS RADIX A.P. JATI		POLYPHENOLS IN THERAPY OF OBESITY AND DIABETES	
1 Introduction	81	12. Anthocyanins and Diabetes Regulation	135
2 Free Radicals and Antioxidants	81	HONGHUI GUO, MIN XIA	
3 Anthocyanins	82	1 Introduction	135
4 Legume Anthocyanin as Antioxidant	82	2 Chemical Properties of Anthocyanins	135
5 Conclusion	90	3 Dietary Anthocyanin Sources	137
References	90	4 Anthocyanin Bioavailability	137
 		5 Antidiabetic Effects of Anthocyanins and the Underlying Mechanisms	138
9. Tomato Polyphenolics: Putative Applications to Health and Disease	93	6 Conclusion and Perspective	142
SENA BAKIR, SENEM KAMILOGLU, MERVE TOMAS, ESRA CAPANOGLU		Acknowledgments	143
1 Introduction	93	References	143
2 Health Effects of Tomato Phenolics	94	 	
3 Concluding Remarks	99	13. The Role of Direct and Indirect Polyphenolic Antioxidants in Protection Against Oxidative Stress	147
References	100	LARS PORSKJÆR CHRISTENSEN	
 		1 Introduction	147
10. Polyphenolic Compounds in Sweet Cherries: A Focus on Anthocyanins	103	2 Cytoprotective Proteins (Phase 2 Enzymes)	149
KATHERINE KENT, NADINE HÖLZEL, NIGEL SWARTS		3 Induction of Cytoprotective Proteins	150
1 An Overview of the Nutritive and Nonnutritive Properties of Sweet Cherries	103	4 Direct and Indirect Antioxidants and Their Role in Protection Against Oxidative Stress	150
2 A Focus on Anthocyanins in Sweet Cherries	104	5 Polyphenol and Polyphenol-Derived Inducers of Cytoprotective Proteins (Indirect Antioxidant Effect)	152
3 Anthocyanin Biosynthesis in Sweet Cherries	105	6 Conclusions	170
4 Measurement of Anthocyanin Content in Sweet Cherries	106	References	171
5 Pre- and Postharvest Factors That Impact on Anthocyanins in Sweet Cherries	106	 	
6 Patterns of Global Growth and Economic Importance of Sweet Cherry Production	107	14. Role of Protocatechuic Acid in Obesity-Related Pathologies: An Update	181
7 Important Sensory Attributes and Traditional Quality Indicators of Sweet Cherries	109	MASSIMO D'ARCHIVIO, BEATRICE SCAZZOCCHIO, ANNALISA SILENZI, CLAUDIO GIOVANNINI, ROBERTA MASELLA	
8 Consumer Preference for Sweet Cherries May Not Be Driven by Health	110	1 Introduction	181
9 Sweet Cherry Consumption and Contribution to Habitual Anthocyanin Consumption	111	2 Protocatechuic Acid: Food Content and Bioavailability	181
10 Sweet Cherries and Health Outcomes: Potential Mechanisms of Action	112	3 Obesity: A Global Challenge Yet Today	183
11 Conclusion: Major Gaps in Literature and Future Research Direction	115	4 Mechanism of Action of PCA	184
Acknowledgments	116	5 Conclusion	189
References	116	References	189
11. Citrus Fruit Polyphenols and Flavonoids: Applications to Psychiatric Disorders	119	15. Exposure to Polyphenolic Compounds Modulates Type 1 Diabetes: The Case of Genistein	193
MARIA ROSARIA ANNA MUSCATELLO, ROCCO ANTONIO ZOCICALI, ANTONIO BRUNO		GUANNAN HUANG, JOELLA XU, TAI L. GUO	
1 Introduction	119	1 Introduction	193
2 The Global Burden of Mental Illness	119	2 Pathogenesis of T1D	193

3 Polyphenolic Compounds and T1D	194
4 Mechanisms of T1D Modulation by Polyphenolic Compounds: Gut Microbiota	196
5 Mechanisms of T1D Modulation by Polyphenolic Compounds: Epigenetics	199
6 Other Potential Mechanisms	200
7 Conclusion	200
Acknowledgments and Funding Support	200
References	200

III

MECHANISMS OF POLYPHENOLS ANTIOXIDANT EFFECTS

16. Chocolate/Cocoa Polyphenols and Oxidative Stress	207
JUDITH E ALLGROVE, GLEN DAVISON	

1 Introduction	207
2 Antioxidant Properties	207
3 Bioavailability	208
4 Research on Cocoa and Oxidative Stress	208
5 Summary	216
References	217

17. An Overview of Dietary Polyphenols and Their Therapeutic Effects	221
PALLAVI KESAVAN, ANTARA BANERJEE, ANUSHKA BANERJEE, RAMACHANDRAN MURUGESAN, FRANCESCO MAROTTA, SURAJIT PATHAK	

1 Introduction	221
2 Structural Classification of Polyphenols	221
3 Dietary Intake and Content of Polyphenols	224
4 Bioavailability and Distribution of Polyphenols	225
5 Epigenetic Modifications and Polyphenol Metabolism	226
6 Nutritional Genomics and Dietary Polyphenols	228
7 Novel Therapeutics Using Polyphenols	232
Acknowledgments	232
References	232
Further Reading	235

18. The Polyphenolic Compound Resveratrol Attenuates Pain: Neurophysiological Mechanisms	237
MAMORU TAKEDA, SHIORI TAKEHANA, YOSHIHITO SHIMAZU	

1 Introduction	237
2 Classification of Pain	238
3 Pain Pathway in the Trigeminal System	238
4 Modulatory Mechanism of Resveratrol on the Nociceptive Pain	239
5 Modulatory Mechanism Underlying the Effect of Resveratrol on Pathological Pain	241
6 Functional Significance for Modulation of Pain Relief	243

7 Future Direction	244
8 Concluding Remarks	245
References	245

19. Possible Benefits and Risks of Polyphenols Supplementation During Pregnancy	249
ANTONIO GONZALEZ-BULNES, SUSANA ASTIZ, BEATRIZ ISABEL, MARTA VAZQUEZ-GOMEZ, CONSOLACION GARCIA-CONTRERAS	

Outline	249
1 Introduction	249
2 The Role of Intrauterine Environment in Pregnancy Development	250
3 The Role of the Intrauterine Environment in Postnatal Traits	250
4 Preventive Strategies and Therapies for IUGR	251
5 Alternative Tools for Prevention and Treatment of IUGR: Amino Acids and Antioxidants	252
6 Implications and Evidence for Beneficial Effects of Polyphenols Supplementation During Pregnancy	253
7 Possible Risks of Polyphenols Supplementation During Pregnancy	255
8 Concluding Remarks and Future Research	256
Acknowledgments	256
References	256

20. Flavonoids as Modulators of Neutrophils' Oxidative Burst: Structure-Activity Relationship	261
DANIELA RIBEIRO, EDUARDA FERNANDES, MARISA FREITAS	

1 Introduction	261
2 Neutrophils Morphology	261
3 Neutrophil Phagocytosis	262
4 Production of Reactive Oxygen Species	262
5 Production of Reactive Nitrogen Species	264
6 Flavonoids	265
7 Effect of Flavonoids on Neutrophils' Oxidative Burst	266
8 Catechol Group in the B-Ring	272
9 3-OH in the C-Ring	273
10 C2–C3 Double Bond	274
11 Conclusion	274
Acknowledgments	274
References	274

21. Manipulation of Mitochondrial Function by Polyphenols for New Treatment Strategies	277
CORINA T. MADREITER-SOKOLOWSKI, WOLFGANG F. GRAIER	

1 Introduction	277
2 Mitochondria	278
3 Polyphenols	280
4 Manipulation of Mitochondrial Function by Polyphenols	281
5 Polyphenols as Treatment Strategies to Manipulate Mitochondrial (Dys)Function in Diseases	284
6 Conclusion	287
References	288
Glossary	292

IV

BIOAVAILABILITY AND EFFECTS
ON METABOLISM22. Bioavailability of Flavonoids: The Role of Cell
Membrane Transporters 295JOVANA ČVOROVIĆ, LOVRO ZIBERNA, STEFANO FORNASARO,
FEDERICA TRAMER, SABINA PASSAMONTI

1 Introduction	295
2 Principles of Membrane Transport	296
3 Indirect Evidence Supporting the Existence of Flavonoid Membrane Transporters	297
4 Anatomical Distribution of Flavonoid-Related Membrane Transporters	301
5 Issues Related to the Low Bioavailability of Flavonoids	310
6 Transporter-Based Flavonoid-Drug Interactions	311
7 Conclusion	312
Acknowledgments	313
References	313

23. Interaction of Polyphenols With the
Intestinal and Placental Absorption of Some
Bioactive Compounds 321ELISA KEATING, CONCEIÇÃO CALHAU, ANA FARIA,
FÁTIMA MARTEL

1 Introduction	321
2 Effect of Polyphenols on the Transport of 1-Methyl-4- Phenylpyridinium	322
3 Effect of Polyphenols on the Transport of Folates	324
4 Effect of Polyphenols on the Transport of Thiamine	326
5 Effect of Polyphenols on the Transport of Glucose	328
6 Conclusions	332
References	332

24. Analyzing Ingredients in Dietary Supplements
and Their Metabolites 337

JEEVAN K. PRASAIN, STEPHEN BARNES, J. MICHAEL WYSS

1 Introduction	337
2 Anthocyanins	338
3 Flavanols	339
4 Flavones and Flavonols	340
5 Isoflavones	340
6 Extraction of Isoflavones	342
7 In Vivo Metabolism of Isoflavones	344
8 Conclusions	345
References	345

25. Metabolism of Dietary Polyphenols by Human
Gut Microbiota and Their Health Benefits 347SURAJIT PATHAK, PALLAVI KESAVAN, ANUSHKA BANERJEE,
ANTARA BANERJEE, GULCIN SAGDICOGLU CELEP, LAURA BISSI,
FRANCESCO MAROTTA

1 Introduction	347
2 Dietary Intake of Polyphenols	349

3 Absorption, Metabolism, and Bioavailability of Polyphenols	349
4 Metabolism of Polyphenols by the Gut Microbiota	350
5 Enzymes in the Metabolism of Polyphenols	353
6 Modulation of Gut Microbiota by Polyphenols	353
7 Health Benefits of Polyphenols and Their Microbial Metabolites	354
8 Conclusions	355
Acknowledgments	356
References	356

26. Bioavailability and Biochemistry of Quercetin
and Applications to Health and Diseases 361GABRIELE CARULLO, MARIATERESA BADOLATO,
FRANCESCA AIELLO

1 Chemical Features of Quercetin	361
2 Bioavailability, Absorption and Metabolism of Quercetin	362
3 Mechanistic and Preclinical Studies of Quercetin and Its Metabolites	364
4 Esters of Quercetin and Their Therapeutic Applications	365
5 Conclusion	367
References	368
Further Reading	371

27. Effects of Quercetin and Its Combinations on
Health 373S.K. SHEBEKO, I.A. ZUPANETS, O.S. POPOV, O.O. TARASENKO,
A.S. SHALAMAY

1 Introduction	373
2 Basic Pharmacological Properties of Quercetin	374
3 Pharmacokinetic Properties of Quercetin and Ways of Modifying Them	376
4 Gastroprotective Effects of Quercetin	379
5 Angioprotective Activity of Quercetin	379
6 Effects of Quercetin on Hemostasis	379
7 Cardioprotective Properties of Quercetin	380
8 Application of Quercetin-Based Drugs in Chronic Kidney Disease	382
9 Quercetin-Based Drugs in Joint Diseases	386
10 Conclusion	391
References	392

V

POLYPHENOLS IN DISEASE

28. Green Tea Polyphenols in the Amelioration of
Osteoarthritis: Memoir on the Preclinical
Observations 397NAVEEN JOSEPH MATHAI, DAVANAGERE MURALI SUJAYENDRA,
MOHAMMED ADNAN, TARESH SHEKAR NAIK, THOMAS GEORGE,
SONIYA ABRAHAM, MANJESHWAR SHRINATH BALIGA

1 Introduction	397
2 Green Tea in Arthritis	398
3 Phytochemistry of Green Tea	398
4 Traditional and Validated Uses	399

5 Free Radical Scavenging and Antioxidant Properties	399	7 Effect of Green Tea Phytochemicals on Hepatotoxicity of Lead	417
6 Green Tea Increases Antioxidant Enzymes and Reduces Lipid Peroxidation	399	8 Effect of Tea Phytochemicals on Hepatotoxicity of Azathioprine	417
7 Antiinflammatory Effects	399	9 Effect of Tea Phytochemicals on Galactosamine-Induced Liver Damage	417
8 Green Tea Polyphenols Inhibit the Activation of Mitogen-Activated Protein Kinases	400	10 Effect of Tea Phytochemicals on Lipopolysaccharide-Induced Liver Damage	417
9 Green Tea and Its Polyphenols Decrease Activation of NF- κ B	400	11 Effect of Tea Phytochemicals on Fumonisin B1-Induced Liver Damage	418
10 EGCG and Its Influence on Matrix Metalloproteinases	400	12 Effect of Tea on Hepatotoxicity of Aflatoxins	418
11 Chondroprotective Effects of EGCG	400	13 Effect of Tea Phytochemicals on Phenobarbital-Induced Liver Damage	418
12 EGCG Inhibits Osteoclast Activation and Differentiation	401	14 Effect of Tea on Hepatocarcinogenesis	418
13 Conclusion	401	15 Effect of Tea Polyphenols on Fatty Liver Disease	419
References	401	16 Effect of Tea Polyphenols on Obesity-Induced Liver Damage	419
29. Polyphenolics Evoke Healing Responses: Clinical Evidence and Role of Predictive Biomarkers	403	17 Conclusions	419
RUSSELL JAFFE, JAYASHREE MANI		References	419
1 Polyphenolic Consumption	403	31. CAPE and Tympanosclerosis	421
2 Flavanoids and Flavonols	404	İBRAHİM AĞRI, ARZU ERDAL AĞRI, DOĞUKAN ÖZDEMİR, ABDULKADİR ÖZGÜR	
3 Measurements of Antioxidant Capacity	404	1 The Effect of Caffeic Acid Penethyl Ester on Tympanosclerosis	421
4 Quercetins	406	2 Caffeic Acid Phenethyl Ester	421
5 Synergistic Polyphenols: Quercetin Dihydrate and Soluble Orthoproanthocyanidin	406	3 CAPE and Oxidative Stress	422
6 Orthoproanthocyanidins (Soluble OPCs)	408	4 CAPE and Inflammation	423
7 Ellagic Acid Content: Pomegranate Juice	409	5 Tympanosclerosis	423
8 Clinical Considerations: Whole Fruit and Fruit Juice	409	6 CAPE and Tympanosclerosis	427
9 Predictive Biomarkers Referenced to Goal Values: Personalized Care	410	References	428
10 Conclusions	411	Further Reading	430
References	412	32. The Polyphenolic Compound Hesperidin and Bone Protection	431
30. Hepatoprotective Effects of Green Tea and Its Polyphenols: A Revisit	415	JENALYN L. YUMOL, WENDY E. WARD	
MANJESHWAR SHRINATH BALIGA, ARNADI RAMACHANDRAYYA SHIVASHANKARA, PAUL SIMON, SURESH RAO, PRINCY LOUIS PALATTY		1 Introduction	431
1 Introduction	415	2 Nutrition as a Strategy for Maintaining Healthy, Strong Bones	432
2 Tea Protects Against Alcohol-Induced Hepatotoxicity	415	3 Hesperidin Consumption and Its Effect on Outcomes of Bone Protection	433
3 Tea Protects Against Carbon Tetrachloride-Induced Hepatotoxicity	416	4 Summary	438
4 Effect of Tea on <i>N</i> -Acetaminophen-Induced Hepatotoxicity	416	References	438
5 Tea Is Effective in Viral Hepatitis	417	Glossary	440
6 Effect of Tea on Ischemia Reperfusion Injury	417	Index	441