
Role of Phenolic Phytochemicals in Diabetes Management

Muddasarul Hoda
Shanmugam Hemaiswarya
Mukesh Doble

Role of Phenolic Phytochemicals in Diabetes Management

Phenolic Phytochemicals and Diabetes

 Springer

Muddasarul Hoda
Department of Biotechnology
Indian Institute of Technology Madras
Chennai, Tamil Nadu, India

Shanmugam Hemaiswarya
Department of Biotechnology
Indian Institute of Technology Madras
Chennai, Tamil Nadu, India

Department of Biological Sciences
Aliah University
Kolkata, India

Mukesh Doble
Department of Biotechnology
Indian Institute of Technology Madras
Chennai, Tamil Nadu, India

ISBN 978-981-13-8996-2 ISBN 978-981-13-8997-9 (eBook)
<https://doi.org/10.1007/978-981-13-8997-9>

© Springer Nature Singapore Pte Ltd. 2019

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. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd.
The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

Preface

Diabetes is a major chronic disease characterized by hyperglycaemia, polyuria, polydipsia, and polyphagia. According to the seventh edition of the International Diabetes Federation (IDF) Atlas, approximately 415 million people between the ages of 20 and 79 around the globe have been estimated to suffer from diabetes in the year 2015. This count is further expected to rise to 642 million by the year 2040. The ever-changing lifestyle and dietary habits have immensely contributed to the development of not only chronic but also acute diabetic conditions. The current drugs in the market have their associated toxicity and side effects as well as become ineffective after a certain period of treatment.

Phytomedications are among the oldest remedies for diabetes that have been practiced around the world under various names including *Ayurveda* (Indian subcontinent), *Unani* (West Asia), and *Zhōngyī* (Central Asia). They are essentially mixtures of a variety of phytochemicals in various proportions. The concentrations of these phytochemicals may vary significantly, depending upon the plant source, or even in various organs within the same plant. As per the US Department of Agriculture (USDA) database, approximately 1200 phytochemicals have been reported to reverse/control diabetic conditions via a number of transcriptional, translational, and epigenetic modulations of major signaling molecules. Some of the limitations of phytomedicine include lack of validations of constituents' proportions and ambiguous mechanisms of action against diabetes.

Among the various types of phytochemicals, phenolic compounds have been of particular interest. It is among the major constituents and active principles in various plant extracts. Phenolic compounds are a group of simple and complex molecules, classified together based on the presence of at least one aromatic ring and a hydroxyl group attached to it. Herbs, fruits, and spices, including bitter melon, java plum, and turmeric, are among the vast repository of natural resources from which a variety of phenolic compounds, including flavonoids, aromatic acids, phenylethanoids, alkylresorcinols, and capsaicin, have been identified and isolated. These phenolic phytochemicals have been studied for their therapeutic efficacy against various types of diseases, including cancer, diabetes, arthritis, cardiovascular diseases, and some neurodegenerative disorders.

This book summarizes the current research trends of phytochemical therapy against diabetes. It lists the various phenolics reported to possess anti-diabetic activity and their plant sources. It also discusses the various mechanisms of actions of

these compounds. Each of these pathways may be targeted by the combination of multiple phytophenolics and synthetic drugs, such that their synergistic effects may result in lowering the diabetic conditions or simultaneous lowering of the dependence on synthetic drugs. Phytochemicals have certain shortcomings which include poor aqueous solubility, bioavailability, and shelf life. Nanotechnology-based approaches may overcome some of these problems. The pharmacokinetics, pharmacodynamics, and degradation of phytophenolics also need to be understood for their effective use which is also discussed here. The National Institutes of Health (NIH) and the USDA are among the many agencies that are funding intensive research in phytochemicals as dietary supplements in preventive medicine. The current trends of European markets evidently suggest that phytomedicines are increasingly being preferred as an alternative preventive medicine due to its mild adverse effects and reduced toxicity.

This book could be a useful reference to academicians, scientists working in government and industrial labs, dieticians, alternative therapy practitioners, and the common public. Some of the novel photochemicals reported here could also be a lead molecule for the design of novel anti-diabetic drug.

Chennai, India

Muddasarul Hoda
Shanmugam Hemaiswarya
Mukesh Doble

Contents

1	Diabetes: Its Implications, Diagnosis, Treatment, and Management . . .	1
1.1	Introduction	1
1.2	Epidemiology of Diabetes	2
1.3	Types of Diabetes.	2
1.4	Clinical Implications of Diabetes.	4
1.5	Economic Implications of Diabetes.	5
1.6	Diagnosis Criteria for Diabetes	5
1.7	Diabetes Prevention and Management.	8
1.8	Current Drugs and Their Alternatives in Diabetes Management.	9
1.9	Plant Sources as Alternative Treatment to Synthetic Drugs	9
1.10	Role of Functional Food in Diabetes Management	10
	References.	11
2	Phenolic Phytochemicals: Sources, Biosynthesis, Extraction, and Their Isolation	13
2.1	Introduction	13
2.2	Classification of Phenolic Compounds from Plant Sources	15
2.2.1	Flavonoids	16
2.2.2	Phenolic Acids and Phenyl Alkanoids	19
2.2.3	Quinones	19
2.2.4	Stilbenoids	19
2.2.5	Lignans and Neolignans.	20
2.2.6	Polyphenolic Amides	20
2.2.7	Xanthones and Curcuminoids	20
2.2.8	Dimeric and Polymeric Polyphenols	20
2.3	Biosynthesis of Phenolic Compounds	21
2.3.1	Biosynthesis of Aglycone Phenolic Compounds.	21
2.3.2	Functional Group Derivation of Primary Aglycones.	23
2.4	Extraction and Isolation Processes of Phenolic Compounds.	24
2.4.1	Sample Preparation	24
2.4.2	Phytochemical Extraction and Isolation	25
2.4.3	Isolation of Specific Phenolic Compounds	29

2.5	Identification and Quantification of Phenolic Compounds	30
2.6	Structural Elucidation of Phenolic Compounds.	31
	References.	40
3	Food Sources of Antidiabetic Phenolic Compounds	45
3.1	Introduction	45
3.2	Cereals	46
3.3	Vegetables	49
3.4	Fruits	54
3.5	Spices	54
3.6	Beverages.	55
3.7	Medicinal plants.	55
	References.	74
4	Mechanisms of Action of Phenolic Phytochemicals in Diabetes Management	83
4.1	Introduction to General Mechanisms of Action Against Type 2 Diabetes	83
4.1.1	Transcriptional Modulation of Diabetic Regulatory Genes	85
4.1.2	Modulation of Cell Signaling Pathways of Glucose Homeostasis Regulatory Proteins	85
4.1.3	Modulation of Various Enzymes and Protein Activity Diabetes-Related Metabolism	86
4.1.4	Modulation of Epigenetic Factors That Influence Diabetes	87
4.2	Mechanism of Action of Specific Phytophenolic Compounds	88
4.2.1	Anthocyanins	88
4.2.2	Catechins	88
4.2.3	Resveratrol.	90
4.2.4	Curcumin	93
4.2.5	Silymarin	99
4.2.6	Capsaicin	99
4.2.7	Emodin.	103
4.2.8	Thymoquinone	103
4.2.9	Chlorogenic Acid.	106
4.2.10	Quercetin	106
4.3	Conclusion	109
	References.	111
5	Synergistic Behavior of Phytophenolics with Antidiabetic Drugs	123
5.1	Introduction	123
5.2	Evaluation of Combinations in Diabetes	124
5.3	Herb-Drug Interactions	126
5.3.1	Herb–Biguanide Interaction.	126
5.3.2	Herb–Thiazolidinedione Interaction	129
5.3.3	Herb–Sulfonylurea Interaction.	131
5.3.4	Interaction Between Herb–Alpha Glucosidase Inhibitors	133

5.4	Herb–Herb Interactions	135
5.5	Food–Drug Interaction	136
5.6	Mechanism of Herb–Drug Interaction	137
	References	138
6	Polyphenol Nanoformulations with Potential Antidiabetic Properties	145
6.1	Introduction	145
6.2	Curcumin	146
6.3	Resveratrol	151
6.4	Epigallocatechin Gallate (EGCG)	152
6.5	Green Synthesis of Nanoparticles	153
6.6	Conclusion	154
	References	154
7	Pharmacokinetics and Pharmacodynamics of Polyphenols	159
7.1	Introduction	159
7.2	Interaction of Polyphenols with Saliva	160
7.3	Intestinal Transit of Polyphenols	160
	7.3.1 Transporter Proteins	160
	7.3.2 Gut Microbiota-Mediated Metabolism of Polyphenols	162
7.4	Phase 1 and Phase 2 Metabolism of Polyphenols	166
7.5	Pharmacokinetic (PK) Parameters	167
7.6	Pharmacodynamics	168
	References	169
8	Trends in Research and Development of Phenolic Phytochemicals as Potential Antidiabetic Therapeutics	175
8.1	Introduction	175
8.2	Status of Research and Development of Phenolic Phytochemicals as Therapeutics	177
	8.2.1 Phenolic Compounds as Part of Personalized Medicine in Diabetes Management	179
	8.2.2 Potential Natural Analogs of some Prominent Phenolic Compounds	180
	8.2.3 Research and Development of Isolation, Identification, and Drug-Delivery Methods of Phenolic Phytochemicals	181
8.3	Challenges and Future of Phenolic Phytochemicals as Potential Antidiabetics	181
	References	183
9	Conclusions	185

About the Authors

Muddasarul Hoda Currently Assistant Professor, Department of Biological Sciences, Aliah University, Kolkata. His research interests include nanotechnology in drug targeting and therapeutics, and synergism of phytochemicals against glucose homeostasis imbalance and cancer. He received his PhD from Pondicherry University, and postdoctoral degree from the IIT Madras. He has 7 research publications to his credit.

Shanmugam Hemaiswarya Project Officer, Department of Biotechnology, Indian Institute of Technology, Madras. Her research interests include phytomedicine and studying combinations of phytochemicals with synthetic drugs as effective antibacterial and anticancer agents. She was engaged in a two-year postdoctoral stay at the University of Algarve, Portugal and a three-year research fellowship under Women Scientist Scheme A (DST) at Anna University, Chennai (SR/WOS-A/LS-1231/2014 G). She has 19 research publications to her credit.

Mukesh Doble is a Professor (Emeritus) at the Department of Biotechnology, IIT Madras, Chennai, India. His areas of interest include drug design, natural products and biomaterials. He has previously worked for 23 years in Imperial Chemical Industries (ICI) and General Electric (GE) Technology centres. He holds BTech and MTech degrees in Chemical Engineering from the IIT Madras, a PhD from the University of Aston, UK, and postdoctoral degrees from the University of Cambridge, UK, and Texas A&M, USA. He has authored 310 technical papers, 10 books, and filed 12 patents. He is a fellow of the Royal Society of Chemistry and a recipient of the Herdillia Award for “Excellence in Basic Research” from the Indian Institute of Chemical Engineers. He received the 5th National Award for Technology Innovation in the Field of Petrochemicals and Downstream Plastic Processing Industry, Govt of India for his innovations in “Antimicrobial Food Wrap” (Runner up, 2015). He is also the Director of two biotech start-ups.