

REVIEW

Biosynthesis and Biotransformation of Ether Lipids¹

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Some naturally occurring as well as synthetic ether lipids are biologically active. In certain cases, the effects of these substances are enhanced, in others, they are inhibited by compounds that were isolated from natural sources or prepared by chemical synthesis. The biotransformation of natural or "unnatural" ether lipids in microorganisms, plant or animal tissue also can lead to substances that elicit biological effects. The production of such compounds through various biotechnological techniques is a field wide open for future exploration. In addition to animal cell cultures, plant cell cultures may become useful tools in biomedical studies concerned with ether lipids.

Lipids 22, 789-799 (1987).

Naturally occurring ether lipids (alkoxylipids), once considered to be "dead ends" of lipid metabolism, have been found to be intimately involved in a variety of physiological reactions (1-4). Biologically active ether lipids include compounds containing an alkyl or a 1-alkenyl moiety. The platelet activating factor, for example, a powerful lipid mediator, is a phospholipid containing an alkyl moiety (5,6), whereas, the farnesenes, potent mutagens, are polyunsaturated 1-*O*-(1-alkenyl)glycerols (7).

In recent years, numerous synthetic ether lipids that do not occur in nature have been prepared to find therapeutic agents such as agonists and antagonists of natural lipid mediators (8,9) and compounds that can be of value in the therapy of cancer patients (10-18).

The results of some recent studies indicate that certain biological effects are due to products that are derived, in living systems, from both natural and synthetic "unnatural" ether lipids. The biotransformations that ether lipids undergo in animal and plant cells, therefore, are of great current interest.

The present review describes briefly a few biologically active lipids containing alkyl or 1-alkenyl moieties and, in more detail, various reactions in animal and plant cells involving both natural ether lipids and those having "unnatural" structures.

NATURALLY OCCURRING ETHER LIPIDS

Neutral and ionic lipids containing an alkyl or 1-alkenyl moiety bound to glycerol at position 1 are ubiquitous though, as a rule, minor constituents of animal cells (14-16) but not of plant cells (17). All of these natural products are chiral compounds; their alkyl and 1-alkenyl moieties usually are saturated and monounsaturated and have chains predominantly of 16, 18 and 20 carbon atoms.

Neutral ether lipids include 1-*O*-alkyl-2,3-diacyl-*sn*-glycerols, 1-*O*-(1-alkenyl)-2,3-diacyl-*sn*-glycerols (neutral plasmalogens) and a variety of ether glycolipids such as 3-*O*-alkyl-2-acyl-1- β -D-galactopyranosyl-*sn*-glycerols (2,4,18). Ionic ether lipids are the 1-*O*-alkyl-2-acyl-*sn*-glycero-3-phosphocholines, the 1-*O*-(1-alkenyl)-2-acyl-*sn*-glycero-3-phosphocholines (choline plasmalogens), and the corresponding glycerophosphoethanolamines and glycerophosphoserines (2,4,16).

In addition to ether lipids with a single alkyl moiety, hearts of some mammalian species contain extremely small proportions of phospholipids derived from 1,2-di-*O*-alkylglycerols (19,20). And, besides alkyl and 1-alkenyl ethers of glycerol, traces of ether lipids having a diol backbone occur in nature; these diol lipids also include neutral and ionic compounds (21). Alkyl ethers (22) and 1-alkenyl ethers (23) of cholesterol are found in mammalian heart tissues. In contrast, disteryl ethers that occur in refined edible fats and oils are not natural products. These compounds are formed from sterols of plant and animal origin during the bleaching process (24,25). They are not absorbed in the gastro-intestinal tract, and their



1-*O*-Alkyl-2,3-diacyl-*sn*-glycerols and 1-*O*-(1-alkenyl)-2,3-diacyl-*sn*-glycerols

¹Presented at the symposium on "Ether Lipids in Oncology," Göttingen, Federal Republic of Germany, December 1986.

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Biologically Active Ether Lipids

**Abel Lajtha, Guido
Tettamanti, Gianfrancesco Goracci**



Biologically Active Ether Lipids:

Metabolism and Functions of Bioactive Ether Lipids in the Brain Akhlaq A. Farooqui, Tahira Farooqui, Lloyd A. Horrocks, 2008-04-13 Information on bioactive ether lipids and their involvement in neurological disorders is currently scattered throughout the literature in the form of original papers and reviews *Metabolism and Functions of Bioactive Ether Lipids in the Brain* provides readers with a comprehensive description of metabolism of bioactive ether lipids in the brain activities of enzymes involved in their metabolism and their involvement in neurological disorders This book will be particularly useful to neuroscience graduate students academics and researchers Clinicians will find this book useful for understanding molecular aspects of neurodegeneration in acute neural trauma and neurodegenerative diseases that are mediated by plasmalogen selective phospholipase A2 and PAF acetyl hydrolase This monograph will be first to provide a comprehensive description of not only metabolism and role of plasmalogen and platelet activating factor in brain tissue but also the involvement of these lipids with abnormal signal transduction processes in neurological disorders *Ether Lipids* H.K. Mangold, 2012-12-02 *Ether Lipids Biochemical and Biomedical Aspects* is a 21 chapter text that explores the procedures for the analysis synthesis and biomedical application of ether lipids This book surveys first the chromatographic analysis of ether lipids and their characterization by mass spectrometry The following chapter describes the chemical synthesis of lipids containing alkyl or 1 alkenyl chains Three chapters are devoted to the biosynthesis of ether lipids and four others cover unusual ether lipids Significant chapters focus on biologically active ether lipids including the naturally occurring platelet activating factor and synthetic alkyl analogs of lysophosphatidylcholines which exhibit cancerostatic properties This text further discusses the application of these and related substances in biomedical research as well as in clinical diagnosis and therapy The remaining chapters highlight the use of ether lipids in studies aimed at elucidating the structure of membranes and their functions Organic chemists biochemists and researchers in the biomedical field will find this book invaluable

Biologically Active Ether Lipids Pierre Braquet, Helmut K. Mangold, B. B. Vargaftig, 1988 *Biochemistry of Lipids, Lipoproteins and Membranes* J.E. Vance, Dennis E. Vance, 1991-12-17 The second edition of this book on lipids lipoprotein and membrane biochemistry has two major objectives to provide an advanced textbook for students in these areas of biochemistry and to summarise the field for scientists pursuing research in these and related fields Since the first edition of this book was published in 1985 the emphasis on research in the area of lipid and membrane biochemistry has evolved in new directions Consequently this second edition has been modified to include four chapters on lipoproteins Moreover the other chapters have been extensively updated and revised so that additional material covering the areas of cell signalling by lipids the assembly of lipids and proteins into membranes and the increasing use of molecular biological techniques for research in the areas of lipid lipoprotein and membrane biochemistry have been included Each chapter of the textbook is written by an expert in the field but the chapters are not simply reviews of current literature Rather they are written as current readable summaries of these

areas of research which should be readily understandable to students and researchers who have a basic knowledge of general biochemistry The authors were selected for their abilities both as researchers and as communicators In addition the editors have carefully coordinated the chapters so that there is little overlap yet extensive cross referencing among chapters

Biochemistry of Lipids, Lipoproteins and Membranes Dennis E. Vance, J.E. Vance, 2002-12-06 The first edition of this book was published in 1985 The content of the 4th edition reflects the enormous advances that have occurred since that time in the field of lipid biochemistry This publication is unique in that it represents a bridge between the superficial coverage of the lipid field found in basic biochemistry text books and the highly specialized material contained in scientific review articles and monographs The book is not a collection of exhaustive reviews but a current and readable summary of diverse aspects of lipids It is intended as an advanced and up to date textbook for teachers and students who are familiar with the basic concepts of lipid biochemistry and will also serve as a general reference book for scientists studying lipids lipoproteins and membranes

Biochemistry of Lipids, Lipoproteins and Membranes Neale Ridgway, Roger McLeod, 2008-03-14 Research on the biochemistry and molecular biology of lipids and lipoproteins has experienced remarkable growth in the past 20 years particularly with the realization that many different classes of lipids play fundamental roles in diseases such as heart disease obesity diabetes cancer and neurodegenerative disorders The 5th edition of this book has been written with two major objectives The first objective is to provide students and teachers with an advanced up to date textbook covering the major areas of current interest in the lipid field The chapters are written for students and researchers familiar with the general concepts of lipid metabolism but who wish to expand their knowledge in this area The second objective is to provide a text for scientists who are about to enter the field of lipids lipoproteins and membranes and who wish to learn more about this area of research All of the chapters have been extensively updated since the 4th edition appeared in 2002 Represents a bridge between the superficial coverage of the lipid field found in basic biochemistry text books and the highly specialized material contained in scientific review articles and monographs Allows scientists to become familiar with recent developments related to their own research interests and will help clinical researchers and medical students keep abreast of developments in basic science that are important for subsequent clinical advances Serves as a general reference book for scientists studying lipids lipoproteins and membranes and as an advanced and up to date textbook for teachers and students who are familiar with the basic concepts of lipid biochemistry

Bioactive Components of Human Milk David S. Newburg, 2012-12-06 The major emphasis in this book is a compilation and definition of what is known about components of human milk including glycoconjugates that inhibit common pathogens of the infant Also discussed are other bioactive constituents whose relevant biological roles are also beginning to be defined Hormonal and cytokine activity immunomodulating and autoinflammatory agents xenobiotics and conditionally essential nutrients in milk could have roles in the protection of the infant but may also participate in digestive processes maternal infant communication maturation of the gut central nervous system and other

components of infant growth and development Like the protective activities these are discussed in terms of their presence in milk structures potential functions and structure function relationship Components whose role is nutritional support during early development of the infant are also included **Biologically Active Substances of Protozoa** N.N.

Sukhareva-Buell, 2003-07-31 The search for new producers of biologically active substances BAS against human and animal diseases continues to be an important task in biology and medicine Experimental work must be carried out well in advance of need because it takes an average of ten years to develop a new medication as well as additional time to put it on the market Study of the Protozoa forms a special branch of biology protozoology The traditional fields of protozoology are taxonomy phylogeny morphology cytology evolution ecology and host parasite interactions The Protozoa is the only taxon among the microscopic organisms which has not been persistently studied as a source of BAS This book then is the result of the research on the project Biologically active substances of the Mastigophora Flagellates The research was carried out at the Laboratory of Antibiotics Department of Microbiology Biological Faculty of Moscow State University Articles of other authors on the matter have been considered as the important part of this reference book The goal of the reference book is to elucidate scientific approaches which lead to obtaining biologically active substances from cultures of protozoa the book reviews the historical background in connection with contemporary development of the field N N Sukhareva

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Khorokhorina my colleagues at Moscow State University Yu Kozlov and I Oxidative Stress in Vertebrates and Invertebrates Tahira Farooqui, Akhlaq A. Farooqui, 2011-10-24 This volume presents a unique comparative treatment of the role oxidative stress plays in vertebrates and invertebrates in multiple organ systems with regards to cell death development aging and human diseases and anti oxidant therapy It offers comprehensive reviews of the current understanding of oxidative stress mediated physiology and pathology as well as directions for future research It also provides current information on the role of oxidative stress in neurodegenerative diseases cardiovascular diseases and various types of cancer mediated by oxidative stress **Platelet-Activating Factor and Related Lipid Mediators** F. Snyder, 2013-11-11 Platelet activating

factor PAF is the commonly used name for a group of potent biologically active ether linked phospholipids the alkylacetyl glycerophospho cholines Following the identification of the chemical structure of P AF in 1979 much progress has been made in our understanding of these phospholipid mediators This is particularly true from the points of view of their molecular structural requirements for expression of biological activity their biosynthesis and catabolism their diverse range of biological activities evidence for their specific receptors at the cell surface the development of specific antagonists for use in receptor studies and for testing as potential anti PAF drugs and implications about their involvement in health and disease Chapters in this book cover the current status of these general areas of PAF research Although an enormous amount of

information has been published about this interesting new type of phospholipid mediators questions about their mechanism of action regulatory controls and the precise role and relative importance of PAF in specific diseases and physiological functions remain to be answered Since the 1979 discovery the PAF field has brought together scientists from a variety of different biomedical disciplines The diversity of scientists now in PAF research is very apparent from the number of PAF publications appearing in a wide array of scientific journals ranging from molecular biology to clinical medicine Publications related to PAF continue to increase at an amazingly rapid rate with the pace reminiscent of the period following the discovery of prostaglandins

Cumulated Index Medicus, 1986 *Handbook of Organophosphorus Chemistry* Robert Engel, 1992-06-19 This practical work summarizes the development of organophosphorus chemistry in topical areas and details the discipline's current state providing applications and experimental procedures throughout Written by 18 leading authorities in the field the *Handbook of Organophosphorus Chemistry* examines advances in the mechanistic understanding of the Perkow and related organophosphorus reactions describes methods for the reduction of quinquivalent to trivalent phosphorus and their applications to standard synthetic procedures emphasizes the preparation of phosphonates bearing hydroxy amino and thiol functions at the alpha position relative to the phosphoryl group reviews the basics of NMR as it applies to the ^{31}P nucleus considering the use of the latest measurement techniques in solving structural and mechanistic problems compares the characteristics of polymer based and monomeric materials and presents recent progress in the design of insecticides and covers their chemical and biological characteristics Generously referenced with close to 3000 bibliographic citations the *Handbook of Organophosphorus Chemistry* is an important volume for organic medicinal and agricultural chemists and biochemists pharmacists chemical engineers and graduate level students in these disciplines

Handbook of Neurochemistry and Molecular Neurobiology Abel Lajtha, Guido Tettamanti, Gianfrancesco Goracci, 2009-10-27 Contents include Biochemistry and molecular biology of neural lipids Advances in lipid analysis lipidomics Metabolism and enzymology of glycerolipids Lipid metabolism in brain development and aging Cellular and subcellular localization of neural lipids and much more

[News & Features from NIH](#), 1983 **Platelet Activating Factor Receptor** Shivendra D. Shukla, 1992-10-23 Platelet activating factor PAF is the most potent phospholipid agonist known to date PAF has a wide variety of physiological effects and has also been implicated in pathophysiology of cells Since the structural elucidation of PAF in 1979 several laboratories have embarked upon characterizing the PAF receptor and its signaling pathways This book focuses on this aspect and presents the first comprehensive account of research in the area It also examines developments on the PAF receptor its cloning molecular features coupling to multiple signaling pathways and relationship to nuclear gene expression This is an excellent reference volume for all researchers studying PAF

Neurochemical Aspects of Excitotoxicity Akhlaq A. Farooqui, Wei-Yi Ong, Lloyd A. Horrocks, 2007-11-20 In the past decade our understanding of the biochemistry molecular biology and neuropathology of the glutamate transporters and

receptors has exploded It is becoming increasingly evident that molecular mechanisms which govern the transfer of the death signal from the neural cell surface to the nucleus depend on lipid mediators and on cross talk among excitotoxicity oxidative stress and neuroinflammation and that interactions among these three processes play a major role in neuronal cell death during acute neural trauma and neurodegenerative disease These processes may be primary initiating points in neurodegeneration or they may be the end result of the neurodegenerative process itself *Neurochemical Aspects of Excitotoxicity* provides extensive insight into glutamate transporters and receptors including their role in the brain with other neurochemical parameters in excitotoxicity and possible treatments This book will be of interest scientists already working in the field of excitotoxicity who are interested in gaining a broader understanding of this complicated subject area as well as graduate students and neurologists who are curious about a common cause of neuronal injury and neurological disorders

Annual Reports in Medicinal Chemistry, 1989-09-08 *Annual Reports in Medicinal Chemistry Bioactive Ceramides in Health and Disease* Johnny Stiban, 2019-09-09 This book is about the various roles of bioactive ceramides and other sphingolipids in cellular biology The enigmatic biophysical and biochemical properties of ceramides and their propensity to influence membranes whether as rafts or protein permeable channels are heavily discussed Metabolism of ceramides and their metabolites is also focused with ceramide synthase family of proteins being a target of extensive review Ceramide 1 phosphate and other sphingolipids are also presented in cellular physiology and pathophysiology Prokaryotic origins of mitochondria at the level of membranes and the occurrence of apoptosis in bacteria are presented Many aspects of ceramide and sphingolipid biology are addressed in this book Its focus is the metabolism of ceramide in normal and diseased states and the biophysical and biochemical mechanisms governing the bioactivity of these molecules Sphingolipid research has surged over the past thirty years and this book gathers the recent findings of various aspects of sphingolipid biochemistry World renowned scientists from the field of lipid biology specifically sphingolipid biochemistry were gathered to write this book Scholars from most continents of the globe committed to write diligently about their expertise and the newest findings in the relevant fields This book came to fruition after almost a year and a half of laborious preparation and diligent writings This book is targeted to the experienced reader who is looking to read about the various aspects of bioactive ceramide signaling as well as to the newcomer into the field as the topics are explained in concise yet very informative manner The authors and editor wish all readers a pleasant time reading this volume and are adamant that this book will meet all expectations

Current Catalog National Library of Medicine (U.S.), First multi year cumulation covers six years 1965

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






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