Available online at www.sciencedirect.com

ScienceDirect

Progress in Lipid Research 47 (2008) 233–306

Progress in Lipid Research

www.elsevier.com/locate/plipres

Review

Biosynthesis and function of polyacetylenes and allied natural products

Robert E. Minto [*], Brenda J. Blacklock

Department of Chemistry and Chemical Biology, Indiana University–Purdue University Indianapolis, 402 North Blackford Street,
Indianapolis, IN 46202, United States

Received 4 December 2007; received in revised form 25 February 2008; accepted 28 February 2008

Abstract

Polyacetylenic natural products are a substantial class of often unstable compounds containing a unique carbon–carbon triple bond functionality, that are intriguing for their wide variety of biochemical and ecological functions, economic potential, and surprising mode of biosynthesis. Isotopic tracer experiments between 1960 and 1990 demonstrated that the majority of these compounds are derived from fatty acid and polyketide precursors. During the past decade, research into the metabolism of polyacetylenes has swiftly advanced, driven by the cloning of the first genes responsible for polyacetylene biosynthesis in plants, moss, fungi, and actinomycetes and the initial characterization of the gene products.

The current state of knowledge of the biochemistry and molecular genetics of polyacetylenic secondary metabolic pathways will be presented together with an up-to-date survey of new terrestrial and marine natural products, their known biological activities, and a discussion of their likely metabolic origins.

Keywords: Acetylenes; Polyacetylenes; Secondary metabolism; Desaturases; Lipids; Polyketides

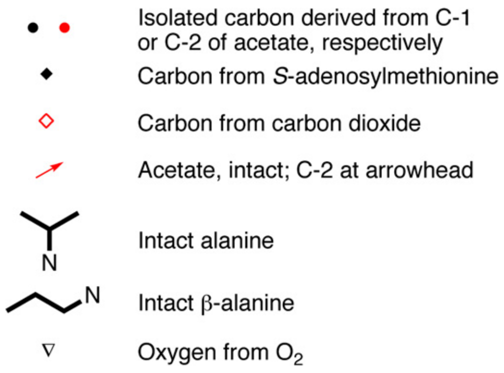
Contents

Abbreviations: ACP, acyl carrier protein; AT, acyltransferase; CoA, coenzyme A; CDP-CPT, cytidine diphosphocholine diacylglycerol choline phosphotransferase; CFA, cyclopropanyl fatty acid; COX, cyclooxygenase; CYP_{450}, cytochrome P_{450}; DAG, diacylglycerol; DGAT, diacylglycerol:acyl-CoA, acyltransferase; DGDG, digalactosyldiacylglycerol; DH, b-hydroxyacyl dehydratase; DHAP, dihydroxyacetone phosphate; Dhoea, 2,2-dimethyl-3-hydroxy-7-octenoic acid; Dhoya, 2,2-dimethyl-3-hydroxy-7-octynoic acid; dNDP, deoxynucleotide diphosphate; %ee, percent enantiomeric excess; EPA, eicosapentenoic acid; ER, endoplasmic reticulum; FAR, fatty acyl-CoA reductases; FAS, fatty acid synthase; Hmpa, 2-hydroxy-3-methylpentanoic acid; LIP, lipase; LPAAT, lysophosphatidic acid acyltransferase; KASA, ketoacyl synthase A; KIE, kinetic isotope effect; KR, b-ketoacyl reductase; KS, b-ketoacyl synthase; MCFA, medium-chain fatty acid; Me, methyl; MEP, methylerythritol-4-phosphate; MGDG, monogalactosyldiacylglycerol; *N*-MeVal, *N*-methylvaline; NADH, nicotinamide adenine dinucleotide, reduced form; NADPH, nicotinamide adenine dinucleotide phosphate, reduced form; NRPS, non-ribosomal peptide synthase; nt, nucleotide; OPP, pyrophosphate; ORF, open-reading frame; PA, phosphatidic acid; PBAN, pheromone biosynthesis activating neuropeptide; PC, phosphatidylcholine; PCR, polymerase chain reaction; PE, phosphatidylethanolamine; PI, phosphatidylinositol; PKS, polyketide synthase; PK, polyketide; PL, phospholipase; PPTE, 4′-phosphopantetheinyl thioesterase; r.a., relative activity; TAG, triacylglycerol; TFA, total fatty acids; VLCFA, very long-chain fatty acids.

[*] Corresponding author. Tel.: +1 317 274 6869; fax: +1 317 274 4701.
E-mail address: minto@chem.iupui.edu (R.E. Minto).

0163-7827/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.plipres.2008.02.002

Biosynthesis.



Key to the experimentally determined isotopic labeling patterns that are superimposed on structures found in, e.g., Figs. 5, 12, etc.

1. Introduction to acetylenic natural products

Acetylenic natural products include all compounds with a carbon–carbon triple bond or alkynyl functional group. While not always technically accurate, the term "polyacetylenes" is often used interchangeably to describe this class of natural products, although they are not polymers and many precursors and metabolites may contain only a single acetylenic bond. Acetylenic natural products are widely distributed, occurring in plants, moss and lichens, fungi, marine algae, sponges, tunicates, insects, frogs, and, in traces quantities, humans. The compounds themselves tend to be unstable, succumbing either to oxidative, photolytic, or pH-dependent decomposition, which originally provided substantial challenges for their isolation and characterization.

The earliest isolated alkyne-bearing natural product was dehydromatricaria ester (**1A**), which was isolated, but not fully characterized, in 1826 (Fig. 1). No compound was characterized as being acetylenic until 1892 (tariric acid, **5T**) [1,2], after which only a handful of compounds were isolated before 1952 (Fig. 1). A lecture by Sörensen to the Royal Chemical Society in Glasgow describes the early history of polyacetylenic natural product chemistry [3]. From the 1960s to the late 1980s, natural products began to yield to the increasing powers of separation and analysis, bolstered by the ability of organic chemists to synthesize