

Review

Allenic and cumulenenic lipids [☆]

Valery M. Dembitsky ^{a,*}, Takashi Maoka ^b

^a Department of Medicinal Chemistry and Natural Products, School of Pharmacy,
P.O. Box 12065, Hebrew University, Jerusalem 91120, Israel

^b Research Institute for Production Development, 15 Shimogamo-Morimoto-Cho, Sakyo-Ku, Kyoto 606-0805,
Kyoto Pharmaceutical University, Japan

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Abstract

Nowadays, about 200 natural allenic metabolites, more than 2700 synthetic allenic compounds, and about 1300 cumulenenic structures are known. The present review describes research on natural as well as some biological active allenic and cumulenenic lipids and related compounds isolated from different sources. Intensive searches for new classes of pharmacologically potent agents produced by living organisms have resulted in the discovery of dozens of such compounds possessing high anticancer, cytotoxic, antibacterial, antiviral, and other activities. Known allenic and cumulenenic compounds can be subdivided on several structural classes: fatty acids, hydrocarbons, terpenes, steroids, carotenoids, marine bromoalenes, peptides, aromatic, cumulenenic, and miscellaneous compounds. This review emphasizes the role of natural and synthetic allenic and cumulenenic lipids and other related compounds as an important source of leads for drug discovery.

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Keywords: Fatty acids; Lipids; Triacylglycerides; Hydrocarbons; Allenic; Cumulenenic; Anticancer; Antiviral; Antibacterial; Terpenoids; Carotenoids; Steroids; Peptides; Aromatic; Synthetic

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Abbreviations: AADC, aromatic acid decarboxylase; ABA, abscisic acid; α -Allenic-DOPA allenic analog of amino acid L-3,4-dihydroxyphenylalanine (L-DOPA); GABA, γ -aminobutyric acid; HepG2, human hepatocellular liver carcinoma cell line; HUVEC, umbilical vein endothelial cells; LM, leucomycin; LOX, lipoxygenase; LPS, lipopolysaccharide; MGC, mammalian gene collection; MTT assay is a laboratory test and a standard colorimetric assay for measuring cellular proliferation; NF-kappa B, factor-kappa B; OAT, optically active triglycerides; Raji cells are a line of EBV-transformed lymphocytes with surface F_c receptors; TNF-alpha, tumor necrosis factor; VDR, vitamin D nuclear receptor.

[☆] See Ref. [1] for a previous article giving additional information.

* Corresponding author. Tel./fax: +972 2 590 2947.

E-mail address: dvalery@cc.huji.ac.il (V.M. Dembitsky).

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1. Introduction

Fatty acids constitute an abundant class of natural compounds and are major constituents of many complex lipids. Fatty acids differ in the number of olefinic bonds, extent of branching, the length of the hydrocarbon chain, and the number of functional groups. Allenic fatty acids which are one of the most interesting groups among the naturally occurring lipids, are often neglected in the literature [2,3]. Allenic fatty (carboxylic) acids and other lipophilic metabolites contain the $[-HC=C=CH-]$ group, and cumulenic fatty (carboxylic) acids and related compounds contain the $[-HC=C=C=CH-]$ group. Both these lipid groups are rare in nature [2–4]. Graphic chemical structures both groups are shown in Fig. 1.

Natural occurrence, structures, and biosynthetic pathways have partly been reported in several publications [4–8]. Among naturally occurring allenic fatty acid derivatives are a large group compounds which show cytotoxic, antibacterial, antiviral and other activities, [2,8,9]. Synthesis of allenes, cumulenes, and acetylenes has also been reviewed [8–14].

The chemistry of allenes began from Jacobus Henricus van't Hoff (awarded the first Nobel Prize in Chemistry, 1901), who predicted the structures of allenes and cumulenes paper, in 1875 [15]. The first allenic dicarboxylic acid, named glutinic acid (2,3-pentadienedioic acid) was isolated from leaf resin of *Alnus glutinosa* (Betulaceae, also called 'European alder'), in 1908 by Hans [16]. The first allenic carotenoid, named fucoxanthin was found in extracts of three species of marine brown algae, *Fucus*, *Dictyota* and *Laminaria*, in 1914 by Willstätter and Page [17]. More recently, fucoxanthin was isolated from other algae, invertebrates, plants, and other species [18–24].

The first allenic sesquiterpene named panacene was isolated from mixture of $H_2O-Et_2O-MeOH$ extract of a perennial shrub Korean ginseng (also called *Panax ginseng*) in 1915 by Kondo and Tanaka [25]. In 1931, Min re-discovered the sesquiterpene previously named panacene from *Panax ginseng* and *Panax quinquefolius* [26]. In 1964, Lee and Lee confirmed the presence of sesquiterpene panacene in *Panax ginseng* [27]. More recently, brominated analog of panacene was isolated from the sea hare *Aplysia brasiliiana*, and it acts as a fish antifeedant [28]. The second allenic fatty acid, named mycomycin, which was produced by a mold-like Actinomycete and was active against the *Bacilli* sp. of human tuberculosis was discovered in 1947 by Johnson and Burdon [29]. The structure of mycomycin and its physical, chemical, and tuberculostatic properties were reported soon after [30–34].

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