Review

Hydrobiological Aspects of Saturated, Methyl-Branched, and Cyclic Fatty Acids Derived from Aquatic Ecosystems: Origin, Distribution, and Biological Activity

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Abstract: This review focuses on the hydrobiological aspects of saturated, methyl-branched, and cyclic fatty acids (FA) derived from aquatic ecosystems. This short review presents the distribution of about 60 FA in various living organisms inhabiting the aquatic environment as well as in marine and freshwater sediments. In addition, it is important to determine the biological activity of saturated, methyl-branched, and cyclic fatty acids. An interesting finding was that some cyclic FA show antiplatelet activity. The generalized and presented data are of interest to hydrobiologists, chemists, and pharmacologists.

Keywords: aquatic organisms; saturated; cyclic; fatty acids; biological activity

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1. Introduction

Fatty acids (FA) are important components of complex lipids such as mono-, di-, and triglycerides, glycolipids, phospholipids, and steryl esters [1–25]. In addition, FA are the building blocks of fat both in the bodies of animals and in food that living organisms eat [1–3,13–15]. Typically, FA are carboxylic acids with aliphatic chains of various lengths: short chain (C1–C7), medium chain (C8–12C), long chain (C13–C22), and very long chain (C24–C36). The most common FA chain length range is between C14 and C20 [1,4–10,16–25]. During digestion, the body breaks down dietary fats into FA, which then enter the bloodstream. FA molecules combine in groups of three FA to form a molecule called triglyceride [15]. Complex lipids are the basis of the biological membranes of marine organisms, algae, plants, fungi, animals, and microorganisms [1–3,5–12,17–22]. The biochemistry and chemistry of FA are well studied, made up of aliphatic chains that contain a carboxyl group (–COOH) [1,2]. The most naturally occurring FA have an unbranched chain with an even number of carbon atoms, from 4 to 36; however, odd FA are also widely present, especially in microorganisms [1,3]. In either of these forms, fatty acids are important dietary fuel sources for animals and important structural components for cells. FA can be both saturated and non-saturated. The full names of lipids and fatty acids can be found in a published article titled: ‘*The nomenclature of lipids*’ [2].

2. Acyclic Aliphatic Fatty (Carboxylic) Acids

The saturated FA shown in Figure 1 are the most abundant in a variety of natural sources. The first on this list is caprylic acid (1), which was first found in goat milk along with caproic acid (C6) and capric acid (2), and these acids together make up over 15% of the FA in goat milk fat [26,27].

The n-saturated (1–9, see Figure 1), iso- (16–22, see Figure 2) and anteiso- (29–35, see Figure 2), branched-chain (48–53, see Figure 3) FA series occur in many bacteria as the major acyl constituents of membrane lipids. In addition, ω-cyclohexyl (58) and ω-cycloheptyl (59) FA are present in several bacterial species [28,29]. Cyclopropane FA, containing three carbon rings located at different sites of the FA chain (55–57, see Figure 3), occur widely

in several microorganisms as major lipid components and in certain eukaryotes including protozoa, fungi, and plants [30–33].

Figure 1. Saturated FA derived from different sources.

Figure 2. An *iso*- and *anteiso*-FA derived from different sources.

Figure 3. Cyclic and miscellaneous FA derived from different sources.

Bacillus is a genus of Gram-positive rod-shaped bacteria whose FA composition is the most well-studied. Thus, FA produced by 22 strains of 10 species of the genus *Bacillus* (see Figure 4) were studied. All 10 species, *B. alvei*, *B. brevis*, *B. cereus*, *B. circans*, *B. licheniformis*, *B. macerans*, *B. megaterium*, *B. polymyxa*, *B. pumilus*, and *B. subtilis*, produced eight unusual fatty acids, six branched (*anteiso*-15:0, *anteiso*-17:0, *iso*-14:0, *iso*-15:0, *iso*-16:0, and *iso*-17:0) and two n-14:0 and n-16:0. In all cases, the six branched chain FA accounted for more than 60% of the total FA. In addition to the eight FA, *B. cereus* produced four additional FA, three branched (*anteiso*-13:0, *iso*-12:0, and *iso*-13:0) and one monoene-n-C16 [29,34,35].

Figure 4. Gram-positive, rod-shaped bacteria belonging to the genus *Bacillus*: (a) *B. subtilis*, (b) *B. cereus*, (c) *B. megaterium*, and (d) *B. polymyxa*, widely found in water and soil, are producers of saturated, *iso*-, *anteiso*-, and branched-chain and cyclic FA. All photos are taken from sites where permission is granted for non-commercial use.

n-Straight chain, *iso*-, and *anteiso*-acids from different sedimentary environments of the North Atlantic have also been studied. Acids cover the range from C7 to C21. Normal and *iso*-acids occur at every number; *anteiso*-acids occur only at odd carbon numbers within the same range. It is suggested that the *iso*- and *anteiso*-acids may provide markers for the bacterial contribution, and the isoprenoid acid markers for the contribution of animal and plant lipids to the organic matter of recent sediments [36]. Sediment samples were taken from a mangrove swamp in the Low Islands, North Queensland, in the Great Barrier Reef, Australia. The FA composition consisted of n-saturated (1–13, structures in Figure 1), *iso*- (15–22, structures in Figure 2) and *anteiso*- (32–34, structures in Figure 2), branched (49), and cyclopropane containing (55 and 56, Figure 3) FA [37]. The authors believe that FA found in marine sediments are of bacterial origin.

The composition of FA extracted from the cyanobacteria *Synechocystis* sp. PCC 6803, *Anabaena variabilis* ATCC 29413 (see Figure 5), *Synechococcus* sp. PCC 7002, and *Cyanothece* sp. ATCC 51142 strains were reported, and the thylakoid membrane contained: C8:0 (caprylic), C10:0 (capric), C12:0 (lauric), C16:0 (palmitic), and C18:0 (stearic) acids [38]. The microalgae *Arthrospira platensis* (see Figures 5 and 6), *A. maxima* and *A. pacifica* contained 3.7 to 4 percent caprylic acid, while this FA ranged between 0.26 and 4 percent in *Chlorella vulgaris* and *C. pyrenoidosa* [39].

Figure 5. Cyanobacteria: (a) *Anabaena planctonica*; (b) *Nostoc commune*; (c) *Arthrospira platensis*; (d) *Lyngbya* sp. living in aquatic environments and producing saturated and branched FA.

Figure 6. *Arthrospira* is a free-floating filamentous cyanobacterium that naturally occurs in tropical and subtropical lakes or stagnant rivers and swamps. Several types of *Arthrospira* are cultivated in many countries around the world and are used as a feed additive in aquaculture, aquariums, and poultry farming. All *Arthrospira* species contain saturated and methyl-branched FA.

A more detailed analysis of FA using gas chromatography-mass spectrometry (GC-MS) of various cyanobacteria species showed that these organisms contain caprylic, capric, and lauric acids in low proportions from 0.15 to 0.5 percent. n-Saturated FA (1–9), iso-FA

(14–18), and ω -cyclic FA (58) in six freshwater wild cyanobacteria (*Chroococcus minutus*, *Lyngbya ceylanica* (see Figure 5), *Merismopedia glauca*, *Nodularia sphaerocarpa*, *Nostoc linckia*, and *Synechococcus aeruginosus*) collected from different lakes and springs of Israel were found [40]. In addition, these FA were found in three species of wild terrestrial strains of the genus *Chroococcidiopsis* (see Figure 7): *C. supralittoralis*, *C. umbratilis*, and *C. versatilis*, which were collected from Lake Kinneret, Dead Sea, and Ein Kerem (Jerusalem) [41].

Figure 7. Microphotograph of the strain *Chroococcidiopsis versatilis*, originally isolated from the sublittoral hypersaline solar pond at the Dead Sea.

Low molecular, hydroxy, dioic, saturated (1–11, 14–21, 27–34), and unsaturated FA were identified in about 50 cyanobacterial species belonging to the genus *Nostoc* (see Figure 5) and in different habitats: freshwater, terrestrial as well as symbionts. There were large variations in individual fatty acid contents according to species and location of the genus *Nostoc*. Statistical analysis of the variability of fatty acids belonging to the genus *Nostoc* was reported [42]. The FA composition of many species of cyanobacteria, which are summarized in some reviews, show that various types of cyanobacteria contain saturated acids (1–10), *iso*-FA (14–23), and *anteiso*-FA (27–36) [43–49]. Moreover, carboxylic acids (1–40) have been found in the lipopeptides of cyanobacteria [50–53].

It is known that monounsaturated and polyunsaturated FA possess many nutritional properties, and their main sources are marine red, brown, and green algae [48,54–59]. Saturated FA have always been of less interest since they were assumed to have no practical value for human and animal health [60–62].

The genus of green seaweed *Codium* (algae of genus *Codium* are shown in Figure 8) includes about 50 species in different parts of the world's oceans, and the FA composition has only been studied in 12 species. For all studied species, *Codium decorticatum*, *C. dichotomum*, *C. duthiae*, *C. dwarkense*, *C. elongatum*, *C. flabellatum*, *C. flabellatum*, *C. galeatum*, *C. harveyi*, *C. intractum*, *C. iyengarii*, *C. muelleri*, *C. pomoides*, *C. taylorii*, and *C. fragile* were characterized by the presence of saturated FA (2–13) as well as some *iso*- (18–21) and *anteiso*-FA (30–35) [63–65].

Caprylic acid (1) and some other saturated FA such as lauric (3), tridecylic (4), myristic (5), pentadecylic (6), palmitic (7), margaric (8), stearic (9), and nonadecylic (10) acids were found in acetone extracts of the brown algae *Padina pavonica* and *Hormophysa triquetra* and these acids showed antimicrobial activity against Gram-negative bacteria *E. coli* and Gram-positive bacteria *S. aureus* [66].

When studying Chlorophyceae (*Ulva rotundata* and *Enteromorpha intestinalis*), Pheophyceae (*Laminaria saccharina*, *L. digitata*, *Fucus vesiculosus*, *Undaria pinnatifida*, and *Halidrys siliquosa*), and Rhodophyceae (*Porphyra umbilata* and *Gracilaria verrucosa*), the authors showed that 14:0, 16:0, and 18:0 dominated among the saturated FA, while 12:0, 13:0, 15:0, 17:0, and 20:0 were found among minor FA [67]. Samples of marine brown algae are shown in Figure 9, and red algae are shown in Figure 10.

FA from more than twenty aquatic and terrestrial moss species were studied and among the saturated acids, n-saturated (2–13), *iso*- (16–21), *anteiso*- (30–36), and branched (49–51) have been found [68–70].

Figure 8. Green algae belonging to the genus *Codium*: (a) *C. capitatum*; (b) *C. dwarkense*; (c) *C. taylorii*; and (d) *Codium* sp. live in different zones of the world's oceans and contain different types of saturated and methyl-branched FA.

Figure 9. Marine brown algae: (a) *Fucus vesiculosus*; (b) *Laminaria digitata*; (c) *Padina pavonica*; and (d) *Undaria pinnatifida* contain a wide range of saturated and methyl-branched FA.

Figure 10. Marine red algae: (a) *Asparagopsis taxiformis*; (b) *Corallina officinalis*; (c) *Porphyra umbilicalis*; and (d) *Gracilaria verrucosa* contain an interesting spectrum of saturated and methyl-branched FA.

Freshwater and marine invertebrates contain a wide variety of saturated FA [71–75]. For instance, freshwater sponges *Lubomirskia baikalensis*, *Baikalospongia bacillifera*, and *B. intermedia* from Lake Baikal contain n-saturated (2–13), iso- (16–26), anteiso- (29–39), and other acids (49–51) [76–78]. Very-long-chain and multibranched polyunsaturated and saturated FA of three freshwater sponges, *Ephydatia syriaca*, *Nudospongilla* sp. and *Cortispongilla barroisi* belonging to the family Spongillidae (class Demospongia) were studied and the saturated FA were found to be like the acids found in Baikal freshwater sponges [79–81]. Examples of freshwater sponges from Lake Baikal are shown in Figure 11, whereas further examples of freshwater sponges are shown in Figure 12.

Figure 11. Endemic freshwater sponges of Lake Baikal, living at depths from 100 to 1500 m: (a) *Lubomirskia* sp.; (b) *Lubomirskia baikalensis*; (c) *Lubomirskia* sp. and (d) *Lubomirskia baikalensis*. All these sponge species contain saturated and methyl-branched FA.

Figure 12. Samples of freshwater sponges: (a) *Ephydatia fluviatilis*; (b) *Spongilla* sp.; (c) *Spongilla lacustris*; (d) *Ephydatia* sp. living in rivers and lakes synthesize a different FA including saturated, branched, and unsaturated.

Marine sponges are of particular interest to scientists due to their ability to synthesize many different chemically interesting and unusual molecules. FA of marine sponges are no exception and are of great practical importance both for chemists, pharmacologists, and physicians due to their high biological activity. Almost all the saturated acids (1–57) that are presented in this article were found in various marine sponges, of which more than 600 species have been studied [82–90]. Several specimens of marine sponges found in various regions of the oceans are shown in Figure 13.

Figure 13. Photos of samples of marine sponges. These invertebrates synthesize a wide variety of biologically active and unusual metabolites including saturated, *iso*-, *anteiso*-, and branched-chain FA.

Molluscs are one of the most diverse and widespread groups of invertebrates in freshwater and marine habitats. Unfortunately, due to human activities, freshwater and

marine taxa of molluscs are among the most endangered invertebrates on Earth, and many species are on the verge of extinction [91–96].

The study of the composition of saturated FA of molluscs living in sea, fresh, or brackish waters has shown no fundamental difference in the qualitative composition of acids, but there are significant differences in the quantitative composition [97–106]. The main fatty acids that have been found in marine and freshwater molluscs are saturated (4–11), *iso*- (17–23), *anteiso*- (31–35), and other (49–51, 53). Examples of freshwater molluscs are shown in Figure 14, whereas some species of nudibranch molluscs are shown in Figure 15.

Figure 14. Samples of freshwater snails that have been tested for FA content. Experiments have shown that the lipids of these mollusks contain saturated, methyl-branched, and unsaturated FA.

Figure 15. Examples of nudibranchs, a group of soft-bodied marine gastropods that shed their shells after the larval stage. Nudibranchs are often called sea slugs and contain a range of saturated, methyl-branched, and unsaturated FA.

3. Comparison of Biological Activities of Natural Saturated Fatty Acids

It is known that the chemical structure of both natural molecules predetermines biological activity, which makes it possible to analyze the structure–activity relationships (SAR). This concept was first proposed by Brown and Fraser more than 150 years ago in 1868 [107]. According to other sources [108], SAR was used from the field of toxicology, according to which Cros, in 1863, determined the relationship between the toxicity of primary aliphatic alcohols and their solubility in water. More than 30 years later, Richet in 1893 [109], Meyer in 1899 [110], and Overton in 1901 [111] separately found a linear correlation between lipophilicity and biological effects. By 1935, Hammett [112,113] presented a method for accounting the effect of substituents on reaction mechanisms using an equation that considered two parameters: the substituent constant and the reaction constant. Complementing Hammett’s model, Taft in 1956 proposed an approach to separate the polar, steric, and resonance effects of substituents in aliphatic compounds [114]. Combining all previous developments, Hansch and Fujita laid out the mechanistic basis for the development of the QSAR method [115], and the linear Hansch equation and Hammett’s electronic constants are detailed in the book by Hansch and Leo published in 1995 [116].

Some popular computer programs can, with some degree of reliability, estimate the pharmacological activity of organic molecules isolated from natural sources or synthesized compounds [117–119]. It is known that classical SAR methods are based on the analysis of (quantitative) structure–activity relationships for one or more biological activities by using organic compounds belonging to the same chemical series as the training set [120].

The computer program PASS (prediction of activity spectra for substances), which has been continuously updated and improved for the past thirty years [121], is based on the heterogeneous training set algorithm, which includes information on more than 1.3 million known biologically active compounds that correlates with the data on about 10,000 types of biological activity [122]. Chemical descriptors implemented in PASS, which reflect the peculiarities of ligand–target interactions, and the original realization of the Bayesian approach for the elucidation of structure–activity relationships provide the average accuracy and predictivity for several thousand biological activities equal to about 96% [123]. In several comparative studies, it was shown that PASS outperforms, in predictivity, some other recently developed methods for the estimation of biological activity profiles [124,125]. Freely available via the Internet, the PASS Online web-service [126] is used by more than thirty thousand researchers from almost a hundred countries to determine the most promising biological activities for both natural and synthetic compounds [127,128]. To reveal the hidden pharmacological potential of the natural substances, researchers have successfully used the past fifteen years [129,130].

In the current study, we obtained PASS predictions for about 60 saturated fatty acids produced by different living organisms. PASS estimates are presented as Pa values, which correspond to the probability of belonging to a class of “actives” for each predicted biological activity. The higher the Pa value, the higher the confidence in the predicted biological activity [131].

Saturated FA (1–13) are complex lipids and are found in almost all living organisms. The biological activities of some of these acids have been studied and are shown in Table 1. The biological activity that was found using the PASS program is also provided in Table 1. For all saturated acids, the property as a regulator of lipid metabolism is dominant with a reliability of 86% to 91%. Of greatest interest are acids 9, 10, 11, and 12 since their reliability exceeds 91% and Figure 16 shows the 3D graph of the predicted and calculated biological activity of these saturated FA.

Table 1. Biological activity of saturated FA.

No.	Predicted Biological Activity, Pa *	Reported Activity	Ref.
1	Lipid metabolism regulator (0.860), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638) Atherosclerosis treatment (0.634), Antiprotozoal (Coccidial) (0.514)	Antibacterial Anti-fungal Anti-protozoan Antiviral	[132]
2	Lipid metabolism regulator (0.860), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638) Atherosclerosis treatment (0.634), Antiprotozoal (Coccidial) (0.514)	Antibacterial Anti-protozoan Anti-fungal Antiviral	[132]
3	Lipid metabolism regulator (0.860), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638)	Antibacterial Anti-fungal Anti-protozoan	[132]
4	Lipid metabolism regulator (0.860), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638)	Antibacterial Antiviral	[132]
5	Lipid metabolism regulator (0.860), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638)	Antibacterial Anti-fungal	[132]
6	Lipid metabolism regulator (0.860), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638)	Antibacterial	[132]
7	Preneoplastic conditions treatment (0.836), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638)	Antibacterial Anticancer	[132,133]
8	Lipid metabolism regulator (0.860), Antiviral (Arbovirus) (0.833) Anti-inflammatory (0.709), Antiviral (Picornavirus) (0.706) Anti-hypercholesterolemic (0.646), Antibacterial (0.638)	Antibacterial Anti-breast cancer	[132,134]
9	Lipid metabolism regulator (0.913), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Antiviral (Arbovirus) (0.705), Antiviral (Picornavirus) (0.617)	Antibacterial Antiviral Hemolytic	[132]
10	Lipid metabolism regulator (0.913), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Antiviral (Arbovirus) (0.705), Antiviral (Picornavirus) (0.617)	No experimental data	
11	Lipid metabolism regulator (0.913), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Antiviral (Arbovirus) (0.705), Antiviral (Picornavirus) (0.617)	No experimental data	
12	Lipid metabolism regulator (0.913), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Antiviral (Arbovirus) (0.705), Antiviral (Picornavirus) (0.617)	No experimental data	
13	Lipid metabolism regulator (0.817), Hypolipemic (0.784) Antiviral (Arbovirus) (0.768), Antineurotic (0.752) Antiviral (Picornavirus) (0.683), Antifungal (0.567)	No experimental data	

* Only activities with Pa > 0.5 are shown.

It is known that *iso*-FA (14–26), which are part of complex lipids and are found in almost all living organisms, are produced by many bacteria. The biological activity of some of these acids was studied and shown in Table 2, and the structures are shown in Figure 2. The biological activity that was found using the PASS program is provided in Table 2. For many *iso*-acids, the dominant property is as a regulator of lipid metabolism with a reliability of more than 81%. Among the published activities of *iso*-acids, anti-breast cancer activity is characteristic. Three acids 17, 18 and 19 are of interest since their reliability is

81% and Figure 17 provides the 3D graph of the predicted and calculated biological activity of these FA.

Figure 16. The 3D graph shows the predicted and calculated biological activity of saturated FA (compound numbers: 9, 10, 11, and 12) showing the highest degree of confidence of more than 91%. The red zone is the dominant activity that is characteristic of all acids.

Figure 17. The 3D graph shows the predicted and calculated biological activity of *iso*-FA (compound numbers: 17, 18, and 19) showing the highest degree of confidence, more than 81%. In the red zone, there are two dominant activities (two peaks), which are characteristic of these acids. The first property is a regulator of lipid metabolism with a confidence level of 81%, and the second property is the treatment of precancerous conditions with a confidence level of more than 80%.

Table 2. Biological activity of acyclic aliphatic *iso*-FA.

No.	Predicted Biological Activity, Pa *	Reported Activity	Ref.
14	Sclerosant (0.878), Anesthetic general (0.849), Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805) Acute neurologic disorders treatment (0.723), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	No experimental data	
15	Sclerosant (0.878), Anesthetic general (0.849), Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805) Acute neurologic disorders treatment (0.723), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	No experimental data	
16	Sclerosant (0.878), Anesthetic general (0.849), Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805) Acute neurologic disorders treatment (0.723), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134,135]
17	Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134,135]
18	Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134]
19	Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134,135]
20	Lipid metabolism regulator (0.810), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)		
21	Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134,135]
22	Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134]
23	Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134]
24	Lipid metabolism regulator (0.810), Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649)	Anti-breast cancer	[134]
25	Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649), Antimutagenic (0.532)	No experimental data	
26	Preneoplastic conditions treatment (0.805), Antiviral (Arbovirus) (0.716), Antiviral (Picornavirus) (0.649), Antimutagenic (0.532)	No experimental data	

* Only activities with Pa > 0.5 are shown.

Anteiso-FA (27–39), which are part of complex lipids, are found in almost all living organisms, and many bacteria produce them in significant quantities. The biological activity that was found using the PASS program is shown in Table 3, and the structures are shown in Figure 2. For many *anteiso*-acids, the dominant property is as a regulator of lipid metabolism with a confidence level of more than 91%. Of interest are four acids 30, 31, 35, and 39, and the reliability of their activity is more than 91%, and Figure 18 represents the 3D graph of the predicted and calculated biological activity of these *anteiso*-FA.

Table 3. Biological activity of acyclic aliphatic *anteiso*-FA.

No.	Predicted Biological Activity, Pa *
27	Anti-hypercholesterolemic (0.801), Preneoplastic conditions treatment (0.793) Hypolipemic (0.768), Acute neurologic disorders treatment (0.718) Atherosclerosis treatment (0.679), Antineoplastic (0.566), Antiparasitic (0.526)
28	Anti-hypercholesterolemic (0.801), Preneoplastic conditions treatment (0.793) Hypolipemic (0.768), Acute neurologic disorders treatment (0.718) Atherosclerosis treatment (0.679), Antineoplastic (0.566), Antiparasitic (0.526)
29	Anti-hypercholesterolemic (0.801), Preneoplastic conditions treatment (0.793) Hypolipemic (0.768), Acute neurologic disorders treatment (0.718) Atherosclerosis treatment (0.679), Antineoplastic (0.566), Antiparasitic (0.526)
30	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
31	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
32	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
33	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
34	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
35	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
36	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
37	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
38	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)
39	Lipid metabolism regulator (0.913), Anti-hypercholesterolemic (0.801), Hypolipemic (0.768) Acute neurologic disorders treatment (0.718), Anticonvulsant (0.717) Atherosclerosis treatment (0.679), Antifungal (0.592), Antiparasitic (0.526)

* Only activities with Pa > 0.5 are shown.

Methyl-branched and cyclic FA (40–59), which are complex lipids, are found in many aquatic organisms including marine and freshwater sponges, molluscs, and other organisms. Bacteria produce cyclic FA. The biological activity that was found using the PASS program is shown in Table 4, whereas the structures are shown in Figure 3. Of greater interest are two cyclic FA (58 and 59) that have been shown to prevent the growth of blood clots and break down blood clots. This is a rare property that FA 58 and 59 exhibit. Figure 19 provides the 3D graph of the predicted and calculated biological activity of cyclic FA.

Figure 18. 3D graph showing the predicted and calculated biological activity of *anteiso*-FA (compound numbers: 30, 31, 35, and 39) showing the highest degree of confidence of more than 91%.

Figure 19. 3D graph showing the predicted and calculated biological activity of ω -cyclo-17,11-cyclohexyl undecanoic acid (58, cyclohexyl 16:0) with the highest degree of confidence of more than 91%. Both ω -cyclohexyl FA (58 and 59) were found in two strains of *Curtobacterium pusillum* and other strains of the genus *Alicyclobacillus*. ω -Cyclohexyl undecanoic acid (58) constituted 12% to 96% of the total FA in the bacteria [136–138].

Table 4. Biological activity of methyl-branched and cyclic FA.

No.	Predicted Biological Activity, Pa *
40	Lipid metabolism regulator (0.905), Anti-hypercholesterolemic (0.789), Hypolipemic (0.757)
41	Lipid metabolism regulator (0.817), Anti-hypercholesterolemic (0.674) Atherosclerosis treatment (0.643)
42	Lipid metabolism regulator (0.905), Anti-hypercholesterolemic (0.789) Atherosclerosis treatment (0.682)
43	Lipid metabolism regulator (0.853), Hypolipemic (0.767) Anti-hypercholesterolemic (0.699), Atherosclerosis treatment (0.694)
44	Hypolipemic (0.863), Lipid metabolism regulator (0.803) Atherosclerosis treatment (0.655), Anti-hypercholesterolemic (0.610)
45	Lipid metabolism regulator (0.877), Hypolipemic (0.809) Atherosclerosis treatment (0.701), Anti-hypercholesterolemic (0.656)
46	Lipid metabolism regulator (0.877), Hypolipemic (0.809) Atherosclerosis treatment (0.701), Anti-hypercholesterolemic (0.656)
47	Lipid metabolism regulator (0.877); Hypolipemic (0.809) Atherosclerosis treatment (0.701), Anti-hypercholesterolemic (0.656)
48	Lipid metabolism regulator (0.865), Hypolipemic (0.781) Anti-hypercholesterolemic (0.721), Atherosclerosis treatment (0.659)
49	Lipid metabolism regulator (0.854), Anti-hypercholesterolemic (0.766) Hypolipemic (0.740), Atherosclerosis treatment (0.685)
50	Lipid metabolism regulator (0.860), Anti-hypercholesterolemic (0.790) Hypolipemic (0.769), Atherosclerosis treatment (0.692)
51	Hypolipemic (0.833), Acute neurologic disorders treatment (0.830) Lipid metabolism regulator (0.771), Anti-hypercholesterolemic (0.701) Atherosclerosis treatment (0.698), Anti-inflammatory (0.662)
52	Lipid metabolism regulator (0.790) Anti-hypercholesterolemic (0.757), Hypolipemic (0.677)
53	Lipid metabolism regulator (0.854), Anesthetic general (0.793) Anti-hypercholesterolemic (0.766), Hypolipemic (0.740)
54	Hypolipemic (0.833), Acute neurologic disorders treatment (0.830) Lipid metabolism regulator (0.771), Neuroprotector (0.676)
55	Mucositis treatment (0.842), Fibrinolytic (0.821); Antithrombotic (0.635), Antimutagenic (0.566)
56	Anti-eczematic (0.893), Mucositis treatment (0.842); Fibrinolytic (0.821), Anti-inflammatory (0.704)
57	Anti-eczematic (0.893), Mucositis treatment (0.842); Fibrinolytic (0.821), Anti-inflammatory (0.704)
58	Fibrinolytic (0.915), Cardiovascular analeptic (0.715), Antithrombotic (0.688) Anti-ischemic, cerebral (0.655), Platelet antagonist (0.581), Anticoagulant (0.515)
59	Fibrinolytic (0.915), Cardiovascular analeptic (0.715), Antithrombotic (0.688) Anti-ischemic, cerebral (0.655), Platelet antagonist (0.581), Anticoagulant (0.515)

* Only activities with Pa > 0.5 are shown.

4. Conclusions

This review focused on the hydrobiological aspects of saturated, methyl-branched, and cyclic FA derived from aquatic ecosystems and their distribution. The review presents about 60 that are found in various living organisms as well as in marine and freshwater sediments such as rivers, lakes, and sea bays. Particularly interesting was the determination of the biological activity of saturated, methyl-branched, and cyclic FA. The pharmacological

activity of the presented acids was determined using the popular computer program PASS. According to PASS data, saturated FA are of interest as regulators of lipid metabolism as well as processes associated with the metabolism and synthesis of cholesterol. In addition, some acids exhibited antiviral and other properties. Methyl-branched acids exhibited similar properties. Interestingly, some cyclic FA exhibited antiplatelet, fibrinolytic, and anticoagulant activities. The obtained and presented data are of interest to hydrobiologists, biologists, chemists, and pharmacologists.

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