Chapter

Introductory Chapter: Fatty Acids in Modern Times

Viduranga Y. Waisundara

1. Introduction to lipids and fatty acids

Before going into the chemical structure and properties of fatty acids, it is important to mention that they are merely one component of the major nutrient group commonly known as lipids. Lipids are biological compounds, which are soluble only in nonpolar solvents. They are typically known as fats and oils as well. However, fats and oil differ from each other based on their physical characteristics. The term "fats" is used to refer solid lipids at room temperature such as lard and butter, while "oils" are liquid lipids at room temperature such as sunflower oil, olive oil, etc. The classification of lipids is shown in **Figure 1**. Fatty acids appear under "triglycerides" since it is a component of this particular category of lipids.

To provide a brief introduction on fatty acids at a very basic level, they are the building blocks of the fat, which is physiologically present and obtained from the food we eat. During digestion, the body breaks down fats in the food products into fatty acids, which are subsequently absorbed into the blood. Upon absorption, fatty acid molecules are typically joined in groups of three, forming a molecule called a triglyceride. It has to be noted in this instance that triglycerides can even be made up from the carbohydrates in the food that we consume. There are several important functions of fatty acids in the body, including being a medium of storing energy

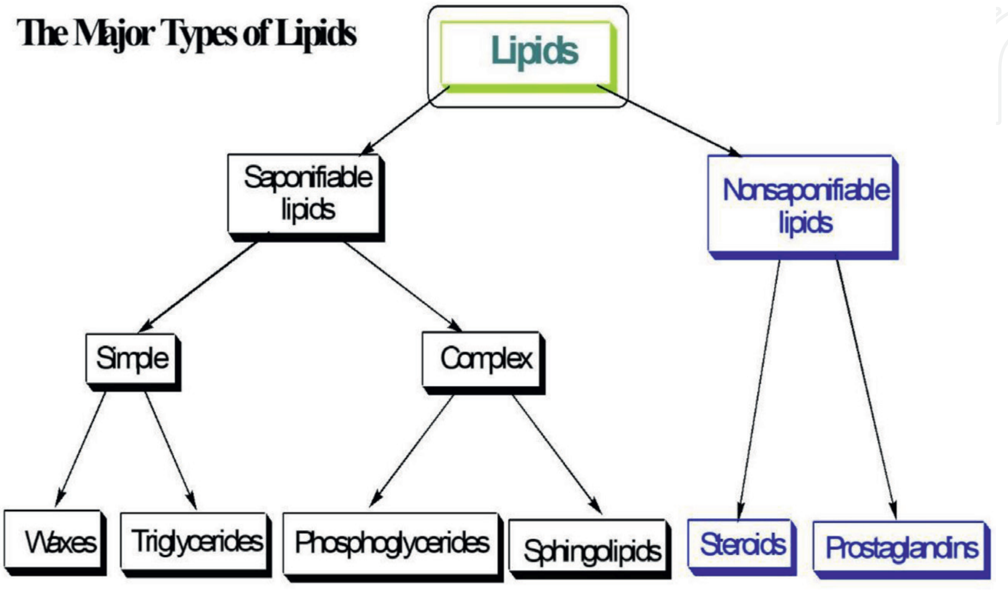

Figure 1.
Major types of lipids: fatty acids come under triglycerides according to this classification.

and being involved in the cellular composition in the forms of phospholipids and cholesterol esters. When glucose is unavailable for generation of energy in the cellular mechanism, the body uses fatty acids as fuel instead.

In terms of the chemical structure, a fatty acid is a carboxylic acid. It has an aliphatic chain, which is either saturated (having only single bonds) or unsaturated (having double bonds). Most of the naturally occurring fatty acids do not have branches in the aliphatic chain and contain an even number of carbon atoms (i.e., from 4 to 28). The long nonpolar tails of the fatty acids are responsible for the hydrophobic characteristics of fats and oils, while the carboxyl group of the fatty acids is polar or hydrophilic. Because of having both the hydrophobic and hydrophilic nature, when fatty acids are placed in an aqueous solution, they form spherical clusters or micelles. The micelles are arranged in such a way that the nonpolar straight chain is extended toward the interior of the structure and away from the water, while the polar carboxyl groups face outward in contact with the water.

There are two major types of classification of fatty acids, among many others. One classification is based on the length of the aliphatic chain, which is as follows:

- Short-chain fatty acids (SCFAs): less than five carbons in the aliphatic chain
- Medium-chain fatty acids (MCFA): aliphatic tails of 6–12 carbons, which form medium-chain triglycerides
- Long-chain fatty acids (LCFA): aliphatic tails of 13–21 carbons
- Very long-chain fatty acids (VLCFA): aliphatic tails of 22 carbons or more

Another classification is based on the level of saturation:

- Saturated fatty acids: no double bonds in the aliphatic tails. The general formula for saturated fatty acids is $C_nH_{2n+1}COOH$.
- Unsaturated fatty acids: one or more double bonds in the aliphatic tails.

Unsaturated fatty acids can be divided into *cis-* and *trans*-fatty acids. A *cis* configuration means that the two hydrogen atoms adjacent to the double bond appear on the same side of the aliphatic chain, whereas *trans* configuration means that the adjacent two hydrogen atoms lie on the opposite sides of the chain. Unsaturated fatty acids can also be divided based on the number of double bonds, where monounsaturated fatty acids would have only one double bond in the aliphatic tail and polyunsaturated fatty acids would have two or more double bonds. Polyunsaturated fatty acids may have the double bonds next to each other as conjugated double bonds or alternatively between single bonds as nonconjugated double bonds.

The *cis* configuration of unsaturated fatty acids will create a bend in the fatty acid chain that is not found in saturated fatty acids. These bends prevent unsaturated fatty acids from packing closely together. As a result, they form less London dispersion forces between the fatty acids. This leads to *cis*-fatty acids having lower melting points. *Trans*-fatty acids, on the other hand, are obtained via hydrogenation of polyunsaturated fatty acids, e.g., margarine. *Trans*-fatty acids will not pack as well as saturated fatty acids, but do not produce a bend as in *cis*-fatty acids. Therefore, the melting points of *trans*-fatty acids are between the melting points of saturated fatty acids and *cis*-fatty acids of the same carbon length.

2. Fatty acids and health

Fatty acids have gained much attention over the past few decades owing to its implications on human health. Much of this is due to the fact that the western diet has changed with the advent of "fast" and "convenient" foods [1]. These food products are energy dense, have a low dietary fiber content, and produce a comparatively lower satiety and satiation signals than low-energy-dense foods [2]. This newly introduced diet is markedly different to the historical diet of humans that the gut was adapted to over several millennia [3]. According to current evidence for most of the history on the human lineage, the diet consisted of more indigestible plant material, such as grasses, sedges, and tubers, than the present and is therefore likely to have contained a larger nondigestible component [4]. Recent systematic reviews of randomized trials [5, 6] and prospective cohort studies [7] have called for the re-evaluation of dietary guidelines based on these dietary transitions, primarily in terms of the intake, and a reappraisal of the effects of fatty acids on health. It is heartening to observe, nevertheless, that public health efforts to remove *trans* fats from the food supply in several countries have intensified [8].

Saturated fatty acids contribute to approximately 10% of energy to the North American diet [9, 10]. According to De Souza et al. [8], the main sources of fatty acids in the food supply of North Americans are animal-based food products, such as butter, cows' milk, meat, salmon, and egg yolks, and a few plant products such as chocolate and cocoa butter, coconut, and palm kernel oils. Despite attempts to completely remove *trans* fats from the diet, they evidently contribute to approximately 1–2% of energy in the North American diet [8, 11–13] and are primarily produced through industrial processing such as partial hydrogenation of liquid plant oils in the presence of a metal catalyst, vacuum, and high heat. Production of *trans* fats can also occur naturally in meat and dairy products, where ruminant animals biohydrogenate unsaturated fatty acids via bacterial enzymes [8]. According to De Souza et al. [8], the major industrially produced *trans*-fatty acids in the food supply are elaidic acid isomers, while the major ruminant-derived *trans*-fatty acid is vaccenic acid. Both these chemical compounds share the characteristic of having at least one double bond in the *trans*-configuration. Present dietary guidelines recommend that saturated fats should be limited to <10% (5–6% for those who would benefit from lowering of low-density lipoprotein, LDL cholesterol) and *trans* fats to <1% of energy or as low as possible in view of reducing the risk of ischemic heart disease and stroke [14–19].

3. Short-chain fatty acids (SCFAs)

There is increased attention on SCFAs given its importance in the human gut microbiota. The human microbiota is primarily the collection of microbes that live on and in our body, where the largest and most diverse cluster of microorganisms inhabits the gut [20]. Evidence has surfaced that the gut microbiota has coevolved with the host, which provides the microbes with a stable environment, while the microbes provide the host with a broad range of functions such as digestion of complex dietary macronutrients, production of nutrients and vitamins, defense against pathogens, and maintenance of the immune system [20]. Interactions between the microbiota and the distal gut are currently considered as fundamental determinants of human health.

As previously mentioned, SCFAs are a subset of saturated fatty acids containing six or less carbon molecules which include acetate, propionate, butyrate, pentanoic (valeric) acid, and hexanoic (caproic) acid. SCFAs are the primary end products of fermentation of nondigestible carbohydrates that become available to the gut microbiota [21]. SCFAs represent the major flow of carbon from the diet, through the gut microbiome to the host. It was discovered recently that SCFA appears to be the natural ligands for free fatty acid receptors 2 and 3 (FFAR 2/3), found on a wide range of cell types, including enteroendocrine and immune cells [22–24]. This unearthing has led to renewed interest in the role of SCFA in human health.

SCFAs are mainly produced through saccharolytic fermentation of carbohydrates which are able to escape digestion and absorption in the small intestine [21, 25]. The pathways of SCFA production are well understood at present and have been recently described in detail recently by Flint et al. [26]. The major products formed as a result of the saccharolytic fermentation are formate, acetate, propionate, and butyrate. Lactate is also a major organic acid produced from the fermentation of selected often rapidly fermentable nondigestible carbohydrates [21]. Relatively minor amounts of branched-chain fatty acids are also produced in this biochemical pathway, mainly through the fermentation process of protein-derived branched-chain amino acids [27, 28].

Acetate is the most abundant SCFA in the colon and makes up more than half of the total SCFA detected in feces [29, 30]. The majority of acetate is produced by most of the enteric bacteria present in the gut as a result of carbohydrate fermentation [30]. In addition, approximately one-third of the colonic acetate has been detected to come from acetogenic bacteria, which are able to synthesize it from hydrogen and carbon dioxide or formic acid through the Wood-Ljungdahl pathway [25, 31].

It is evident from the insurmountable evidence on microbial interactions with dietary polysaccharides and the resulting SCFAs that these particular fatty acids are important energy and signaling molecules. It is becoming increasingly accepted that SCFA-producing bacteria have several beneficial effects on human health. However, it is still unclear whether beneficial effects are driven by the SCFAs per se or whether in combination with other metabolites produced from the gut bacteria [20]. It should be noted and understood in this instance that the gut microbiota produces many other classes of metabolites such as bile acids and amino acid derivatives, which may also have several essential signaling functions leading to health and wellness of the human physiological systems.

4. Conclusion(s)

Fatty acids remain an important component in human nutrition with growing amounts of scientific studies focusing on elucidating its roles in the biochemical pathways as well as its benefits upon consumption. Out of all fatty acids, the two most important types, which have garnered much attention, are *trans*-fatty acids, which are primarily not recommended and have a zero tolerance level of presence in food, and SCFAs owing to their vitality in maintaining the gut microbiota. The knowledge of the role of fatty acids in determining health and nutritional well-being among global consumers has expanded dramatically in the past few decades. The role of fatty acids in neonatal and infant growth and development, health maintenance, the prevention of cardiovascular disease, diabetes, cancers, and age-related functional decline is an aspect, which has been recognized by many experts; thus, despite several highlights of adverse effects of excessive fatty acid consumption, as a class of chemical components, fatty acids remain important to human health, and a complete elimination of fatty acids from the diet is definitely not considered as an intellectual recommendation. As briefly mentioned earlier, fatty acids are the major components of the cell membrane structure, which participate in modulating gene transcription, function as cytokine precursors, and serve as energy sources in complex, interconnected systems. Therefore, it is indeed apparent that dietary fatty acids are vital for many of the physiological functions and, thereby, affect human health.

Conflict of interest

The author has no conflicts of interest to declare, financial or otherwise.

Author details

Viduranga Y. Waisundara
Australian College of Business and Technology, Kandy, Sri Lanka

*Address all correspondence to: viduranga@gmail.com

References

[1] Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. Nutrition Reviews. 2012;**70**:3-21. DOI: 10.1111/j.1753-4887.2011.00456.x

[2] Prentice AM, Jebb SA. Fast foods, energy density and obesity: A possible mechanistic link. Obesity Reviews. 2003;**4**:187-194. DOI: 10.1046/j.1467-789X.2003.00117.x

[3] Eaton SB. The ancestral human diet: What was it and should it be a paradigm for contemporary nutrition? Proceedings of the Nutrition Society. 2006;**65**:1-6

[4] Byrne CS, Chambers ES, Morrison DJ, Frost G. The role of short chain fatty acids in appetite regulation and energy homeostasis. International Journal of Obesity. 2015;**39**:1331-1338. DOI: 10.1038/ijo.2015.84

[5] Chowdhury R, Warnakula S, Kunutsor S, Crowe F, Ward HA, Johnson L, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: A systematic review and meta-analysis. Annals of Internal Medicine. 2014;**160**:398-406. DOI: 10.7326/M13-1788

[6] Harcombe Z, Baker JS, Cooper SM, Davies B, Sculthorpe N, DiNicolantonio JJ, et al. Evidence from randomized controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: A systematic review and meta-analysis. Open Heart. 2015;**2**:e000196. DOI: 10.1136/openhrt-2014-000196

[7] Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. American Journal of Clinical Nutrition. 2010;**91**:535-546. DOI: 10.3945/ajcn.2009.27725

[8] De Souza RJ, Mente A, Maroleanu A, Cozma AI, Ha V, Kishibe T, et al. Intake of saturated and trans unsaturated fatty acids and risk of all-cause mortality, cardiovascular disease, and type 2 diabetes: Systematic review and meta-analysis of observational studies. BMJ. 2015;**351**:h3978. DOI: 10.1136/bmj.h3978

[9] Health Canada, Statistics Canada, Canadian Community Health Survey. Nutrient Intakes from Food: Provincial, Regional and National Data Tables (CCHS Cycle 2.2). Vol. 1-3. Ottawa, Ontario: Health Canada Publications; 2009

[10] Wright JD, Wang CY, Kennedy-Stephenson J, Jacobs Jr DR, Ervin RB. Dietary Intakes of Ten Key Nutrients for Public Health: 1999-2000. Advanced Data; 2003;**17**(334):1-4

[11] Doell D, Folmer D, Lee H, Honigfort M, Carberry S. Updated estimate of trans fat intake by the US population. Food Additives & Contaminants: Part A. 2012;**29**:861-874. DOI: 10.1080/19440049.2012.664570

[12] Kris-Etherton PM, Lefevre M, Mensink RP, Petersen B, Fleming J, Flickinger BD. Trans fatty acid intakes and food sources in the U.S. population: NHANES 1999-2002. Lipids. 2012;**47**:931-940

[13] Ratnayake WM, L'Abbe MR, Farnworth S, Dumais L, Gagnon C, Lampi B, et al. Trans-fatty acids: Current contents in Canadian foods and estimated intake levels for the Canadian population. Journal of AOAC International. 2009;**92**:1258-1276

[14] Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Miller NH, Hubbard VS, et al. AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: A report of the American College of Cardiology/

American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology. 2014;**63**:2960-2984. DOI: 10.1161/01.cir.0000437740.48606.d1

[15] FAO/WHO. Fats and Fatty Acids in Human Nutrition: Report of An Expert Consultation. FAO; 2010

[16] Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, et al. Diet and lifestyle recommendations revision 2006: A scientific statement from the American Heart Association nutrition committee. Circulation. 2006;**114**:82-96

[17] US Department of Agriculture and US Department of Health and Human Services. Dietary Guidelines for Americans, 2010. 7th ed. Washington DC, USA: US Government Printing Office; 2010

[18] EFSA Panel on Dietetic Products NaA. Scientific opinion on dietary reference values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol. Journal of the European Food Standards Agency. 2010;**8**:1461. DOI: 10.2903/j.efsa.2010.1461

[19] Food Standards Australia New Zealand. Trans Fatty Acids. Available from: www.foodstandards.gov.au/consumer/nutrition/transfat/Pages/default.aspx [Accessed: November 1, 2018]

[20] Koh A, De Vadder F, Kovatcheva-Datchary P, Backhed F. From dietary fiber to host physiology: Short-chain fatty acids as key bacterial metabolites. Cell. 2016;**165**:1332-1345. DOI: 10.1016/j.cell.2016.05.041

[21] Morrison J, Preston T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. Gut Microbes. 2016;**7**:189-200. DOI: 10.1080/19490976.2015.1134082

[22] Le Poul E, Loison C, Struyf S, Springael JY, Lannoy V, Decobecq ME, et al. Functional characterization of human receptors for short chain fatty acids and their role in polymorphonuclear cell activation. Journal of Biological Chemistry. 2003;**278**:25481-25489. DOI: 10.1074/jbc.M301403200

[23] Brown AJ, Goldsworthy SM, Barnes AA, Eilert MM, Tcheang L, Daniels D, et al. The orphan G protein-coupled receptors GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids. Journal of Biological Chemistry. 2003;**278**: 11312-11319. DOI: 10.1074/jbc.M211609200

[24] Nilsson NE, Kotarsky K, Owman C, Olde B. Identification of a free fatty acid receptor, FFA2R, expressed on leukocytes and activated by short-chain fatty acids. Biochemical and Biophysical Research Communications. 2003;**303**:1047-1052. DOI: 10.1016/S0006-291X(03)00488-1

[25] Miller TL, Wolin MJ. Pathways of acetate, propionate, and butyrate formation by the human fecal microbial flora. Applied Environmental Microbiology. 1996;**62**:1589-1592

[26] Flint HJ, Duncan SH, Scott KP, Louis P. Links between diet, gut microbiota composition and gut metabolism. Proceedings of the Nutrition Society. 2015;**74**:13-22. DOI: 10.1017/S0029665114001463

[27] Macfarlane S, Macfarlane GT. Regulation of short-chain fatty acid production. Proceedings of the Nutrition Society. 2003;**62**:67-72. DOI: 10.1079/PNS2002207

[28] Russell WR, Gratz SW, Duncan SH, Holtrop G, Ince J, Scobbie L, et al. High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to

colonic health. American Journal of Clinical Nutrition. 2011;**93**:1062-1072. DOI: 10.3945/ajcn.110.002188

[29] Louis P, Scott KP, Duncan SH, Flint HJ. Understanding the effects of diet on bacterial metabolism in the large intestine. Journal of Applied Microbiology. 2007;**102**:1197-1208. DOI: 10.1111/j.1365-2672.2007.03322.x

[30] Ríos-Covián D, Ruas-Madiedo P, Margolles A, Gueimonde M, de los Reyes-Gavilán CG, Salazar N. Intestinal short chain fatty acids and their link with diet and human health. Frontiers in Microbiology. 2016;**7**:185. DOI: 10.3389/fmicb.2016.00185

[31] Louis P, Hold GL, Flint HJ. The gut microbiota, bacterial metabolites and colorectal cancer. Nature Reviews Microbiology. 2014;**12**:661-672. DOI: 10.1038/nrmicro3344