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REVIEW

The Properties of Lauric Acid and Their Significance in Coconut Oil

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Abstract The primary fatty acid of coconut oil is lauric acid, which is present at approximately 45–53 %. The metabolic and physiological properties of lauric acid account for many of the properties of coconut oil. Coconut oil is rapidly metabolized because it is easily absorbed and lauric acid is easily transported. Detailed studies have shown that the majority of ingested lauric acid is transported directly to the liver where it is directly converted to energy and other metabolites rather than being stored as fat. Such metabolites include ketone bodies, which can be used by extrahepatic tissues, such as the brain and heart, as an immediate form of energy. Studies on the effect of lauric acid on serum cholesterol are contradictory. Among saturated fatty acids, lauric acid has been shown to contribute the least to fat accumulation. Lauric acid and monolaurin have demonstrably significant antimicrobial activity against gram positive bacteria and a number of fungi and viruses. Today there are many commercial products that use lauric acid and monolaurin as antimicrobial agents. Because of the significant differences in the properties of lauric acid relative to longer chain fatty acids, they are typically differentiated as medium-chain fatty acids covering C6–C12, and long-chain fatty acids covering C14 and longer.

Keywords Coconut oil · Lauric acid · Medium-chain fatty acid · Medium-chain triglyceride · Monolaurin

Symbols and abbreviations

C6	Caproic acid
C8	Caprylic acid
C10	Capric acid
C12	Lauric acid
C14	Myristic acid
C16	Palmitic acid
C18:0	Stearic acid
C18:1	Oleic acid
C18:2	Linoleic acid
C18:3	Linolenic acid
LCFA	Long-chain fatty acid(s)
LCT	Long-chain triglyceride(s)
MCFA	Medium-chain fatty acid(s)
MCT	Medium-chain triglyceride(s)
MLG-1	1-Monolaurin, 1-monolauryl glyceride
MLG-2	2-Monolaurin, 2-monolauryl glyceride
TAG	Triacylglyceride(s)

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Introduction

Coconut oil is an edible oil present in and recovered from the meat of the coconut. It is unique because it contains lauric acid (C12) as its major fatty acid, accounting for 45–53 % of the overall fatty acid composition. Because coconut oil is widely consumed in the tropics, [1] lauric acid is a significant component of the diet in these parts of the world.

Objectives of this review. Although the properties of a vegetable oil cannot be fully accounted for by a single fatty acid component, this review aims to show that many of the properties of coconut oil can indeed be attributable to the properties of lauric acid. In particular, this review will discuss the role of lauric acid in the metabolism of medium-chain triglycerides and will focus on the metabolism of lauric acid itself. The role of lauric acid in health issues such as cholesterol and fat accumulation and storage will also be discussed. Finally, the well-documented antimicrobial activities of lauric acid and monolaurin will be presented. In

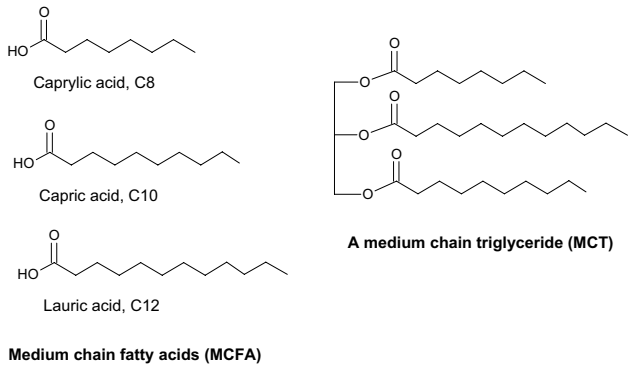


Fig. 1 Examples of medium-chain fatty acids (MCFA) and medium-chain triglycerides (MCT)

these discussions, the one common observation that emerges is that lauric acid, a medium chain fatty acid, has numerous properties that differentiate it from long chain fatty acids.

Medium chain fatty acid (MCFA) and medium chain triglyceride (MCT). There is no generally accepted definition of the term "medium-chain fatty acid" (MCFA). This term is commonly used to refer to two fatty acid groupings: C8 and C10 and C6–C12. Similarly, the term medium-chain triglyceride (MCT) is used to refer to two main types of triglycerides: a commercial triglyceride mixture containing only C8 and C10 fatty acids and a triglyceride mixture which is made up predominantly of C6–C12 fatty acids (Fig. 1).

The definition of MCT as C8 and C10 arose when these fatty acids, which were obtained industrially from fractionation of hydrolyzed coconut oil, were used to manufacture special dietary oils containing C8 and C10 only, while the more commercially more important C12 was used in the surfactant industry [2]. In 1968, Harkins and Sarett [3] developed a synthetic triglyceride mixture composed of 75 % C8 and 25 % C10, which was called "MCT oil" [4]. MCT oil was found to be digested and absorbed more readily than vegetable oils with longer chain fatty acids (LCFA), such as corn oil. MCT oil was found to be useful for nutritional management of patients with impaired fat digestion. Aside from its use in clinics, MCT oil is used today by athletes as a source of quick energy and by medical researchers.

In 1982, Bach and Babayan [5] reviewed the metabolism and action of saturated fatty acids in the liver and extrahepatic tissues. Based on the metabolic and physiological properties of the various fatty acids, Bach and Babayan proposed that medium-chain fatty acids be defined to include C6–C12 and long-chain fatty acids as C14 and longer. Thus the definition of MCT as C8 and C10 only has its origin in commerce, while the definition of MCFA as C6–C12 is based on metabolic and physiological behavior. This article shall use the definition of Bach and Babayan for the terms MCFA and MCT.

Fatty Acids and Triglycerides of Coconut Oil

There are three common ways of analyzing the composition of vegetable oils (Fig. 2). The most common method is by determining the fatty acid composition of the oil by chemical hydrolysis, methylation and analysis by gas chromatography (GC) (method A). The second method entails the separation of the oil into triglyceride fractions using GC or high performance liquid chromatography (HPLC), followed by determination of the fatty acid composition of each triacylglyceride (TAG) fraction by chemical hydrolysis (method B). The third method entails the use of lipase to hydrolyze each TAG fraction (method C). The third method enables the regiospecific identification of the fatty acids on the *sn*-1/*sn*-3 and *sn*-2 positions. The first method, which is the most common method, gives the fatty acid profile of the vegetable oil but does not give the profile of TAG which is unique for each vegetable oil.

The Codex Standard for Named Vegetable Oils [6] lists the fatty acid profile of coconut oil which is obtained by chemical hydrolysis of the oil. Bezard and co-workers [7] used GC to separate the TAG of coconut oil followed by chemical hydrolysis (method B) and determined the fatty acid composition of the main TAG as: trilaurin (3C12), caprodilaurin (C10 + 2C12), caprolauromyristin (C10 + C12 + C14), and dilauromyristin (2C12 + C14). Marina and co-workers [8] analyzed twelve coconut oil samples from Indonesia and Malaysia by HPLC using TAG standards to identify the fractions. The fractions were collected, hydrolyzed and then analyzed by GC to obtain their respective fatty acid compositions. They determined the fatty acid composition of the main TAG and quantified them as follows: trilaurin (3C12, 23.6 %), capryldilauryl glyceride (C10 + 2C12, 19.8 %), dicapryllauryl glyceride (2C10 + C12, 15.4 %), and dilaurylmyristyl glyceride (2C12 + C14, 15.2 %). Lauric acid was found to be present in 92 % of all coconut TAG and MCT were calculated to make up almost 60 % of coconut oil.

On the other hand, Pham and co-workers [9] analyzed coconut oil from the Philippines using pancreatic lipase which has specificity for *sn*-1 and *sn*-3 positions. They determined that 54.3 % of the coconut TAG has lauric acid in the *sn*-1 and -3 positions and 44.1 % in the *sn*-2 position. The presence of capric acid in the same positions was 4.9 and 1.6 %, respectively (Fig. 3). This means that at least 59.2 % (54.3 % + 4.9 %) of coconut TAG has MCFA in the *sn*-1 and *sn*-3 positions and at least 45.7 % (44.1 % + 1.6 %) have MCFA in the *sn*-2 position.

Freshly pressed coconut oil (for example, virgin coconut oil) is a mixture of triglycerides, diglycerides, monoglycerides, and free fatty acids. Using thin layer chromatography (TLC), Pham and co-workers [10] estimated the composition

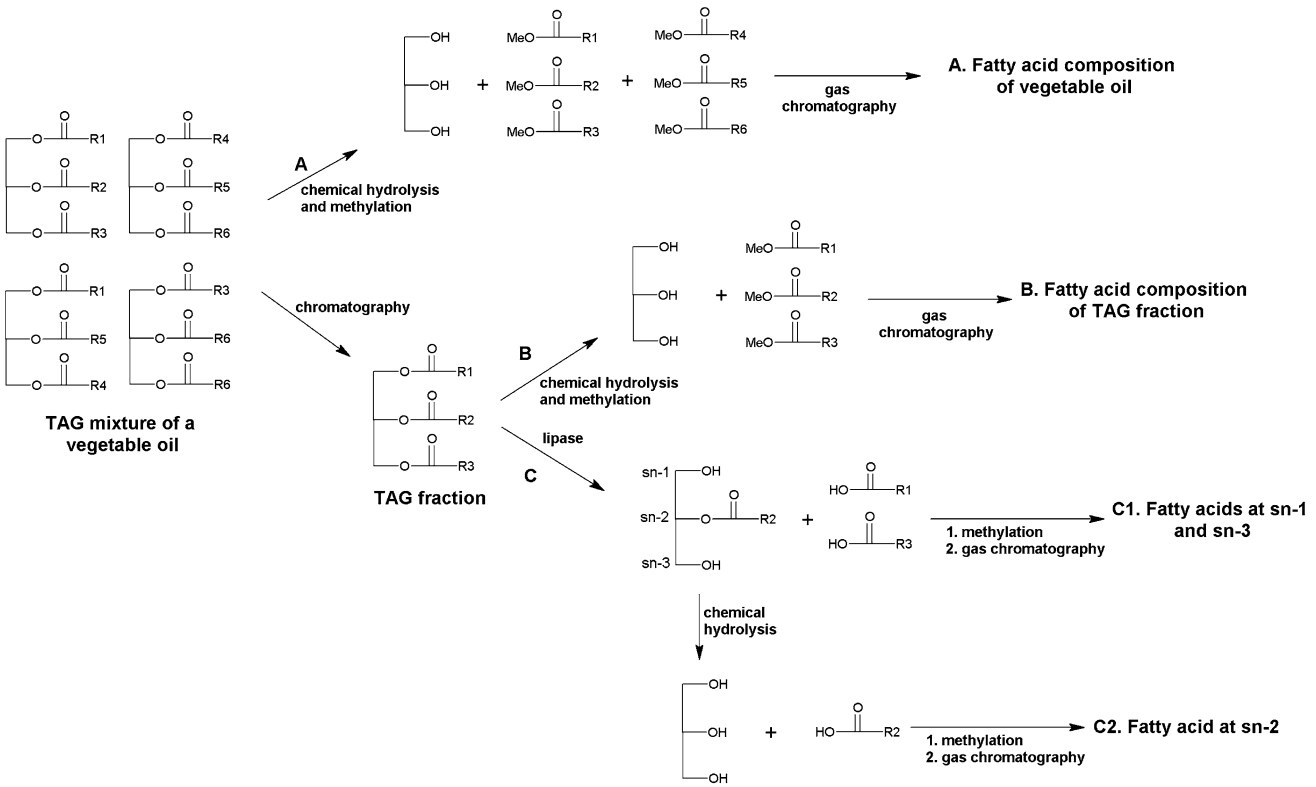


Fig. 2 Analysis of vegetable oils. **a** Chemical hydrolysis gives the fatty acid composition of the vegetable oil. **b** Chemical hydrolysis of a TAG fraction yields the fatty acid composition of the TAG fraction. **c** Hydrolysis using lipase enzymes enables the identification of the fatty acids in the *sn*-1/*sn*-3 positions and the *sn*-2 position (regiospecific analysis)

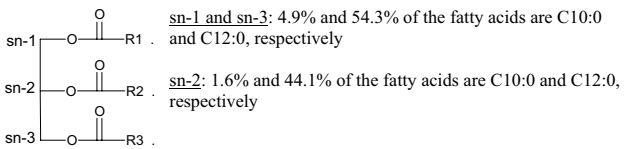


Fig. 3 Lauric acid in the TAG structure of coconut oil [10]

to be approximately 85 % triglycerides, 7 % diglycerides, and 3 % monoglycerides, while Dayrit and co-workers [11] employed nuclear magnetic resonance (NMR) spectroscopy to determine non-TAG components to be 1.5 % diglycerides, 0.01 % 1-monoglycerides, and 0.13 % free fatty acids.

Although coconut oil and palm kernel oil have similar fatty acid profiles (using method A), they have distinctly different triglyceride compositions. Bezard [12] analyzed palm kernel oil and reported a different profile for two of its major TAG: trilaurin (3C12) and dilauromyristin (2C12 + C14). In a comparative study of various vegetable oils, Karupaiah and Sundram [13] determined the regiospecific TAG profiles of coconut and palm kernel oil. They reported that the most dominant regiospecific TAG species in coconut oil were (with assigned *sn*-positions): 1,2,3-trilauryl glyceride (C12-C12-C12), 1-capro,2,3-dilauryl glyceride (C10-C12-C12), and 1-capro,2-lauryl,3-myristyl glyceride (C10-C12-C14), whereas the dominant TAG in palm kernel oil were: 1,2,3-trilauryl glyceride (C12-C12-C12), 1-myristyl,2-stearyl,3-lauryl glyceride (C14-C18-C12), and 1,3-oleyl,2-lauryl glyceride (C18:1-C12-C18:1).

Regiospecific analysis of coconut oil has revealed its triglyceride structure and positional distribution of lauric acid. The presence of lauric acid in the *sn*-1/*sn*-3 positions and the *sn*-2 position has important consequences with respect to the digestion of coconut oil.

Digestion of Coconut Oil

The digestion of triglyceride oils involves both physical and enzymatic processes. Coconut oil, which has a large proportion of MCT, is more water soluble and more rapidly hydrolyzed by lipase than other vegetable oils, which are predominantly LCT.

Hydrolysis by lingual, gastric and pancreatic lipase is regiospecific and the rate is more rapid if MCFA occupy the *sn*-1 and *sn*-3 positions in the TAG as opposed to LCFA [14, 15]. Since 54.3 % of coconut oil TAG contains lauric

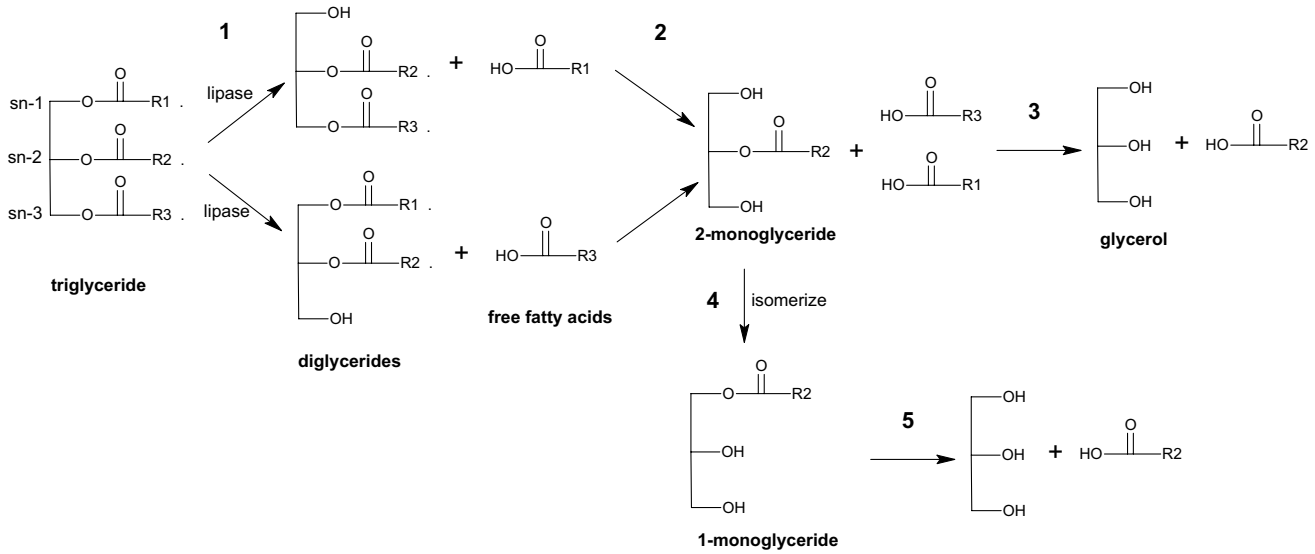


Fig. 4 MCT undergo step-wise hydrolysis upon ingestion

acid in *sn*-1 or -3 positions (and almost 60 % if capric acid is included), [16] coconut oil is very rapidly absorbed. On the other hand, lipase hydrolyzes TAG with LCFA and long-chain polyunsaturated fatty acids (PUFA) in the *sn*-1 and -3 positions less efficiently, leading to slower absorption of such fats and oils [17].

Initial hydrolysis forms 1,2-diglycerides and free fatty acids (Fig. 4, step 1). The second hydrolysis step yields 2-monoglyceride and another free fatty acid. The 2-monoglyceride undergoes competitive hydrolysis (step 3) or isomerization to 1-monoglyceride (step 4). Because lauric acid is present in the *sn*-2 position in 44.1 % of coconut TAG, [18] a relatively large amount of monolaurin is produced.

The third hydrolysis step yields glycerol and the free fatty acid from the *sn*-2 position. The monoglyceride and free fatty acids can be absorbed by the intestinal cells, via specific carrier molecules but possibly also by passive diffusion depending on their chain length. Because of the high proportion of lauric acid in coconut oil, it may be assumed that monolaurin and lauric acid are present in the stomach immediately after ingestion of coconut oil.

Bragdon and Karmen [19] fed coconut oil to human volunteers and then compared the fatty acid composition of the fed oil with the chylomicrons collected from the volunteers 6 h after feeding. The chylomicrons contained 68 % less MCFA (C8–C12) while the LCFA (≥C14) were significantly higher as compared to the starting coconut oil. From this, they estimated that about two-thirds of the MCFA in coconut oil are transported via the portal vein and one-third is brought to the lymph and stored in chylomicrons. However, other studies also showed that the distribution of MCFA between the portal vein and lymph depends on the amount of MCT consumed in proportion to the total diet [20]. That is, the body adjusts to variations in the nature of fats and oils that are consumed.

Overall, studies have shown that lauric acid has properties similar to capric acid (C10) and distinctly different from palmitic acid (C16). Further, the metabolic properties of triglycerides that contain C6–C12 are distinctly different than triglycerides with fatty acids C14 and longer. Thus, the definition proposed by Bach and Babayan [21] of MCT that includes lauric acid (C6–C12) is valid.

Metabolism of Lauric Acid

After the release of lauric acid from the triglyceride, it is either transported directly to the liver via the portal vein or reformed into new triglycerides which enter the lymphatic system. McDonald and co-workers [22] studied the route of portal venous transport in rat intestine by intraduodenal infusion of various fatty acids. Under conditions where only one fatty acid is administered, they determined that 72 % of lauric acid, 58 % of myristic acid, 41 % of palmitic acid, and 28 % of stearic acid bypassed the lymphatic pathway. That is, LCFA have a greater tendency to enter the lymphatic pathway than lauric acid. This experiment also showed that lauric acid may also enter the lymphatic pathway in the absence of longer chain fatty acids.

The fate of lauric acid in the blood stream has been studied in rats. Using isotopically-labeled lauric acid and palmitic acid, Goransson [23] observed that lauric acid disappeared more rapidly than palmitic acid from the blood, and

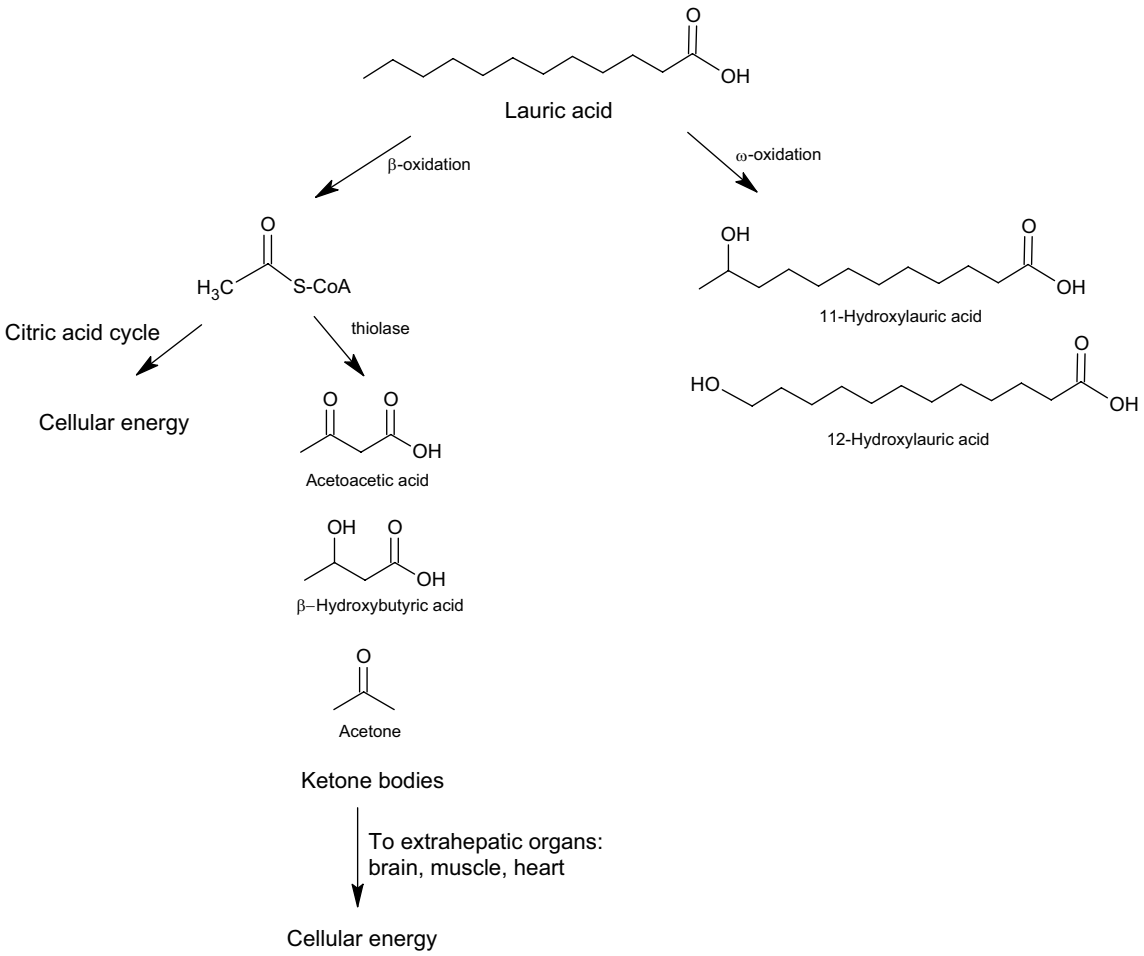


Fig. 5 Metabolism of lauric acid in the liver

was also oxidized more rapidly. He also showed that small amounts of lauric acid are found in the liver as triglycerides and that it is not incorporated into phospholipids. However, he noted that these trends may not apply if rats are overfed. Consistent with this result, lauric acid was not detected in lymph lipids of rats 8 h after dietary administration, while myristic acid and longer saturated fatty acids were detected [24]. This suggests that, while some of the ingested lauric acid enters the blood stream, it is rapidly metabolized and only a small amount is stored in the liver as triglycerides. Mass spectrometric analysis of lipids from liver tissue samples from humans detected only LCFA (≥C14) [25].

In the liver, fatty acids are metabolized for energy in the mitochondria. Depending on its chain length, a fatty acid can cross the mitochondrial membrane either by passive diffusion or by carnitine-assisted transport. Gharlid and co-workers [26] showed that lauric acid is rapidly transported across the membrane bilayer by non-ionic passive diffusion. Measurements using dynamic NMR spectroscopy showed that MCFA are able to diffuse more rapidly than LCFA across the membrane through a "flip-flop" mechanism; a lengthening of the carbon chain by two carbons slows down the rate of diffusion by about 100 times [27]. Consistent with this, lauric acid has been shown to diffuse freely across the mitochondrial membrane, while longer chain fatty acids require carnitine [28]. Thus, lauric acid can be rapidly transported into the mitochondria via physical diffusion or with assistance from carnitine.

Lauric acid is rapidly metabolized in the liver in a number of ways. (Fig. 5) β-Oxidation accounts for the major pathway for fatty acid metabolism producing acetyl-CoA for the citric acid cycle. In humans, four different acyl-CoA dehydrogenase enzymes have been identified. The preferred substrates were determined for each identified enzyme as follows: short-chain acyl-CoA dehydrogenase (SCAD): C4, C6, with the highest activity for C4; medium-chain acyl-CoA dehydrogenase (MCAD): C4–C14, with the highest activity at C6; long-chain acyl-CoA dehydrogenase (LCAD): C6–C22, with the highest activity at C16; and very-long-chain acyl-CoA (VLCAD): C12–C22, with the highest activity at C16. Two of the enzymes—MCAD and LCAD—have high activity for lauric acid.[29.]

In liver mitochondria, acetyl-CoA can also be converted to acetoacetic acid and then to beta-hydroxybutyric acid and acetone; these compounds are collectively called ketone bodies. Although the liver synthesizes ketone bodies, it has little β-ketoacyl-CoA transferase and is therefore not able to utilize ketone bodies. The ketone bodies are transported to other tissues such as the brain, muscle and heart which have the enzymes to convert ketone bodies to acetyl-CoA to serve as energy source.

The presence of ketone bodies in the blood stream induces an increase in insulin secretion and hypoglycaemia. Feeding an oral load of MCT (C6–C12) to rats, Bach and co-workers [30] observed a decrease in plasma levels of lactate, pyruvate and glucose together with a slight increase in plasma insulin levels. LCT (≥C14) had no effect on these plasma levels which suggests that LCT are not able to generate ketone bodies efficiently.

ω-Oxidation is a minor pathway that accounts for less than 10 % of total liver fatty acid oxidation under normal physiological conditions. However, under conditions of starvation or intake of certain dietary fats, the activity of ω-hydroxylases may increase [31]. Lauric acid is used as the model substrate for ω-oxidation by cytochrome P450 enzymes. A number of cytochrome P450 enzymes in the liver have been shown to catalyze the ω-1 and ω-2 oxidation of lauric acid. Cytochrome P 450 IVA1 (also known as lauric acid hydroxylase, LAH) forms 11- and 12-hydroxyl lauric acids [32]. In the human liver, the microsomal enzymes cytochrome P450 4A and cytochrome 2E1 were shown to catalyze the ω-1 hydroxylation of lauric acid efficiently [33, 34]. Lauric acid can also be used to form longer chain fatty acids in the liver. Using radiolabeled 1–^{14}C lauric acid, Rioux and co-workers showed that lauric acid can also be elongated to produce myristic and palmitic acids [35].

Another organ of the body where lipids play a significant role is the skin. The endogenous triglycerides on the skin surface are composed of C16 and C18 fatty acids with monounsaturates and branched chains. Lauric acid is also naturally present at lower amounts in the skin triglycerides [36]. When applied to the outer layer of the skin (*stratum corneum*), lauric acid was shown to have the highest affinity to skin due to its optimal partition coefficient, solubility parameter and conformation. In a 12-h skin penetration experiment, lauric acid showed the greatest penetration into human skin [37].

These studies show that the metabolism and oxidation of lauric acid differ from longer chain fatty acids.

Cholesterol, Fat Accumulation and Lauric Acid

Lauric acid itself has been shown to act in various ways which can modulate serum cholesterol levels. As discussed above, the saturated fatty acids in the *sn*-1 and *sn*-3 positions of triacylglycerols can lead to different metabolic effects [38]. This means that dietary fats and synthetic MCT oil may have different physiological effects. Because of different experimental designs and feeding periods, there have been inconsistent conclusions regarding the effects of lauric acid on serum cholesterol.

In 1957, Keys hypothesized that dietary saturated fats caused hypercholesterolemia and that high cholesterol was linked to heart disease [39]. Keys narrowed the cholesterol-promoting effect of saturated fatty acids in natural diets to lauric, myristic and palmitic acids. However, since palmitic acid was much more abundant in the American diet than lauric acid and myristic acid, he surmised that palmitic acid may be primarily responsible for raising serum cholesterol levels in Americans [40].

A number of dietary experiments have given results which are at odds with the Keys hypothesis. A human feeding study by Hashim and co-workers [41] using an MCT preparation containing C6-C12 saturated fatty acids showed a transient rise and fall of serum cholesterol. Their results did not support the view that coconut oil with its high MCFA content raises serum cholesterol. In a meta-analysis of 60 controlled trials on the effects of dietary fatty acids, German and Dillard [42] concluded that lauric acid increased both total cholesterol (TC) and high density lipoproteins (HDL). The overall effect was a decrease in the ratio of TC to HDL which is associated with desirable cardiovascular outcomes.

In a review of the literature, Denke [43] concluded that all of the saturated fatty acids from C8 to C16 raised cholesterol, with C14 being the most potent. Recently, Tholstrup and co-workers [44] noted that the position of the fatty acid influences how the body responds to the fat. This may explain some of the contradictory conclusions regarding the health impact of lauric acid in studies that did not use natural coconut oil. Finally, as noted by Kaunitz in 1970, [45] epidemiological data on populations that regularly consume coconut oil in their diet have shown no correlation between coconut oil consumption and coronary heart disease. For example, studies on Polynesians [46, 47] and Bicolanos in the Philippines [48], as free-living populations that consume coconut oil, have shown that coconut oil does not negatively impact cardiovascular health and, in fact, may be beneficial against other indicators, such as atherosclerosis.

In humans, nuclear regulatory protein receptors called peroxisome proliferator-activated receptors (PPAR) have been shown to regulate cell development and metabolism. To date, three PPAR have been identified in various organs in the human body: PPARα (liver, kidney, heart, muscle, adipose tissue, others), PPARγ (heart, muscle, adipose tissue, others), and PPARβ or PPARδ (brain, adipose tissue, others). In some cell types, MCFA from C8 to C12 bind PPARγ; however, in others, only C8 and C10

MCFA activate transcription. Ligand binding pockets for MCFA have been identified in crystal structures of PPARγ [49]. The interaction of lipids with PPAR can be seen as a molecular mechanism whereby dietary fatty acids can modulate lipid homeostasis. Lauric acid can regulate fatty acid homeostasis via PPARα and γ [50].

Brown adipose tissue (BAT) is a fat cell that specializes in burning fat. It is responsible for adaptive, nonshivering thermogenesis in mammals. BAT is brown because of the presence of a high amount of iron-containing mitochondria. Thermogenesis refers to the generation of body heat directly from dietary fat without producing ATP. The thermogenic ability of BAT is due to uncoupling protein 1 (UCP1, also called thermogenin), a unique BAT-specific transport protein of the mitochondrial membrane, which facilitates the return of protons after they have been pumped out of the mitochondria by the electron transport chain. UCP1 dissipates the proton motive force that is needed to drive the synthesis of cellular ATP and the energy from the mitochondrial electrochemical gradient is released in the form of heat. Several studies have been conducted on the ability of various fatty acids as activators of UCP1, but the conclusions from various papers have been divergent. For example, Shabalina and co-workers [51] showed that MCFA were potent UCP1 activators and lauric acid was shown to activate UCP1 in a cell-free system [52]. Samartsev and co-workers [53] showed that the uncoupling activity of short-chain fatty acids may be higher than that of LCFA while Fedorenko and co-workers [54] favoured activation by LCFA. Clearly, much still needs to be studied to fully understand the mechanism of thermogenesis and the specific contribution of lauric acid to this phenomenon.

DeLany and co-workers [55] designed an experiment to determine the tendency of the various dietary fatty acids to cause fat formation and obesity. They fed individual ^{13}C-labelled fatty acids to normal-weight men as part of their meal for one week and measured the liberated $^{13}CO_2$ in the breath. The diet, which contained 40 % of energy as fat, included the following fatty acids fed in random order: lauric, palmitic, stearic, oleic, elaidic (the trans isomer of oleic), linoleic, and linolenic acids. Cumulative oxidation of labelled fats ranged from a high of 41 % for lauric acid to a low of 13 % for stearic acid, with polyunsaturated fats giving intermediate values. These results show that among dietary fatty acids, lauric acid is the most highly oxidized and contributes the least to fat accumulation and obesity.

Antimicrobial Properties of Lauric Acid and Monolaurin

Numerous reports have been published on the antimicrobial properties of lauric acid and monolaurin both *in vitro* and *in vivo*. Among the saturated fatty acids, lauric acid and monolaurin have been shown to be very active against gram positive bacteria and a number of viruses and fungi.

The antimicrobial activity of lauric acid, monolaurin, and other ester derivatives can be classified under three main mechanisms: 1 destruction of the cell membrane of gram positive bacteria and lipid-coated viruses by physicochemical processes, 2 interference with cellular processes, such as signal transduction and transcription, and 3 stabilization of human cell membranes. The availability of these multiple mechanisms may be one of the reasons why bacteria have been unable to evolve resistance against the action of these compounds. Table 1 lists representative research findings on the antimicrobial properties of lauric acid and monolaurin.

Early studies on the antimicrobial activity of fatty acids identified lauric acid as the most active among the saturated fatty acids [56, 57]; a systematic study of the *in vitro* anti-microbial activities of fatty acids, monoglycerides and diglycerides showed that lauric acid was the most active fatty acid against gram-positive bacteria [58] and 1-monolaurin as more active than lauric acid [59]. In the presence of lauric acid, the production of infectious vesicular stomatitis virus was inhibited in a dose-dependent and reversible manner: after removal of lauric acid the antiviral effect disappeared. In addition, the chain length of the saturated fatty acid proved to be crucial, as those with shorter or longer chains were less effective or had no antiviral activity [60]. However, the activity of lauric acid was decreased by Mg^{2+} and Ca^{2+} ions while lower pH generally increased its activity. These observations suggested that the uptake of lauric acid is governed by physico-chemical properties of both the acid and the bacterial cell surface [61, 62]. For dental care, lauric acid decreases plaque formation and inhibits hydroxyapatite dissolution [63].

Aside from its antimicrobial activity, monolaurin was also shown to be effective in blocking or delaying the production of exotoxins by pathogenic gram-positive bacteria [64]. The mechanism by which monolaurin inhibits the synthesis of staphylococcal toxins and other exoproteins was shown to be at the level of transcription. Further, it was shown that monolaurin can block the induction of β-lactamase by interfering with signal transduction [65]. Monolaurin inhibited the expression of virulence factors in *Staphylococcus aureus* and the induction of vancomycin resistance in *Enterococcus faecalis*. It was suggested that monolaurin acted by blocking signal transduction [66].

Among the series of fatty acids and monoglycerides, lauric acid and monolaurin have been shown to possess strong activity against *Helicobacter pylori* [67]. Further, there was a low spontaneous development of resistance by *H. pylori* to the bactericidal activity of monolaurin [68]. The susceptibility of *Candida albicans* to several fatty

Table 1 Antimicrobial activity of lauric acid and its derivatives

Microorganisms tested	Activity	Reference
Staphylococcus aureus, *S. epidermidis*, beta-hemolytic streptococci (group A and non-group A), group D streptococcus, *Bacillus subtilis*, *Sarcina lutea*, *Micrococcus* sp., *Candida albicans*, *Nocardia asteroids*, *Corynebacterium* sp., and Pneumococcus	*In vitro* screening study Among fatty acids tested from C6–C18: C12 had the highest inhibitory activity C18:2 had a higher inhibitory activity than C12	[58]
Pneumococci, *Streptococcus* group A, *Streptococcus* beta-hemolytic non-group A, *Candida*, *S. aureus*	*In vitro* screening study. Among fatty acids tested from C6–C18: C12 had the highest inhibitory activity C18:2 had a higher inhibitory activity than C12 *Candida* and *S. aureus* were the most resistant among the bacteria tested	[63]
Pseudomonas aeruginosa, *Streptococcus* group A, *Staphylococcus aureus*, *Candida albicans*	*In vitro* screening study. The following fatty acids were tested: C6–C18, C18:1, C18:2, C18:3 All fatty acids were inactive against *P. aeruginosa* C12 had similar inhibitory activity as C18:2 against *Streptococcus* group A C12 had higher inhibitory activity than C18:1 but lower activity than C18:2 against *S. aureus* and *C. albicans*.	[80]
Streptococcus group A, *S. aureus*	*In vitro* screening study. Among all monoglycerides tested: C2–C18; C18:1, C18:2: MLG-1 had the highest inhibitory activity MLG-1 was approx. twice as active as MLG-2	[80]
Streptococcus groups A, B, F, and G	For application in humans. MLG was active at 10–20 μg/mL MLG reduced exotoxin production, including pyrogenic exotoxins and hemolysins	[66]
Staphylococcus aureus	MLG was active at 100–300 μg/mL MLG inhibited production of hemolysin, toxic shock syndrome toxin 1, and exfoliative toxin A	
Escherichia coli, *Salmonella minnesota*	MLG was inactive	
Vesicular stomatitis virus	Among the fatty acids tested: C6, C8, C10, C16, C18: C12 had highest activity (60 μg/mL). Other fatty acids tested were 100–1,000 times less active	[61]
Staphylococcus aureus	MLG inhibited the synthesis of most staphylococcal toxins and other exoproteins at the level of transcription	[67]
Helicobacter pylori	Among the fatty acids tested: C4–C17: C12 was the only bactericidal fatty acid MLG was the most active bactericidal monoglyceride	[70]
Staphylococcus aureus	MLG inhibited the expression of virulence factors C12 which is produced from hydrolysed MLG showed identical activity as MLG	[68]
Enterococcus faecalis	MLG inhibited induction of vancomycin resistance C12 which is produced from hydrolysed MLG showed identical activity as MLG	

Table 1 continued

Microorganisms tested	Activity	Reference
Candida albicans	Study for human application.	[71]
	Fatty acids tested: C8–C14, C16:1, C18:1	
	C10 caused the fastest and most effective killing	
	C12 was the most active at lower concentrations and after a longer incubation time	
	The corresponding monoglycerides were inactive	
Junin virus (JUNV)	Fatty acids tested: C10–C18	[72]
	C12 was the most active inhibitor	
Helicobacter pylori	Study for human application	[69]
	Fatty acids tested: C4–C16, C14:1, C16:1, C18:1, C18:2, C18:3	
	C12, C18:2, C18:3 had the strongest bactericidal activity. Among the monoglycerides tested: C12–C16:	
	MLG and monomyristyl (C14) glyceride had the strongest bactericidal activities which were twice as strong as the corresponding fatty acids; monopalmityl (C16) glyceride had five times weaker activity	
Clostridium perfringens	Study for use in animals	[93]
	Fatty acids tested: C8–C14, C18:1	
	Order of antimicrobial activity: C12 > C14 > C10 > C18:1 > C8	
Staphylococcus aureus	Study for use in humans and cows. Substances tested: C10, C12, MLG, C14, C18:2$\Delta^{c9,t11}$, C18:2$\Delta^{t10,c12}$	[92]
	C10, C12, MLG, and C14 behaved similarly and reduced overall growth	
Superantigen TSST-1 and β-hemolysin from *Staphylococcus aureus* RN4220	To counter endotoxins from gram-positive bacterial pathogens	[94]
Superantigen SEB and R-hemolysin from *Staphylococcus* strain MNJA	MLG (20 μg/mL) prevented superantigen-induced cytokine secretion by human vaginal epithelial cells (HVECs)	
Superantigen SPE A from *Escherichia coli*	MLG (250 μg) inhibited TSST-1 administered vaginally in rabbits	
Streptolysins O and S from Streptococcal group A strain T18P	MLG (10 μg/mL) inhibited action of anthrax toxin, hemolysins from *Staphylococcus* and	
Hemolysins and anthrax toxin from *Bacillus anthracis*	*B. anthracis*, and was nontoxic to mammalian cells (up to 100 μg/mL)	
	MLG stabilized mammalian cell membranes	
E coli O_{157}:H_7	MLG showed significant inhibitory effect against *E coli* O_{157}:H_7 in dairy products	[69]

1-Monolaurin is designated as: MLG-1. If position is not specified in publication, it is designated as: MLG

acids and their 1-monoglycerides showed that C10 acted the fastest whereas C12 was the most active at lower concentrations and after a longer incubation time. Further, these fatty acids showed no toxicity to skin and mucosa making them ideal for topical application [69]. In a comparison among the saturated fatty acids C10–C18 against Junin virus (JUNV) infection, lauric acid was shown to be the most active inhibitor. From mechanistic studies, it was concluded that lauric acid inhibited a late maturation stage in the replicative cycle of JUNV [70].

The mechanism of action of lauric acid and its derivatives, including monolaurin, has attracted considerable interest. Transmission electron microscopy imaging of *Clostridium perfringens* as it was being treated with lauric acid showed the separation of inner and outer membranes and cytoplasmic disorganization of cells. Again, lauric acid was found to be the most active saturated fatty acid in the series C8–C14 [71]. In a study that compared saturated chains with cationic, anionic and non-ionic groups, Kabara concluded that in general, cationic species (e.g., with ammonium groups) were more active than anionic and non-ionic counterparts and that the optimum chain length was 10–16 carbon atoms. However, the toxicity of cationic species is higher than anionic species [72]. Non-ionic monoglycerides were shown to be active, especially when the ester group was lauryl [73].

Other researchers have proposed that the unique activity of monolaurin may be due to the antimicrobial action of the compound itself and its hydrolysis product, lauric acid. The antimicrobial activities of a number of lauric acid derivatives, including monolaurin, support this hypothesis (see Table 2; Fig. 6). A comparison of the activities of 1-monolaurin (MLG-1) and 1-monolaurylglyceryl ether (MLE-1), the ether analogue of 1-monolaurin, is illustrative. *In vivo*, MLG-1 inhibits the growth of *S. aureus*, but is degraded by *S. aureus* lipase. On the other hand, MLE-1 is stable to *S. aureus* lipase *in vivo* and but is less effective than MLG-1 [74]. The critical difference between MLG-1 and MLE-1 is the ability of MLG-1 to release C12, another antimicrobial compound, upon hydrolysis. Once C12 is released, it is metabolized slowly and this prolongs its effect [75]. Thus, MLG-1 is a more effective anti-staphylococcal topical anti-infective agent than MLE-1.

Various compounds which contain lauryl esters have been shown to be antimicrobial. Peptides which are conjugated with lauric acid show higher antimicrobial activity compared to the unconjugated peptides. This increase in antimicrobial activity was attributed to a change in the helical structure due to lauric acid which enabled the peptides to better interact with the bacterial membrane [76]. The possibility that the increase in the antimicrobial activity could be due to lauric acid itself was not considered. Carbohydrate lauric acid derivatives have shown strong promise as growth inhibitors of food pathogens. For example, the lauric ester of methyl alpha-D-mannopyranoside showed successful control of Listeria and other gram-positive pathogens [77] while laurates of galactose and fructose showed strong inhibition of cell growth of *Streptococcus mutans* [78].

Recently, bioassay-guided fractionation of the aerial parts of the traditional medicinal plant *Siegesbeckia glabrescens* (Compositae) using *S. aureus* led to the isolation of the antimicrobial compound 3-(dodecanoyloxy)-2-(isobutyryloxy)-4-methylpentanoic acid, a novel lauryl ester containing natural product. This compound was active against Gram-positive bacteria (*B. subtilis*, *E. faecalis*, *P. acnes*, *S. epidermidis*, *S. schleiferi* subsp. *coagulans*, *S. agalactiae* and *S. pyrogens*), Gram-negative bacteria (*E. coli* and *P. aeruginosa*), and yeast species (*C. alibicans* and *F. neoformans*). As in the case of monolaurin, the laurate ester group may be key to the antimicrobial activity of this compound [79].

An important characteristic of lauric acid and monolaurin is the absence of human toxicity. Human milk contains about 3.5–4.5 % fat, mostly as triglycerides, of which about 4–6 % is lauric acid.[80] As human milk is consumed, the monoglycerides and free fatty acids that are released strongly inhibit enveloped viruses, some bacteria, and protozoans. Among the strongest antimicrobial agents in human milk is monolaurin [81]. The antibacterial activities of MCFA and their 1-monoglycerides were evaluated against gram-positive strains belonging to genera *Staphylococcus*, *Corynebacterium*, *Bacillus*, *Listeria*, and *Streptococcus*. The 1-monoglycerides were more active than the corresponding fatty acids; C12 alone was weakly active. Synergistic relationships were observed between monocaprin and monolaurin. This information was used to understand the antimicrobial properties of human colostrum and to design milk formula for infants [82]. Monolaurin is the only monoglyceride which has been found to be useful as a food preservative. Monolaurin has been shown to protect against food-borne pathogens [83] and to inhibit *E coli* O_{157}:H_7 in dairy milk [84]. Lauric acid and its derivatives have also found important applications in the treatment of difficult microbial infections in animals, such as *Staphylococcus aureus* in dairy cows [85] and *Clostridium perfringens* in poultry, piglets and rabbits [86].

Monolaurin exhibits a third mode of action involving stabilization of mammalian cell membranes. Monolaurin was observed to insert into the human cell membrane thereby preventing signal transduction mechanisms, such as host cell receptor signaling systems which have been usurped by exotoxins. It was also able to stabilize red blood cells against lytic effects [87].

In 1977, Kabara [88] registered synthetic monolaurin under the trade name Lauricidin™ and filed one of the first

Table 2 Chemical structures of lauric acid and its derivatives in relation to their antimicrobial activity. See Fig. 6 for proposed reaction with lipase or other enzyme

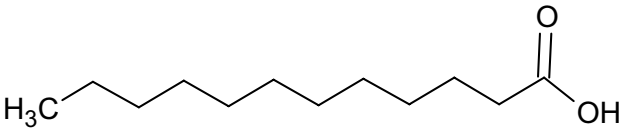
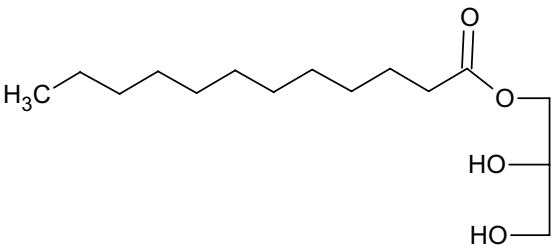
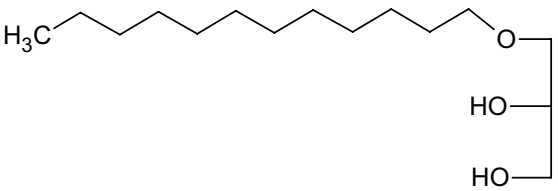
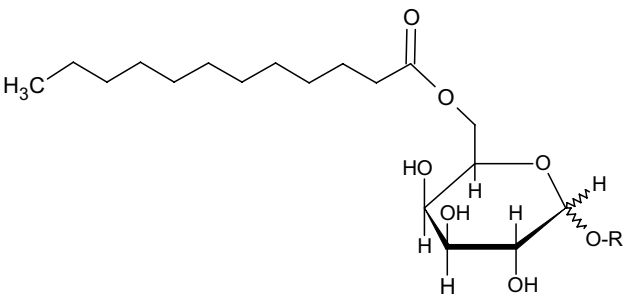
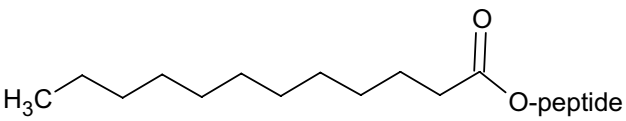
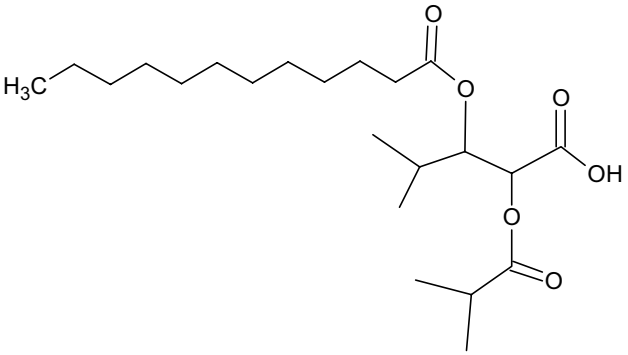
Chemical structure	Mechanism of antimicrobial activity	References
 Lauric acid (C12:0)	Lauric acid is able to disrupt the cell membrane of gram positive bacteria by physico-chemical processes. Once inside the cell, it can interfere with bacterial cell signal transduction and gene transcription processes. Its activity is generally better at low pH and is diminished by Mg^{2+} and Ca^{2+}	[71, 80]
 1-Monolaurin (MLG)	Similar to lauric acid, monolaurin is able to disrupt the cell membrane of gram positive bacteria by physico-chemical processes. In addition, hydrolysis by lipase releases lauric acid which is also antibacterial. 1-Monolaurin is more active than 2-monolaurin. Monolaurin that is made by chemical synthesis is 1-monolaurin	[71, 80, 81]
 1-Monolaurylglycerol ether (MLE)	1-Monolaurylglycerol ether is stable to hydrolysis by lipase *in vivo* and probably acts only at the cell membrane. It is less effective than 1-monolaurin which is hydrolysed by lipase *in vivo*	[81]
 Galactosyl laurate, mixture of positional isomers, R=H, CH_3	The growth-inhibitory effects of 23 carbohydrate lauryl monoesters against *Streptococcus mutans* were determined. Galactosyl laurate (mixture of positional isomers) gave the highest activity among carbohydrate mono-esters of lauric acid	[84, 85]
 Lauryl peptide	Two of three antimicrobial peptides, which were conjugated with lauric acid, showed higher antimicrobial activity compared to the unconjugated peptides. The authors attributed the increase in antimicrobial activity to a lauric acid-modified helical secondary structure which is able to better interact with the bacterial membrane. The antimicrobial activity of lauric acid was not considered	[83]

Table 2 continued

Chemical structure	Mechanism of antimicrobial activity	References
 3-(Dodecanoyloxy)-2-(isobutyryloxy)-4-methylpentanoic acid	3-(Dodecanoyloxy)-2-(isobutyryloxy)-4-methylpentanoic acid, a novel lauryl ester containing natural product, was isolated from *Siegesbeckia glabrescens* by microbial bioassay-guided fractionation. It is active against Gram-positive and Gram-negative bacteria and yeast species. The laurate ester group may be the key factor in the antimicrobial activity of this compound	[86]

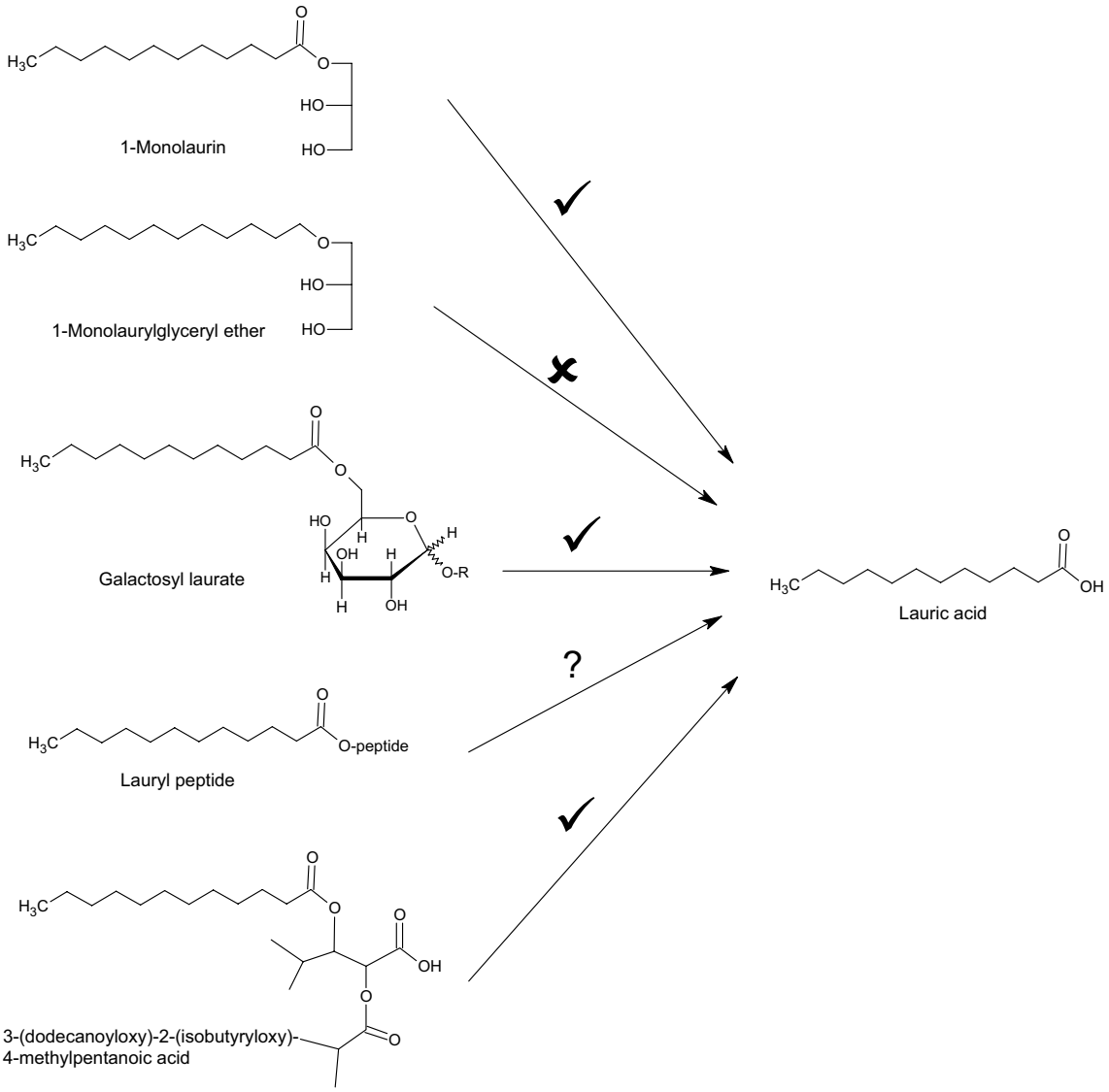


Fig. 6 Lauric acid derivatives may undergo hydrolysis by lipase or other enzymes to release lauric acid inside the cell. See Table 2 for discussion

patents on the commercial use of monolaurin as a food-grade microbicide or microbiostatic agent [89]. Since then, over 100 patents have been filed world-wide on the use of monolaurin in a diverse range of applications covering food and non-food applications, such as medical procedures, disinfection and sanitizing agents, antimicrobial polymer compositions, animal feed supplements, and others [90].

Summary and Conclusions

Lauric acid makes up approximately half of the fatty acids in coconut oil and detailed studies show that lauric acid accounts for many of the properties of coconut oil. The triglyceride structure of coconut oil enables it to be digested more rapidly compared with other vegetable oils with predominantly long chain fatty acids (LCFA). In a normal diet, most of the lauric acid that is ingested is transported directly to the liver via the portal vein. While small amounts of lauric acid may be found in chylomicrons as triglycerides, it is not found in phospholipids. Consistent with these properties, coconut oil has not been shown to contribute to cardiovascular disease and atherosclerosis.

Lauric acid is rapidly transported across the mitochondrial membrane by passive diffusion and does not require carnitine-assisted transport. Lauric acid is rapidly metabolized in the liver in a number of ways. Two acyl-CoA dehydrogenase enzymes are able to rapidly oxidize lauric acid. Lauric acid can be metabolized into ketone bodies, which are important energy sources for extrahepatic organs in the body, such as the brain, heart and muscle. Among all fatty acids, lauric acid contributes the least to fat accumulation. These properties of lauric acid are consistent with the observations that coconut oil is a non-fattening source of energy.

Lauric acid has the strongest antimicrobial activity among all saturated fatty acids against gram-positive bacteria and some viruses and fungi. These compounds are unique in their ability to avoid the development of microbial resistance which may be due to their multiplicity of action, which includes disruption of the cell wall and interference with cell signalling and transcription. In fact, monolaurin has the strongest antimicrobial activity among all monoglycerides. It is able to act as an intact compound and also after hydrolysis which releases lauric acid. There are numerous patents and commercial products based on monolaurin.

Numerous beneficial effects have been claimed for coconut oil. This review on lauric acid provides mechanistic support for many of the beneficial effects of coconut oil. Finally, because MCFA (C6–C12) show sufficiently different metabolic and physiologic properties to LCFA (≥C14), the chain length should be specified when using the term “saturated fatty acid”.

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