J Biosci (2021)46:12
DOI: 10.1007/s12038-020-00133-3

Review

Dietary conjugated linoleic acid and medium-chain triglycerides for obesity management

KHADIGA S IBRAHIM[1]* and EMAN M EL-SAYED[2]

[1]*Environmental and Occupational Medicine Department, National Research Centre, Dokki, Giza, Egypt*

[2]*Nutrition and Food Sciences Department, National Research Centre, Dokki, Giza, Egypt*

**Corresponding author (Email, khadigasalah@yahoo.com)*

MS received 14 April 2020; accepted 7 December 2020

Obesity is considered a serious global health issue. Patients have been predisposed to comorbidities such as dyslipidemia, cardiovascular diseases, diabetes, cancers, and osteoarthritis. Certain fats in the diet have been linked with an increase in obesity, such as saturated and trans-fats. Meanwhile, some dietary fats such as conjugated linoleic acids (CLAs) and medium-chain triglycerides (MCTs) could potentially reduce energy intake. Various mechanisms for reducing weight by CLAs and MCTs, such as increased lipolysis, improved intestinal microbiota, up-regulating peroxisome proliferator-activated receptors (PPARs), increased the expression of uncoupling protein of respiratory chain-1 (UCP-1), and affected satiety hormones are included. These bioactive compounds, CLAs and MCTs, should be used in moderate concentrations to prevent harmful effects such as insulin resistance for CLAs and hypercholesterolemia for MCTs. However, several studies have proposed CLAs or MCTs as adjuvants to the protocol used to minimize bodyweight. Our objective is to summarize the different causes of obesity and to discuss the effects of CLAs or MCTs on body weight and fat deposition in obese animals or humans.

Keywords. Obesity; conjugated linoleic acids; medium-chain triglycerides; lipid metabolism

1. Introduction

Obesity is a state of increase in the mass of adipose tissue with concomitant elevation of body weight greater than the levels of physical requirements. Accumulation of triacylglycerols is believed to be the only manner in which body weight has become excessive. However, obesity cannot be simply defined in terms of body weight solely. In that concept, short individuals are supposed to be lighter than tall ones. There is also a need to standardize body weight against height, which is the body mass index (BMI) (equals a person's weight in kilograms (kg) divided by their height in meters squared (m^2)). The World Health Organization (WHO 1985) defined obesity as BMI > 30 for men and BMI > 28.6 for women.

Obesity is seen as a significant global health concern. More than 2 billion people who are equivalent to 30 percent of the global population are obese or overweight (BMI is greater than or equal to 25 kg/m^2) (Ng *et al*. 2014). It is a major health concern because it predisposes subjects to a variety of comorbidities. Accumulation of excess body fat produces an elevated risk for cardiovascular diseases, multiple forms of cancer, increased mortality, type 2 diabetes, stroke, and osteoarthritis (Björntorp 1993; Guh *et al*. 2009). Recently, there has been tremendous evidence that obesity has a detrimental impact on the brain. Visceral obesity, in particular, is associated with severe metabolic changes in the central nervous system even in younger populations (Kaur *et al*. 2015). Obesity has also been involved in cognitive deficits in dementia patients (Whitmer *et al*. 2007).

Obesity etiology is multi-factorial, both genes and environmental factors may be involved. In particular, increased caloric intake and decreased physical activity

Published online: 03 February 2021

are the main causes of weight gain (Pereira *et al*. 2005; Castro *et al*. 2020). However, there are also secondary reasons for obesity including endocrine disorders and medications (Karam and McFarLane 2007). Also, a deficiency of vitamin D can be a risk factor for obesity (Kaddam *et al.* 2017).

Currently, the available therapies for obesity have not been able to reduce its prevalence. Diet therapy with increased physical activity does not achieve significant short-term weight reduction (Frood *et al*. 2013). Besides, current anorexic drugs and surgical procedures have several harmful side effects that may exceed their benefits (Yanovski and Yanovski 2014). The use of adjuvants in current treatments is therefore a novel, safe, and effective strategy.

These ingredients can help to increase the effectiveness of hypocaloric diets by reducing the side effects associated with low energy intake and avoiding the feeling of hunger (Chambers *et al*. 2014). Many obese individuals tend to eat more foods containing certain functional elements that help to reduce their weight. From these elements, conjugated linoleic acids (CLAs) are known to be antiobesogenic agents in both animals and humans. A variety of studies researched the treatment of CLAs on obesity (den Hartigh *et al*. 2017; van Baak and Mariman 2019; Namazi *et al.* 2019).

Medium-chain triglycerides (MCTs) are triglycerides with saturated fatty acids that have a chain length of 6–12 carbons. Beyond their recognized nutritional values, they substantially minimize bodyweight relative to long-chain triglycerides in mice (Zhang *et al*. 2015; Sung *et al*. 2018). Clinical research also demonstrated that for obese women, MCTs succeeded in lowering body fat and weight (Krotkiewski 2001). CLAs and MCTs also increased satiety and decreased energy consumption, suggesting a possible role in helping to maintain energy balance (Coleman *et al*. 2016; Maher *et al*. 2020).

However, the study of CLAs and MCTs data, concerning their antiobesity effects, is still inconclusive. Hence, the purpose of this article is to summarize the various kinds of literature discussing the effects of CLAs or MCTs on body weight and fat deposition in obese animals or humans. Also, the authors have tried to explore and compare the potential pathways involved in reducing adiposity by both fats. Moreover, the safety of these fat supplements was considered.

2. Adipose tissue and obesity

Fats are stored in adipose tissue, which is classified into anabolic white adipose tissue (WAT) and catabolic brown adipose tissue (BAT). Their roles are different; WAT stores energy as triacylglycerols (TAGs), while the BAT oxidizes lipids to produce energy (Lee *et al*. 2014). The balance between WAT and BAT is necessary to maintain homeostasis energy. Notably, WAT is considered an endocrine organ that secretes many adipokines with autocrine, endocrine, and paracrine functions. It has a functional diversity that can affect most of the body's systems. WAT is also primarily produced by adipocytes but there are different types of cells in this tissue, such as stem cells, lymphocytes, macrophages, preadipocytes, and endothelial cells. Therefore, it has the heterogeneity of cells (Ràfols 2014). WAT secretes various lipid substances mainly fatty acids (released under energy deprivation conditions such as in fasting), prostanoids, cholesterol, and vitamin A (Trayhurn 2005). Besides, sex hormones and glucocorticoids are developed by WAT, as it secretes a large number of protein-grade adipokines that have been classified as adipokines such as leptin, resistin, adiponectin, inflammatory, and anti-inflammatory cytokines (Wozniak *et al*. 2009). However, WAT is distributed across human bodies; Fat deposits are present in the abdomen around the omentum, bowel, and peripheral areas. Subcutaneous fats are also considered to be from the main fat deposits. The locations of WAT determine its metabolic and endocrine properties (Tchkonia *et al*. 2002). WAT is sensitive to glucocorticoids in the neck and the upper back, meanwhile; it is extremely affected by estrogen in the breasts. Intra-abdominal fat secretes adipokines, which are closely linked to inflammation and type 2 diabetes. Under conditions of excess energy or sedentary life, these deposits are increasing and the production of proinflammatory adipokines has increased with the consequent promotion of atherosclerosis (Yudkin *et al*. 2005). Obesity is therefore defined as excess body fat

associated with a risk of type 2 diabetes and cardiovascular disease depending on the location of excess fat.

3. Causes of obesity

The main causes of weight gain are strongly linked to high-calorie intake and a sedentary lifestyle. Obesity can also be secondary to adverse changes in the neuroendocrine system or genes. Such changes can affect the energy imbalance, appetite, fat distribution, and metabolism of lipids and glucose (Karam and McFarlane 2007). Various secondary factors were included.

3.1 *Endocrine disorders*

Obesity is associated with many endocrine disorders such as hypothyroidism (Santini *et al*. 2014), leptin resistance (Sáinz *et al*. 2015), polycystic ovarian syndrome (Lo *et al*. 2006), Cushing's syndrome (Wajchenberg *et al*. 1995), hypothalamic disorders (Srinivasan *et al*. 2004), growth hormone deficiency (Rosen *et al*. 1993), and hypogonadism (Bhasin *et al*. 2003).

3.2 *Vitamin D deficiency*

Vitamin D deficiency is documented in obese patients (Kaddam *et al.* 2017). Vitamin D can contribute to overweight or even obesity through its effects on glucose and fat homeostasis by acting on the pancreas (Delvin *et al*. 2010). Cell culture and animal studies have shown that adipose tissue has a vitamin D receptor (VDR) and also can synthesize vitamin D in its bioactive metabolite (1,25 dihydroxy vitamin D_3).

Vitamin D may increase adipose tissue lipogenesis and adipogenesis (Earthman *et al.* 2012) which leads to obesity. Cases of vitamin D deficiency have reported higher levels of parathyroid hormone (PTH) (Stein *et al*. 2009). Hyperparathyroidism has a potential role in obesity by promoting lipogenesis thus encourages weight gain (Snijder *et al*. 2005). Wakayo *et al.* (2016) have shown that for a unit elevation in the vitamin D serum level of school children, overweight or obesity risk is reduced by 5.8%. Also, weight loss and decrease in blood androgen levels and blood pressure were fulfilled in obese women who had a significant decrease of vitamin D with polycystic ovarian syndrome after three months of vitamin D supplementation (Pal *et al*. 2012). It was found that circulatory vitamin D repletion in extremely obese subjects was achieved by the use of prescribed forms of ergocalciferol (vitamin D_2) or cholecalciferol (vitamin D_3) but the latter is preferable (Stein *et al*. 2009).

3.3 *Genetics*

Obesity is a form of polygenic disease. It is the product of the cumulative action of genetic, epigenetic, and environmental influences (Herrera *et al*. 2011). Several genes have been actively involved in signaling between the hypothalamic satiety and hunger centers and the peripheral leptin, convertase 1, and melanocortin 4 receptors. Mutation of these genes leads to extreme early obesity (Clément *et al*. 1998).

In particular, insulin and leptin stimulate certain neurons in the hypothalamus to produce alpha-melanocyte-stimulating hormone (alpha-MSH), a neurotransmitter that acts on hypothalamus melanocortin receptors (MCR) to reduce food intake. Mutations of genes responsible for alpha-MSH or MCR contribute to obesity (Girardet and Butler 2014). Moreover, another mutation of genes encoding leptin, leptin receptor, or proopiomelanocortin is associated with weight gain. Human obesity may result from polygenic mutations (Comuzzie and Allison 1998).

3.4 *Medications*

Side effects of many drugs may develop obesity among susceptible subjects. Antidiabetic medications such as insulin, thiazolidinediones, and sulfonylurea have been shown to increase body weight gain in diabetic patients (Cheng and Kashyap 2011). Also, several therapies that function centrally as antidepressants (Patten *et al*. 2011), antiepileptics, and antipsychotics may increase body weight gain by operating on brain monoamines (Newcomer and Lieberman 2007).

Besides, the withdrawal of nicotine during smoking cessation was associated with weight gain (Bush *et al*. 2016). Possible mechanisms include declining metabolic resting rate, decreased physical activity, reduced-calorie burn, and increased appetite.

3.5 *Environmental chemicals*

Substances such as endocrine-disrupting chemicals (EDCs) may be related to the obesity epidemic (Baillie-Hamilton 2002). Exposure to EDCs takes place at home, in the workplace, on the farm, in the air we breathe, the food we consume, and the water we drink. Early-life exposure to atmospheric particles increases susceptibility to dietary weight gain, insulin resistance, adiposity, and inflammation (Wei *et al*. 2016). Obesogens are a group of EDCs that may interact with the endocrine system and may contribute to obesity (Janesick and Blumberg 2016).

Bisphenol A (BPA), is used in plastic containers for food and beverage. The composition of BPA is identical to estradiol. Consequently, it binds to estrogen receptors in the body (Do *et al.* 2017). Phthalates can promote obesity through anti-androgenic effects, anti-thyroid activity, and/or activation of peroxisome proliferator-activated receptors (PPARs) (Kim and Park 2014). Atrazine is an herbicide that is widely used. It has been shown to destroy mitochondria in rats, decrease the metabolic rate, and increase abdominal obesity (Lim *et al*. 2009). Organotin polluting tributyltin (TBT) contributes to obesity in humans by increasing the number of fat cells (Grün 2014).

3.6 *Disruption of energy homeostasis*

Continuous disturbance of energy homeostasis contributes to adiposity. The central nervous system (CNS) regulates the feeding activity and thus influences the energy balance. Disturbances in the feeding activity lead to a high incidence of obesity. Energy expenditure includes the basic metabolic rate (BMR), thermogenesis, and physical activity.

BMR is equivalent to about 60–70 percent of the total energy expenditure and it increases with an increase in body weight. However, BMR is centrally regulated (Galgani and Ravussin 2011) that, when dysregulated results in weight gain. It is worth mentioning that physical activity is responsible for 20–30% of overall energy expenditure, except for athletes. A sedentary lifestyle is responsible for major obesity (Bhurosy and Jeewon 2014).

3.7 *Saturated and trans-fats*

Fats and oils in the diet are the main sources of energy as compared to the other macronutrients. High intake of such fats increases the proportion of calories that would be closely associated with overweight or, in some instances, with obesity (Raatz *et al*. 2017). It is well documented that a high intake of saturated fatty acids (SFA) is associated with obesity, especially in obesity-prone carriers of the obesity gene (Phillips *et al*. 2012). Hu *et al*. (2018) exposed mice to 29 types of diets varying in the proportions of fat, carbohydrates, and protein. They found that increased energy intake and adiposity were caused only by elevated dietary fat content. Astrup (2005) findings are consistent with those of Hu *et al*. (2018) since they suggested a low-fat diet to avoid weight gain, obesity, type 2 diabetes, and cardiovascular disease. It was found that the degree of saturation of fatty acids affects their β oxidation (Kien *et al*. 2005). Therefore, SFA increases the deposition of fats in adipose tissue (Piers *et al*. 2003). In addition to classic monoamine systems and leptin in controlling energy balance, there are two opposing systems, one orexigenic and one anorexigenic, which are part of the energy balance regulation. Neuropeptide Y (NPY) and agouti-related protein (AgRP) are orexigenic, increase food consumption, and enhance obesity. Diets with high saturated fats content significantly increased NPY protein expression with concomitant body weight, elevation (Piggott *et al*. 2002).

Trans-fats (TFs) are prepared by the hardening of both vegetable and marine oils by industry. Also, trans-fatty acids are naturally constituted a small content in ruminants, meat, and milk. Koh-Banerjee *et al*. (2003) documented that a high intake of TFs elevated the risk of weight gain and abdominal fat. This could be explained by the role of TFs as ligands for the peroxisome proliferator-activated receptors gamma (PPARγ) system (Mozaffarian *et al*. 2006) and by induction of insulin resistance (Kavanagh *et al*. 2007).

4. Dietary supplements and obesity

Lifestyle modifications by changes in diet and physical activity are expected to be the cornerstone of the management of obesity (Strasser and Fuchs 2016).

However, people are failing to reach their weight-reduction goals. Therefore, the provision of dietary supplements could be helpful for weight reduction. Many animal studies have shown that high consumption of oleuropein (Lepore *et al*. 2015) or oleoresin (Lombardo *et al*. 2018) (olive oil products) is significantly correlated with weight reduction. Merola *et al*. (2017) also proved that citrolive, a commercial extract from the combination of citrus fruit and olive leaf extracts, could ameliorate the metabolic disorders associated with obesity in rats. In humans, consumption of extra virgin olive oil showed a decline in body weight in obese women (Galvão *et al*. 2018). Moreover, weight reduction by enhancing lipid metabolism through activation of AMP-activated protein kinase (AMPK) by tea polyphenols has been reported (Rothenberg *et al*. 2018). Since AMPK can modulate energy homeostasis and lipid metabolism. The results of Yang *et al*. (2018) are consistent with those of Rothenberg *et al.* and added that consumption of 600–900 mg tea catechins substantially reduces weight gain. Furthermore, apple polyphenols have anti-obesity effects through a variety of pathways, including free radical scavenging, regulation of gene expression, and altering signal transduction in fat tissues (Asgary *et al*. 2018). A combination of hibiscus and lemon verbena polyphenolic extracts was consumed by overweight subjects. It exerted an anthropometric measurement improvement, increased anorexigenic hormone (glucagon-like peptide-1), and reduced orexigenic hormone (Ghrelin) through AMPK (Boix-Castejón *et al*. 2018).

Recently the health benefits of fats may vary according to their fatty acid compositions (Schwab *et al*. 2014). Fatty acids that consumed in relatively large amounts are linoleic, oleic, and palmitic, meanwhile, others such as α-linolenic acid (ALA), median chain triacyleglycerols, and omega 3 fatty acids are consumed in smaller quantities, but they have clear health benefits (Oliveira-de-Lira *et al*. 2018) and may be used as dietary supplements (Ludwig *et al*. 2013).

4.1 *Conjugated linoleic acid supplement*

Conjugated linoleic acids (CLAs, 18:2n-6) are natural fatty acids found in meat and dairy products. CLAs are isomers of linoleic acid (LA) but with a double-bond conjugated system. Ruminants have an enzyme that converts omega 6 fatty acids in green plants to CLAs that are stored in animals' meat and milk. They are also present to a lesser degree, in turkeys, chickens, and pigs.

Synthesized CLAs can be also produced by the action of fermentative bacteria in LA (Kishino *et al*. 2002). CLAs have a variety of beneficial effects on cancer, atherosclerosis, and obesity (Koba and Yanagita 2014; den Hartigh 2019; Basak and Duttaroy 2020; O'Reilly *et al*. 2020). The most beneficial effect associated with the intake of trans-10, cis-12 CLAs (t10-c12- CLAs) isomer is the reduction of obesity in both animals and humans (den Hartigh *et al*. 2018; Mądry *et al*. 2016 respectively). CLAs consumption by obese patients with non-alcoholic fatty liver disease often significantly improves their lipid profile, glycemic response, and markedly ameliorates oxidative stress (Ebrahimi-Mameghani *et al*. 2016). On the other hand, for overweight type 2 diabetics, the administration of CLAs for eight weeks does not affect anthropometric measurements and body composition (Shadman *et al.* 2013; Namazi *et al*. 2019). In the meantime, CLAs supplementation for obese postmenopausal women with type 2 diabetes significantly improves both body weight and glycemic parameters (Norris *et al*. 2009; den Hartigh 2019). López-Plaza *et al*. (2013) reported that skimmed milk fortified with 3g of 1:1 mixture of CLAs isomers (c9-t11 and t10-c12) to overweight healthy subjects for 24 weeks significantly decreased both body weight and total fat mass. Also, Kamphuis *et al*. (2003) documented that a mixture of CLAs isomers increased the feeling of fullness and increased satiety after thirteen weeks of supplementation. A reduced weight gain was achieved after six months of intake of mixed isomer CLAs (Watras *et al*. 2007). Both t10-c12 CLAs supplementation and diet restriction in mice exerted equal weight reduction with more fat loss by CLAs followed by increased fat oxidation and energy consumption (den Hartigh *et al.* 2017).

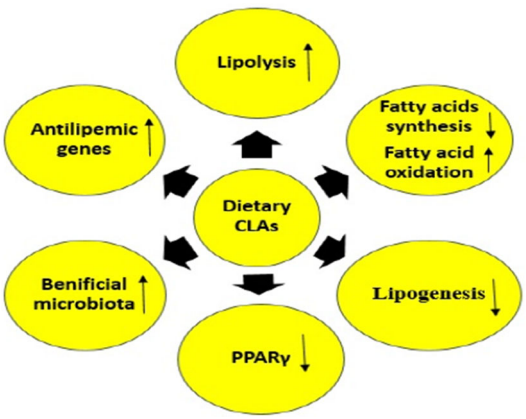

Figure 1. Pathways of CLAs for managing obesity.

4.1.1 *Mechanisms of CLAs:* Many studies demonstrated that CLAs exert their effects by influencing lipid metabolism, modifying enzyme activity, and hormonal profile (Kennedy *et al*. 2010; Lehnen *et al*. 2015). CLAs isomers significantly increase lipolysis in human adipocytes and diminish fatty acids synthesis (Martins *et al*. 2015). They also inhibit the expression of genes that are involved in the differentiation of the pre-adipocytes to mature adipocytes thus reducing lipogenesis (Reardon *et al*. 2012). The peroxisome proliferator-activated receptors (PPARs) are transcription factors in the nucleus that play an important role in the catabolism and the storage of fatty acids. PPARα and β isomers are involved in the expression of proteins responsible for fatty acid oxidation and, PPARγ isomer is associated with adipocytes differentiation (Tavares *et al.* 2007). CLAs inhibits PPARγ leading to the reduction of body fat by altering the gene expression that inhibits cell differentiation and modulates the activity of proteins involved in lipogenesis and lipolysis (Boschini and Garcia Júnior 2005) (figure 1).

PPARγ in the adipocytes regulates the expression of genes of acyl-CoA synthetase, lipoprotein- lipase (LPL), and fatty acid transport protein that is involved in the uptake of fatty acids into the adipocytes (Tavares *et al.* 2007). As a result, the activation of PPARγ increases acyl-CoA synthetase which activates fatty acids, forming an activated complex with carnitine palmitoyl-transferase-1 (CPT-1). This complex enters the mitochondria where it is oxidized to produce adenosine triphosphate (ATP) (Yamashita *et al.* 2008).

CLAs increase the activity of CPT-1consequently and collectively reduce the accumulation of fatty acids in the adipose tissue. Increased β oxidation of mitochondrial fatty acids induced by CLAs also significantly decreases triacylglycerols synthesis with concomitant reduction of adipocyte size (Botelho *et al*. 2005). The reduction of body fat occurred due to a decrease in adipocyte size, not the number.

It is noticed that CLAs significantly elevated the expression of the uncoupling protein of the respiratory chain-1 (UCP-1) that leads to weight loss (Busiello *et al*. 2015). Where, β oxidation of fatty acids results in energy, part of this energy is used for the production of ATP, the rest of the energy is released as heat. UCP-1 also is known as thermogenin, it accelerates the loss of energy as heat. Thus, CLAs increases energy metabolism and expenditure via increasing basal metabolic rate (BMR) or thermogenesis. Consistent with this theory, Shen *et al*. (2013) proved that the CLAs increase the browning of white adipose tissue with a concomitant increase in energy expenditure. The increased brown fat is significantly associated with lower obesity risk in both mice (Almind *et al*. 2007) and humans (Cypess *et al*. 2009). It has been documented that t10-c12 CLA noticeably elevates cyclooxygenase (Cox-2) expression and production of prostaglandin (PG) in the human adipocytes associated with the induction of browning of WAT (Madsen *et al*. 2010).

Coelho *et al*. (2019) demonstrated that dietary fat can regulate obesity through its effects on gut microbiota. Diets supplemented with 0.5 percent t10c12 CLA for eight weeks resulted in enhanced cecum fermentation with the concomitant rise in short-chain fatty acids (SCFAs). The intake of CLAs regulates dysbiosis-induced obesity by gut microbiota modulation (Marques *et al*. 2015). SCFAs induce satiety through the elevation of circulating anorexogenous hormones (Nilsson *et al*. 2013) and the reduction of ghrelin in the blood (Parnell and Reimer 2009).

4.1.2 *Adverse effects of CLAs:* It is noteworthy that some animal and human studies have shown that CLAs administration can increase inflammation and insulin resistance (Risérus *et al*. 2004; Hamilton *et al*. 2015; Shen and McIntosh 2016), where cultured adipocytes treated with t10 C12CLA display inflammatory reactions (den Hartigh *et al*. 2013). Besides, CLAs consumption has been related to reduced insulin signaling in mice (Poirier *et al*. 2006) which is indicative of insulin resistance. Den Hartigh *et al*. (2017) confirmed that CLAs supplementation significantly enhances weight loss associated with insulin resistance. These drawbacks in the consumption of CLAs are significantly related to the dose. High levels of t10-c12CLA might increase inflammatory markers (LaRosa *et al*. 2006). In addition to inflammation, such high doses of CLAs cause an increase in hepatic steatosis that is characterized by an overt appearance of fats in the liver, increased liver weight and triacylglycerol content which may be attributed to insulin resistance (Shen *et al*. 2013). Therefore, controlling the supplemented level or dose of CLAs is a must.

4.2 *Medium-chain triglycerides supplement*

Medium-chain triglycerides (MCTs) are esters formed of glycerol and three fatty acids with a chain length of 6–12 carbon atoms. Dietary medium-chain fatty acids (MCFAs) include caproic acid or hexanoic acid (C_6:0), caprylic acid, or octanoic acid (C_8:0), capric acid, or decanoic acid (C_{10}:0), and lauric acid (C_{12}:0). Natural

sources of MCFAs in the form of MCTs are coconut and palm kernel oils. MCTs differ from long-chain triglycerides (LCTs) by their smaller molecular size. Besides, MCTs are hydrolyzed faster and more extensively during digestion. MCFAs also undergo limited re-esterification as they have a low affinity for anabolic enzymes such as diglyceride acyltransferase. Furthermore, after digestion, both MCFAs and MCTs are directly reached into the liver via the portal system for rapid oxidation (Babayan 1987). MCFAs and MCTs efficiently enter the mitochondria without carnitine esterification (Hoppel, 1982) through the CPT-1 transport system. Unlike long-chain fatty acids (LCFAs) which are packed into chylomicrons for their tissue distribution through the lymphatic system, allowing maximum uptake by adipose tissue for storage as fat. Collectively, MCTs are extremely less likely to be stored, don't produce ectopic fat metabolites which promote insulin resistance and also inflammation (McCarty and DiNicolantonio 2016). MCTs were documented to reduce the accumulation of body fat in both clinical trials and animal studies (Liu *et al*. 2009; Liu *et al*. 2012). Also, St-onge and Jones (2002) have shown that MCTs have important potential in the prevention of obesity.

It is well documented that the consumption of MCTs in ad libitum meals can substantially induce satiety and reduce body weight (Rial *et al*. 2016; Gunasekaran *et al*. 2017). It was also found that when MCTs were added to human breakfast, the consumption at the next meal was reduced (Van Wymelbeke *et al*. 1998). In this context, MCTs supplementation reduces energy intake over the following two days compared to long-chain triglycerides. Decreased energy intake may be mediated by increasing β-hydroxybutyrate concentration and/or delaying gastric emptying (Maher *et al*. 2020). Furthermore, there was reduced intake at the dinner after lunch with MCTs as compared to LCTs or other fat replacements (Van Wymelbeke *et al.* 2001). Interestingly, MCTs consumption resulted in a decrease in food intake either in overweight males (St-Ong *et al*. 2014) or in healthy, non-obese adult males (Van Wymelbeke *et al.* 1998).On the other hand, it has been stated that there is no impact on food intake by MCTs supplement (Poppitt *et al.* 2010). This controversy may be explained by the small dose of MCTs (10 g) in this study. In the meantime, the effective doses in other studies were 20g or more of MCTs. Obese women eating coconut oil had a marked reduction in waist circumference as compared to those who consumed soya bean oil (Assunção *et al*. 2009). McCarty and DiNicolantonio (2016) recommended that lauric acid should be administered instead of LCFAs to manage obesity, as it is less obesogenic and does not intensify obesity. In mice, coconut oil reduced body weight gain and decreased fat deposition after six weeks of treatments (Gunasekaran *et al*. 2017).

4.2.1 *Mechanisms of MCTs:* Zhang *et al*. (2015) fed a high-fat diet with 2% MCTs or LCTs to obese mice for twelve weeks. Their results showed that diet-containing MCTs produced a significant reduction in fat mass. Such a decrease may be partially attributed to the activation of BAT, probably by the norepinephrine (NE) pathway. Since MCTs are significantly irritating to the sympathetic nervous system, an increase in expression of mRNA, and the protein of the beta-3a-drenergic receptors (β3-AR) was observed. NE can trigger many biochemical lipolysis reactions such as the up-regulation of adipose lipase and hormone-sensitive lipase (Liu *et al*. 2012). NE may also induce thermogenesis (Zhao *et al*. 1994). It was proved that an increase in β3-AR expression could cause elevated UCP-1 expression in BAT and thermogenesis (Lowell and Flier 1997).

Very low-calorie diets (VLCD) enriched with MCTs or LCTs have been administered to obese women for 4 weeks. Both body fat and body weight showed a significant reduction in the MCTs' diet. Moreover, the feeling of hunger was lower and directly proportional to the levels of the plasma ketone bodies. Also, MCTs diet-induced lower nitrogen excretion in the urine (Krotkiewski 2001) indicating a protein-sparing effect of MCTs with a concomitant transition to anabolic protein metabolism. Recently, some studies indicate that the net protein catabolism is decreased by 32% in the ketone state such as in cases of fasting and VLCD conditions (Ryde *et al.* 1993). In this case, ketones that are the result of fatty acid oxidation are utilized by the brain and skeletal muscles as an energy source (figure 2). Therefore, they ameliorate the hunger feeling, spare protein conversion to glucose, and increase the synthesis of proteins (Hoffer *et al*., 1982). MCTs produce ketones even in the presence of a large concentration of glycogen (Foster and McGarry 1982) because they have rapid access to the inner mitochondrial matrix in the hepatocytes. The main ketone formed by MCTs is the β-hydroxybutyrate. It decreases appetite and exerts an anorexic effect (Laeger *et al*. 2010).

Many obese patients have a variety of metabolic abnormalities with multifactorial causes. Among these factors, the disturbance of gut microbiota is identified as a causative factor for such complications in obese subjects. MCTs supplementation does not only

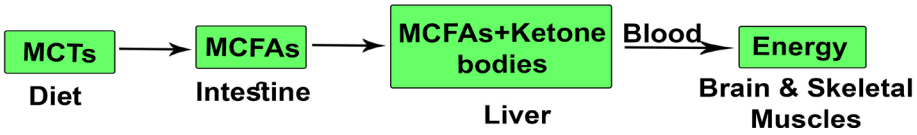

Figure 2. Mechanism of energy production via dietary MCTs.

improve this dysbiosis but also improves intestinal permeability, which helps to manage obesity (Rial *et al.* 2016). Correction of gut microbiota significantly enhances obese well-being and thus increases SCFAs, consequently participates in weight reduction (Parnell and Reimer 2009; Nilsson *et al.* 2013). Moreover, the influence of MCTs on reduction in satiety and food intake is done by a significant increase of MCFAs in plasma after MCTs consumption such as capric, caprylic, and lauric. These fatty acids affect the acylation mechanism of ghrelin, which modulates the feeling of satiety and appetite (Lemarié *et al.* 2016). Each of the capric acid and lauric acid promotes fatty acid oxidation with a concomitant increase of satiety (Lemarié *et al.* 2015). Cholecystokinin (CCK) is the first gut hormone that is found to affect satiety. Ingestion of lipid is linked to the secretion of CCK which depends on the length of the fatty acid chain. It is reported that CCK is considered a mediator of fat-related satiety via delaying gastric emptying (Matzinger *et al.* 1999). It was noticed that CCK was released after the ingestion of either capric or lauric acids (Mclaughlin *et al.* 1999). Furthermore, Feltrin *et al.* (2004) found that C_{12} and C_{10} fatty acids increased CCK release, but the magnitude of this elevation was higher with C_{12}.

Dietary administration of MCTs may likely influence mRNA expression of genes capable of altering the lipogenic capacity of animals (Ferreira *et al.* 2014). MCTs work through PPAR-γ to down-regulate adipogenic genes. Moderate doses of MCTs are required to improve their anti-lipogenic effect otherwise high doses can have lipogenic effects (Marten *et al.* 2006).

Peptide YY (PYY) is an amino acid peptide that belongs to pancreatic peptides. Its secretion is stimulated by the sense of protein and fats. It has an anorexic effect by inhibiting food intake via increasing the C-fos expression in the arcuate nucleus (ARC). ARC reduces food consumption (Riediger *et al.* 2004). MCTs containing 56% octanoic and 43% decanoic acid markedly increased PYY secretion (Maas *et al.* 1998). This finding was supported by Feltrin *et al.* (2007) since they found that decanoic acid could stimulate the PYY release in a dose-dependent manner. Moreover, in overweight men, MCTs administration significantly elevated the concentrations of leptin and PYY but did not affect ghrelin or GLP-1as compared to LCTs (Stonge *et al.* 2014).

4.2.2 *Adverse effects of MCTs:* The MCTs administration as oil may produce a large elevation of plasma ketones which returns to the normal levels within three hours. This can be avoided by the ingestion of intact sources of these MCTs such as coconut oil which causes a less prominent and a delayed rise of ketones (Newport 2013). Also, although MCTs have an important effect on weight loss, they can increase fasting triglycerides and cholesterol levels (Gunasekaran *et al.* 2017). By contrast, Sung *et al.* (2018) demonstrated that MCTs have a potential role in lowering the blood lipids in diabetic rats. Also, this hypercholesterolemia can be considered to be benign (McCarty and DiNicolantonio 2016) and can be avoided by administering moderate amounts of such oils (Marten *et al.*2006). However, it has been shown that MCTs did not have toxicological effects, even with chronic dietary supplementation (Nagao and Yanagita 2010).

5. Conclusion

Obesity is a condition of excessive body weight with an exaggeration of adipose tissue. It plays an important role in several pathophysiological disorders such as atherosclerosis, hypertension, insulin resistance, and diabetes. The etiology of obesity is multifactorial. The primary causes of obesity are higher caloric intake, especially with saturated and/or trans-fats, and a sedentary lifestyle. Meanwhile, secondary factors include several endocrine disorders, vitamin D deficiency, gene mutation, some medications, environmental obesogens, and disruption of energy homeostasis. Many strategies are designed to minimize weight gain; however, each has some adverse effects. Therefore, a trial used a hypocaloric diet with some dietary supplements has shown marked success. Certain dietary fats, besides their role as a source of energy,

can be used as nutraceuticals or dietary supplements to enhance weight reduction. In this context, CLAs and MCTs exhibit a promising issue. Several mechanisms are involved to explain their effects such as increasing satiety, energy expenditure, correcting intestinal microbiota, modifying gene expression, reducing food intake, and increasing mitochondrial oxidation. However, their amounts or doses should be carefully adjusted to avoid unpleasant side effects. Further experimental studies and clinical trials are warranted to confirm the use of such fats as complementary medicine with selected a strategy for weight reduction.

References

Almind K, Manieri M, Sivitz WI, Cinti S and Kahn CR 2007 Ectopic brown adipose tissue in .muscle provides a mechanism for differences in risk of metabolic syndrome in mice. *Proc. Natl. Acad. Sci. USA* **104** 2366–2371

Asgary S, Rastqar A and Keshvari M 2018 Weight loss associated with consumption of apples: a review. *J. Am. Coll. Nutr.* **37** 627–639

Assunção ML, Ferreira HS, dos Santos AF, Cabral CR Jr and Florêncio TM 2009 Effects of dietary coconut oil on the biochemical and anthropometric profiles of women presenting abdominal obesity. *Lipids* **44** 593–601

Astrup A 2005 The role of dietary fat in obesity. *Semin. Vasc. Med*. **5** 40–47

Babayan VK 1987 Medium chain triglycerides and structured lipids. *Lipids* **22** 417–720.

Baillie-Hamilton PF 2002 Chemical toxins: a hypothesis to explain the global obesity epidemic. *J. Altern. Complement.* Med. **8** 185–192

Basak S and Duttaroy AK 2020 Conjugated linoleic acid and its beneficial effects in obesity, cardiovascular disease, and cancer. *Nutrients* **12** 1913

Bhasin S, Woodhouse L and Storer TW 2003. Androgen effects on body composition. *Growth Hormone IGF Res.* **13** S63–S71

Bhurosy T and Jeewon R 2014 Overweight and obesity epidemic in developing countries: a problem with diet, physical activity, or socioeconomic status? *Sci. World J.* **2014** 964236

Björntorp P 1993 Visceral obesity: a "civilization syndrome". Obes. *Rev.* 1 206–222

Boix-Castejón M, Herranz-López M, Pérez Gago A, Olivares-Vicente M, Caturla N, Roche E and Micol V 2018 Hibiscus and lemon verbena polyphenols modulate appetite-related biomarkers in overweight subjects: a randomized controlled trial. *Food Funct*. **9** 3173–3184

Boschini RP and Garcia Júnior JR 2005 UCP2 and UCP3 genic expression: regulation by food restriction, fasting and physical exercise. *Braz. J. Nutr.* **18** 753–764

Botelho AP, Santos-Zago LF, Reis SMPM and Oliveira AC 2005 Conjugated linoleic acid suplementation decreased the body fat in Wistar rats. *Braz. J. Nutr.* **18** 561–565

Bush T, Lovejoy JC, Deprey M and Carpenter KM 2016 The effect of tobacco cessation on weight gain, obesity and diabetes risk. *Obesity* **24** 1834–1841

Busiello RA, Savarese S and Lombardi A 2015 Mitochondrial uncoupling proteins and energy metabolism. *Front. Physiol.* **6** 36

Castro EA, Carraça EV, Cupeiro R, López-Plaza B, Teixeira PJ, González-Lamuño D and Peinado AB 2020 The effects of the type of exercise and physical activity on eating behavior and body composition in overweight and obese subjects. *Nutrients* **12** 557

Chambers L, McCrickerd K and Yeomans MR 2014 Optimising foods for satiety. *Trends Food Sci. Technol.* **41** 149–160

Cheng V and Kashyap SR 2011 Weight considerations in pharmacotherapy for type 2 diabetes. *J. Obes.* **2011** 984245

Clément K, Vaisse C, Lahlou N, *et al*. 1998 A mutation in the human leptin receptor gene causes obesity and pituitary dysfunction. *Nature* **392** 398–401

Coelho OGL, Cândido FG, Alfenas RCG 2019 Dietary fat and gut microbiota: mechanisms involved in obesity control. *Crit. Rev. Food Sci. Nutr.* **59** 3045–3053

Comuzzie AG and Allison DB 1998 The search for human obesity genes. *Science* **280** 1374–7

Coleman H, Quinn P and Clegg ME 2016 Medium-chain triglycerides and conjugated linoleic acids in beverage form increase satiety and reduce food intake in humans. *Nutr. Res.* **36** 526- 533

Cypess AM, Lehman S, Williams G, Tal I, Rodman D, Goldfine AB, Kuo FC, Palmer EL, Tseng YH, Doria A, Kolodny GM and Kahn CR 2009 Identification and importance of brown adipose tissue in adult humans. *N. Engl. J. Med.* **360** 1509–1517

Delvin EE, Lambert M, Levy E, O'Loughlin J, Mark S, Gray-Donald K and Paradis G 2010 Vitamin D status is modestly associated with glycemia and indicators of lipid metabolism in French-Canadian children and adolescents. *J. Nutr.* **140** 987–991

den Hartigh LJ 2019 Conjugated linoleic acid effects on cancer, obesity, and atherosclerosis: a review of pre-clinical and human trials with current perspectives. *Nutrients* **11** 370

den Hartigh LJ, Gao Z, Goodspeed L, Wang S, Das AK, Burant CF, Chait A and Blaser MJ 2018 Obese Mice Losing Weight Due to trans-10,cis-12 Conjugated linoleic acid supplementation or food restriction harbor distinct gut microbiota. *J. Nutr.* **148** 562–572

den Hartigh LJ, Han CY, Wang S, Omer M and Chait A 2013 10E,12 Z-conjugated linoleic acid impairs adipocyte triglyceride storage by enhancing fatty acid oxidation, lipolysis, and mitochondrial reactive oxygen species. *J. Lipid Res.* **54** 2964–2978.

den Hartigh LJ, Wang S, Goodspeed L, *et al*. 2017 Metabolically distinct weight loss by 10,12 CLA and caloric restriction highlight the importance of subcutaneous white adipose tissue for glucose homeostasis in mice. *PLoS One* **12** e0172912

Do MT, Chang VC, Mendez MA and de Groh M 2017 Urinary bisphenol A and obesity in adults: results from the Canadian Health Measures Survey. *Health Promot. Chronic Dis. Prev. Can.* **37** 403–412

Earthman CP, Beckman LM, Masodkar K and Sibley SD 2012 The link between obesity and low circulating 25-hydroxyvitamin D concentrations: considerations and implications. *Int. J. Obes.* **36** 387–396

Ebrahimi-Mameghani M, Jamali H, Mahdavi R, Kakaei F, Abedi R and Kabir-Mamdooh B 2016 Conjugated linoleic acid improves glycemic response, lipid profile, and oxidative stress in obese patients with non-alcoholic fatty liver disease: a randomized controlled clinical trial. *Croat. Med. J.* **57** 331–342

Feltrin KL, Little TJ, Meyer JH, Horowitz M, Smout AJ, Wishart J, Pilichiewicz AN, Rades T, Chapman IM and Feinle-Bisset C 2004 Effects of intraduodenal fatty acids on appetite, antropyloroduodenal motility, and plasma CCK and GLP-1 in humans vary with their chain length. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **287** R524–33

Feltrin KL, Little TJ, Meyer JH, Horowitz M, Rades T, Wishart J and Feinle-Bisset C 2007 Effects of lauric acid on upper gut motility, plasma cholecystokinin and peptide YY, and energy intake are load, but not concentration, dependent in humans. *J. Physiol.* **581** 767–777

Ferreira L, Lisenko K, Barros B, Zangeronimo M, Pereira L and Sousa R 2014 Influence of medium-chain triglycerides on consumption and weight gain in rats: a systematic review. *J. Animal Physiol. Animal Nutr.* **98** 1–8

Foster DW and McGarry JD 1982 The regulation of ketogenesis. *Ciba* Found. *Symp.* **87** 120–131

Frood S, Johnston LM, Matteson CL and Finegood DT 2013 Obesity, Complexity, and the Role of the Health System. *Curr. Obes. Rep.* **2** 320–326

Galgani J and Ravussin E 2011 Principles of Human Energy Metabolism. In: Ahoma RS (ed). *Metabolic Basis of Obesity*. Spriger: New York, pp 1–23. https://link.springer.com/book/10.1007/978-1-4419-1607-5

Galvão CF, Xavier VF, da Silva LE, Gonçalves LCO, Gouveia PMDC and Gonçalves ARC 2018 Consumption of extra virgin olive oil improves body composition and blood pressure in women with excess body fat: a randomized, double-blinded, placebo-controlled clinical trial. *Eur. J. Nutr.* **57** 2445–2455

Girardet C and Butler AA 2014 Neural melanocortin receptors in obesity and related metabolic disorders. *Biochim* Biophys *Acta*. **1842** 482–494

Grün F 2014 The obesogen tributyltin. Vitam. *Horm.* **94** 277–325

Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL and Anis AH 2009 The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health* **9** 88

Gunasekaran R, Shaker MR, Mohd-Zin SW, Abdullah A, Ahmad-Annuar A and Abdul-Aziz NM 2017 Maternal intake of dietary virgin coconut oil modifies essential fatty acids and causes low body weight and spiky fur in mice. *BMC Complement. Altern. Med.* **17** 79

Hamilton M, Hopkins LE, AlZahal O, MacDonald TL, Cervone DT, Wright DC, McBride BW and Dyck DJ 2015.Feeding butter with elevated content of trans-10, cis-12 conjugated linoleic acid to obese-prone rats impairs glucose and insulin tolerance. *Lipids Health Dis*. **14** 119

Herrera BM, Keildson S and Lindgren CM 2011 Genetics and epigenetics of obesity. *Maturitas* **69** 41–49

Hoffer LJ, Bistrian BR, Young VR, Blackburn GL and Matthews DE 1982 Metabolic effects of very low calorie weight reduction diets. *J.* Clin. *Invest.* **73** 750–758

Hoppel CL 1982 Carnitine and carnitine palmitoyltransferase in fatty acid oxidation and ketosis. *Fed. Proc*. **41** 2853–2857

Hu S, Wang L, Yang D, *et al*. 2018 Dietary fat, but not protein or carbohydrate, regulates energy intake and causes adiposity in mice. *Cell Metab.* **8** 415–431.

Janesick AS and Blumberg, B 2016 Obesogens: an emerging threat to public health. *Am. J. Obstet. Gynecol.* **9214** 559–565

Kaddam IM, Al-Shaikh AM, Abaalkhail BA, Asseri KS, Al-Saleh YM, Al-Qarni AA, Al-Shuaibi AM, Tamimi WG and Mukhtar AM 2017 Prevalence of vitamin D deficiency and its associated factors in three regions of Saudi Arabia. *Saudi Med. J.* **38** 381–390

Kamphuis MM, Lejeune MP, Saris WH and Westerterp-Plantenga MS 2003 Effect of conjugated linoleic acid supplementation after weight loss on appetite and food intake in overweight subjects. *Eur. J. Clin. Nutr.* **57** 1268–1274

Karam JG and McFarlane SI 2007 Secondary causes of obesity. *Therapy* **4** 641–650

Kaur S, Gonzales MM, Strasser B, Pasha E, McNeely J, Tanaka H and Haley AP 2015 Central adiposity and cortical thickness in midlife. *Psychosom. Med.* **77** 671–678

Kavanagh K, Jones KL, Sawyer J, Kelley K, Carr JJ, Wagner JD and Rudel LL 2007 Trans-fat Diet Induces Abdominal Obesity and Changes in Insulin Sensitivity in Monkeys. *Obesity* **15** 1675–1684

Kennedy A, Martinez K, Schmidt S, Mandrup S, LaPoint K and McIntosh M 2010 Antiobesity mechanisms of action of conjugated linoleic acid. *J. Nutr.* Biochem. **21** 171–179

Kien CL, Bunn JY and Ugrasbul F 2005 Increasing dietary palmitic acid decreases fat oxidation and daily energy expenditure. *Am. J. Clin. Nutr.* **82** 320–326

Kim SH and Park MJ 2014 Phthalate exposure and childhood obesity. *Ann. Pediatr. Endocrinol. Metab.* **19** 69–75

Kishino S, Ogawa J, Omura Y, Matsumura K and Shimizu S 2002 Conjugated linoleic acid production from linoleic acid by lactic acid bacteria. *J. Am. Oil Chem. Soc.* **79** 159–163

Koba K and Yanagita T 2014 Health benefits of conjugated linoleic acid (CLA). *Obes. Res. Clin. Pract*. **8** e525–e532

Koh-Banerjee P, Chu NF, Spiegelman D, Rosner B, Colditz G, Willett W and Rimm E 2003 Prospective study of the association of changes in dietary intake, physical activity, alcohol consumption, and smoking with 9-y gain in waist circumference among 16 587 US men. *Am. J. Clin. Nutr.* **78** 719–727

Krotkiewski M 2001 Value of VLCD supplementation with medium chain triglycerides. *Int. J. Obes. Relat. Metab. Disord*. **25** 1393–1400

Laeger T, Metges CC and Kuhla B 2010 Role of beta-hydroxybutyric acid in the central regulation of energy balance. *Appetite* **54** 450–455

LaRosa PC, Miner J, Xia Y, Zhou Y, Kachman S and Fromm ME 2006 Trans-10, cis-12 conjugated linoleic acid causes inflammation and delipidation of white adipose tissue in mice: a microarray and histological analysis. *Physiol. Genomics* **27** 282–294

Lee Y, Mottillo EP and Granneman JG 2014 Adipose tissue plasticity from WAT to BAT and in between. *Biochim. Biophys. Acta* **1842** 358–369

Lehnen TE, da Silva MR, Camacho A, Marcadenti A and Lehnen AM 2015 A review on effects of conjugated linoleic fatty acid (CLA) upon body composition and energetic metabolism. *J. Int. Soc. Sports Nutr.* **12** 36

Lemarié F, Beauchamp E, Dayot S, Duby C, Legrand P and Rioux V 2015 Dietary caprylic acid (C8:0) does not increase plasma acylated ghrelin but decreases plasma unacylated ghrelin in the rat. *PLoS* One **10** e0133600

Lemarié F, Beauchamp E, Legrand P and Rioux V 2016 Revisiting the metabolism and physiological functions of caprylic acid (C8:0) with special focus on ghrelin octanoylation. *Biochimie* **120** 40–48

Lepore SM, Morittu VM, Celano M, Trimboli F, Oliverio M, Procopio A, Di Loreto C, Damante G, Britti D, Bulotta S and Russo D 2015 Oral administration of oleuropein and its semisynthetic peracetylated derivative prevents hepatic steatosis, hyperinsulinemia, and weight gain in mice fed with high fat cafeteria diet. *Int.J. Endocrinol.* **2015** 431453

Lim S, Ahn SY, Song IC, Chung MH, Jang HC, Park KS, Lee KU, Pak YK and Lee HK 2009. Chronic Exposure to the Herbicide, Atrazine, Causes Mitochondrial Dysfunction and Insulin Resistance. *PLoS ONE* **4** e5186

Liu Y, Wang J, Zhang R, *et al.* 2009 A good response to oil with medium- and long-chain fatty acids in body fat and blood lipid profiles of male hypertriglyceridemic subjects. *Asia Pac. J. Clin. Nutr.* **18** 351–358

Liu YH, Zhang Y, Xu Q, Yu XM, Zhang XS, Wang J, Xue C, Yang XY, Zhang RX and Xue CY 2012 Increased norepinephrine by medium-chain triglyceride attributable to lipolysis in white and brown adipose tissue of C57BL/6J mice. *Biosci. Biotechnol. Biochem.* **76** 1213–1218

Lo JC, Feigenbaum SL, Yang J, Pressman AR, Selby JV and Go AS 2006 Epidemiology and adverse cardiovascular risk profile of diagnosed polycystic ovary syndrome. *J. Clin.* Endocrinol. *Metab.* **91** 1357–63

Lombardo GE, Lepore SM, Morittu VM, *et al.* 2018 Effects of Oleacein on High-Fat Diet-Dependent Steatosis, Weight Gain, and Insulin Resistance in Mice. Front. *Endocrinol.* **9** 116

López-Plaza B, Bermejo LM, Koester Weber T, Parra P, Serra F, Hernández M, Palma Milla S and Gómez-Candela C 2013 Effects of milk supplementation with conjugated linoleic acid on weight control and body composition in healthy overweight people. *Nutr. Hosp.* **28** 2090–2098

Lowell BB and Flier JS 1997 Brown adipose tissue, beta 3-adrenergic receptors, and obesity. *Annu. Rev. Med.* **48** 307–316

Ludwig T, Worsch S, Heikenwalder M, Daniel H, Hauner H and Bader BL 2013 Metabolic and immunomodulatory effects of n-3 fatty acids are different in mesenteric and epididymal adipose tissue of diet-induced obese mice. *Am. J. Physiol. Endocrinol. Metab.* **304** E1140–E1156

Maas MIM, Hopman WPM, Katan MB and Jansen JBMJ 1998 Release of peptide YY and inhibition of gastric acid secretion by long-chain and medium-chain triglycerides but not by sucrose polyester in men. *Eur. J. Clin. Investig.* **28** 123–130

Mądry E, Chudzicka-Strugała I, Grabańska-Martyńska K, Malikowska K, Grebowiec P, Lisowska A, Bogdański P and Walkowiak J 2016 Twelve weeks CLA supplementation decreases the hip circumference in overweight and obese women. A double-blind, randomized, placebo-controlled trial. *Acta Sci. Pol. Technol. Aliment.***15** 107–113

Madsen L, Pedersen LM, Lillefosse HH, *et al.* 2010 UCP1 induction during recruitment of brown adipocytes in white adipose tissue is dependent on cyclooxygenase activity. *PLoS One* **5** e11391

Maher T, Deleuse M, Thondre S, Shafat A and Clegg ME 2020 A comparison of the satiating properties of medium-chain triglycerides and conjugated linoleic acid in participants with healthy weight and overweight or obesity. *Eur. J. Nutr.* https://doi.org/10.1007/s00394-020-02235-y

Marques TM, Wall R, O'Sullivan O, Fitzgerald GF, Shanahan F, Quigley EM, Cotter PD, Cryan JF, Dinan TG, Ross RP and Stanton C 2015 Dietary trans-10, cis-12-conjugated linoleic acid alters fatty acid metabolism and microbiota composition in mice. *Br. J. Nutr.* **113** 728–738

Marten B, Pfeuffer M and Schrezenmeir J 2006 Medium-chain triglycerides. *Int. Dairy J.* **16** 1374–1382

Martins SV, Madeira A, Lopes PA, Pires VM, Alfaia CM, Prates JA, Moura T and Soveral G 2015 Adipocyte membrane glycerol permeability is involved in the anti-adipogenic effect of conjugated linoleic acid. *Biochem. Biophys. Res. Commun*. **458** 356–361

Matzinger D, Gutzwiller JP, Drewe J, Orban A, Engel R, D'Amato M, Rovati L and Beglinger C 1999 Inhibition of food intake in response to intestinal lipid is mediated by cholecystokinin in humans. *Am. J. Physiol*. **277** R1718–1724

McCarty MF and DiNicolantonio JJ 2016 Lauric acid-rich medium-chain triglycerides can substitute for other oils in cooking applications and may have limited pathogenicity. *Open Heart* **3** e000467

McLaughlin J, Grazia Lucà M, Jones MN, D'Amato M, Dockray GJ and Thompson DG 1999 Fatty acid chain length determines cholecystokinin secretion and effect on human gastric motility. *Gastroenterology* **116** 46–53

Merola N, Castillo J, Benavente-García O, Ros G and Nieto G 2017 The effect of consumption of citrus fruit and olive leaf extract on lipid metabolism. *Nutrients* **9** E1062

Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ and Willett WC 2006 Trans-fatty acids and cardiovascular disease. *N. Engl. J. Med.* **354** 1601–1613

Nagao K and Yanagita T 2010 Medium-chain fatty acids: functional lipids for the prevention and treatment of the metabolic syndrome. *Pharmacol. Res.* **61** 208–212

Namazi N, Irandoost P, Larijani B and Azadbakht L 2019 The effects of supplementation with conjugated linoleic acid on anthropometric indices and body composition in overweight and obese subjects: A systematic review and meta-analysis. *Crit. Rev. Food Sci. Nutr.* **59** 2720–2733

Newcomer JW and Lieberman JA 2007 Comparing safety and tolerability of antipsychotic treatment. *J.* Clin. *Psychiatry* **68** e07

Newport MT 2013 *Alzheimer's disease - what if there were a cure?* 2nd edn. Laguna Beach: Basic Health Publications

Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, Mullany E C, Biryukov S, Abbafati C, Stapelberg N and et al 2014 Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* **384** 766–781

Nilsson A, Johansson E, Ekström L, and Björck I 2013 Effects of a brown beans evening meal on metabolic risk markers and appetite regulating hormones at a subsequent standardized breakfast: a randomized cross-over study. *PLoS One* **8** e59985

Norris LE, Collene AL, Asp ML, Hsu JC, Liu LF, Richardson JR, Li D, Bell D, Osei K, Jackson RD and Belury MA 2009 Comparison of dietary conjugated linoleic acid with safflower oil on body composition in obese postmenopausal women with type 2 diabetes mellitus. *Am. J. Clin. Nutr.* **90** 468–476

Oliveira-de-Lira L, Santos EMC, de Souza RF, Matos RJB, Silva MCD, Oliveira LDS, Nascimento TGD, Schemly PALS and Souza SL 2018 Supplementation-dependent effects of vegetable oils with varying fatty acid compositions on anthropometric and biochemical parameters in obese women. *Nutrients* **10** E932

O'Reilly ME, Lenighan YM, Dillon E, Kajani S, Curley S, Bruen R, Byrne R, Heslin AM, Moloney AP, Roche HM and McGillicuddy FC 2020 Conjugated linoleic acid and alpha linolenic acid improve cholesterol homeostasis in obesity by modulating distinct hepatic protein pathways. *Mol. Nutr. Food Res.* **64** e1900599

Pal L, Berry A, Coraluzzi L, Kustan E, Danton C, Shaw J and Taylor H 2012 Therapeutic implications of vitamin D and calcium in overweight women with polycystic ovary syndrome. Gynecol. *Endocrinol.* **28** 965–968

Parnell JA and Reimer RA 2009 Weight loss during oligofructose supplementation is associated with decreased ghrelin and increased peptide YY in overweight and obese adults. *Am. J. Clin. Nutr.* **89** 1751–1759

Patten SB, Williams JV, Lavorato DH, Khaled S and Bulloch AG 2011 Weight gain in relation to major depression and antidepressant medication use. *J. Affect. Disord.* **134** 288–293

Pereira MA, Kartashov AI, Ebbeling CB, Van Horn L, Slattery ML, Jacobs DR Jr, Ludwig DS 2005 Fast-food habits, weight gain, and insulin resistance (the CARDIA study): 15-year prospective analysis. *Lancet* **365** 36–42

Phillips CM, Kesse-Guyot E, McManus R, Hercberg S, Lairon D, Planells R, Roche HM 2012 High dietary saturated fat intake accentuates obesity risk associated with the fat mass and obesity-associated gene in adults. *J. Nutr.* **142** 824–831

Piers LS, Walker KZ, Stoney RM, Soares MJ and O'Dea K 2003 Substitution of saturated with monounsaturated fat in a 4-week diet affects body weight and composition of overweight and obese men. *Br. J.Nutr.* **90** 717–727

Piggott M, Owens J, O'Brien J, Paling S, Wyper D, Fenwick J, Johnson M, Perry R and Perry, E 2002 Comparative distribution of binding of the muscarinic receptor ligands pirenzepine, AF-DX 384, (R,R)-I-QNB and (R,S)-I-QNB to human brain. *J. Chem. Neuroanat.* **24** 211–223.

Poirier H, Shapiro JS, Kim RJ and Lazar MA 2006 Nutritional supplementation with trans-10, cis-12-conjugated linoleic acid induces inflammation of white adipose tissue. *Diabetes* **55** 1634–41

Poppitt SD, Strik CM, MacGibbon AK, McArdle BH, Budgett SC and McGill AT 2010 Fatty acid chain length, postprandial satiety and food intake in lean men. *Physiol. Behav.* **101** 161–167

Raatz SK, Conrad Z, Johnson LK, Picklo MJ, Jahns L 2017 Relationship of the reported intakes of fat and fatty acids to body weight in US adults. *Nutrients* **9** E438

Ràfols ME 2014 Adipose tissue: Cell heterogeneity and functional diversityTejido adiposo: heterogeneidad celulary diversidad functional. *Endocrinol. Nut.* **61** 100–112

Reardon M, Gobern S, Martinez K, Shen W, Reid T and McIntosh M 2012 Oleic acid attenuates trans-10, cis-12 conjugated linoleic acid-mediated inflammatory gene expression in human adipocytes. *Lipids* **47** 1043–1051

Rial SA, Karelis AD, Bergeron KF and Mounier C 2016 Gut Microbiota and Metabolic Health: The Potential Beneficial Effects of a Medium Chain Triglyceride Diet in Obese Individuals. *Nutrients* **8** E281

Riediger T, Bothe C, Becskei C, Lutz TA 2004 Peptide YY directly inhibits ghrelin-activated neurons of the arcuate nucleus and reverses fasting-induced c-Fos expression. *Neuroendocrinol* **79** 317–326

Risérus U, Vessby B, Arner P and Zethelius B 2004 Supplementation with trans10cis12-conjugated linoleic acid induces hyperproinsulinaemia in obese men: close association with impaired insulin sensitivity. *Diabetologia* **47** 1016–1019

Rosen T, Bosaeus I, TöIli J, Lindstedt G and Bengtsson B 1993 Increased body fat mass and decreased extracellular fluid volume in adults with growth hormone deficiency. *Clin. Endocrinol.* **38** 63–71

Rothenberg DO, Zhou C and Zhang L 2018 A Review on the Weight-Loss Effects of Oxidized Tea Polyphenols. *Molecules*. **23** E1176

Ryde SIS, Saunders NH, Birks JL, Ali PA, Thomas DW, Morgan VD, Evans CJ, Al-Zeibak A, Dutton J and Sivyer A 1993 The effects of VLCD on body composition. In: Krietzman SN, Howard AN (eds). *The Swansea trial*. Smith Gordon: London, pp 31 – 54.

Sáinz N, Barrenetxe J, Moreno-Aliaga MJ and Martínez JA 2015 Leptin resistance and diet-induced obesity: central and peripheral actions of leptin. *Metabolism* **64** 35–46

Santini F, Marzullo P, Rotondi M, Ceccarini G, Pagano L and Ippolito S 2014 Mechanisms in endocrinology: the crosstalk between thyroid gland and adipose tissue: signal integration in health and disease. *Eur. J. Endocrinol.* **171** R137–R152

Schwab U, Lauritzen L, Tholstrup T, Haldorssoni T, Riserus U, Uusitupa M and Becker W 2014 Effect of the amount and type of dietary fat on cardiometabolic risk factors and risk of developing type 2 diabetes, cardiovascular diseases, and cancer: a systematic review. *Food Nutr. Res.* **10** 58

Shadman Z, Taleban FA, Saadat N and Hedayati M 2013 Effect of conjugated linoleic acid and vitamin E on glycemic control, body composition, and inflammatory markers in overweight type2 diabetics. *J. Diabetes Metab. Disord.* **12** 42.

Shen W, Chuang CC, Martinez K, Reid T, Brown JM, Xi L, Hixson L, Hopkins R, Starnes J and McIntosh M 2013 Conjugated linoleic acid reduces adiposity and increases markers of browning and inflammation in white adipose tissue of mice. *J. Lipid Res.* **54** 909–922

Shen W and McIntosh MK 2016 Nutrient Regulation: Conjugated Linoleic Acid's Inflammatory and Browning Properties in Adipose Tissue. *Annu. Rev. Nutr.* **36** 183–210

Snijder MB, van Dam RM, Visser M, Deeg DJ, Dekker JM, Bouter LM, Seidell JC and Lips P 2005 Adiposity in relation to vitamin D status and parathyroid hormone levels: a population-based study in older men and women. *J. Clin Endocrinol. Metab.* **90** 4119–23

Srinivasan S, Ogle GD, Garnett SP, Briody JN, Lee JW and Cowell CT 2004 Features of the metabolic syndrome after childhood Craniopharyngioma. *J. Clin. Endocrinol. Metab.* **89** 81–6

Stein EM, Strain G, Sinha N, Ortiz D, Pomp A, Dakin G, McMahon DJ, Bockman R and Silverberg SJ 2009 Vitamin D insufficiency prior to bariatric surgery: risk factors and a pilot treatment study. *Clin. Endocrinol*. **71** 176–183

St-Onge MP and Jones PJH 2002 Medium chain triglyceride consumption increases energy expenditure relative to long chain triglyceride in overweight men. Am. *J. Clin.* Nutr. **75** 340S

St-Onge MP, Mayrsohn B, O'Keeffe M, Kissileff HR, Choudhury AR and Laferrère B 2014 Impact of medium and long chain triglycerides consumption on appetite and food intake in overweight men. *Eur. J. Clin. Nutr.* **68** 1134–1140

Strasser B and Fuchs D 2016 Diet Versus Exercise in Weight Loss and Maintenance: Focus on Tryptophan. *Int. J.* Tryptophan *Res.* **9** 9–16

Sung MH, Liao FH and Chien YW 2018 Medium-Chain Triglycerides Lower Blood Lipids and Body Weight in Streptozotocin-Induced Type 2 Diabetes Rats. *Nutrients* **10** pii: E963

Tavares V, Hirata MH and Hirata RDC 2007 Peroxisome proliferator-activated receptor gamma (PPARgamma): molecular study in glucose homeostasis, lipid metabolism and therapeutic approach. *Arch. Endocrinol. Metabol.* **51** 526–533

Tchkonia T, Giorgadze N, Pirtskhalava T, Tchoukalova Y, Karagiannides I, Forse RA, DePonte M, Stevenson M, Guo W, Han J, Waloga G, Lash TL, Jensen MD and Kirkland JL 2002 Fat depot origin affects adipogenesis in primary cultured and cloned human preadipocytes. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* **282** R1286–R1296

Trayhurn P 2005 Endocrine and signalling role of adipose tissue: new perspectives on fat. *Acta Physiol. Scand.* **184** 285–293

van Baak MA and Mariman ECM 2019 Dietary strategies for weight loss maintenance. *Nutrients*. **11** 1916

Van Wymelbeke V, Himaya A, Louis-Sylvestre J and Fantino M 1998 Influence of medium-chain and long-chain triacylglycerols on the control of food intake in men. *Am. J. Clin. Nutr.* **68** 226–234

Van Wymelbeke V, Louis-Sylvestre J and Fantino M 2001 Substrate oxidation and control of food intake in men

after a fat-substitute meal compared with meals supplemented with an isoenergetic load of carbohydrate, long-chain triacylglycerols, or medium-chain triacylglycerols. *J.Clin. Nutr.* **74** 620–630

Whitmer RA, Gunderson EP, Quesenberry Jr CP, Zhou J and Yaffe K 2007 Body mass index in midlife and risk of Alzheimer disease and vascular dementia. *Curr. Alzheimer Res.* **4** 103–9

Wajchenberg BL, Bosco A, Marone MM, Levin S, Rocha M, Lerário AC, Nery M, Goldman J and Liberman B 1995 Estimation of body fat and lean tissue distribution by dual energy X-ray absorptiometry and abdominal body fat evaluation by computed tomography in Cushing's disease. *J.* Clin. *Endocrinol. Metab.* **80** 2791–2794

Wakayo T, Whiting SJ and Belachew T 2016 Vitamin D deficiency is associated with overweight and/or obesity among school children in central ethiopia: a cross-sectional study. Nutrients **8** 190

Watras AC, Buchholz AC, Close RN, Zhang Z and Schoeller DA 2007 The role of conjugated linoleic acid in reducing body fat and preventing holiday weight gain. *Int. J. Obes.* **31** 481–487

Wei Y, Zhang JJ, Li Z, Gow A, Chung KF, Hu M, Sun Z, Zeng L, Zhu T, Jia G, Li X, Duarte M and Tang X 2016 Chronic exposure to air pollution particles increases the risk of obesity and metabolic syndrome: findings from a natural experiment in Beijing. FASEB *J.* **30** 2115–2122

World Health Organization (WHO) 1985 Energy and protein requirements : report of a Joint FAO/WHO/UNU Expert Consultation – Geneva, Switzeland Technical Report Series no. 724

Wozniak SE, Gee LL, Wachtel MS and Frezza EE 2009 Adipose tissue: the new endocrine organ? A review article. *Dig. Dis. Sci.* **54** 1847–1856

Yamashita AS, Lira FS, Lima WP, Carnevali LC, Gonçalves DC, Tavares FL and et al 2008 Influence of aerobic physical training in the motochondrial transport of long chain fatty acids in the skeletal muscle: role of the carnitine palmitoil transferase. *Rev. Bras. Med. Esporte*. **14** 150–154

Yang CS, Wang H and Sheridan ZP 2018 Studies on prevention of obesity, metabolic syndrome, diabetes, cardiovascular diseases and cancer by tea. *J. Food Drug Anal.* **26** 1–13

Yanovski SZ and Yanovski JA 2014 Drugs for the treatment of obesity–reply. *JAMA* **311** 1807

Yudkin JS, Eringa E and Stehouwer CD. 2005 "Vasocrine" signalling from perivascular fat: a mechanism linking insulin resistance to vascular disease. *Lancet* **365** 1817–1820

Zhang Y, Xu Q, Liu YH, Zhang XS, Wang J, Yu XM, Zhang RX, Xue C, Yang XY and Xue CY 2015 Medium-Chain Triglyceride Activated Brown Adipose Tissue and Induced Reduction of Fat Mass in C57BL/6J Mice Fed High-fat Diet. *Biomed. Environ. Sci.* **28** 97–104

Zhao J, Unelius L, Bengtsson T, Cannon B and Nedergaard J 1994 Coexisting beta-adrenoceptor subtypes: significance for thermogenic process in brown fat cells. *Am. J. Physiol.* **267** C969–C979

Corresponding editor: Ullas Kolthur-Seetharam