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Virgin Coconut Oil in Ketogenic Diet

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Abstract. A ketogenic diet consists of high fat, with moderate to low protein content, and very low carbohydrates, which forces the body to use fat instead of glucose to produce energy which is called ketosis. Ketogenic diets are commonly used in patients suffering from neurological disorders, and mostly epilepsy. Fat is a mixture of different triacylglycerol molecules formed by esterification of glycerol with three fatty acids. Based on the length of fatty acids in triacylglycerols, fats and oils can be classified into two groups; medium chain triglycerides composed of short and medium chain fatty acids containing 4 to 12 carbon atom, and long chain triglycerides composed of long chain fatty acids containing 14 to 22 carbon. Metabolism of medium chain triglycerides is different from that of long chain triglycerides. Classic or old ketogenic diet use long chain triglycerides as fat component may cause side effects such as dislipidemia and hence increase cardiovascular disease risk.This drawback may be reduced by replacing long chain triglycerides with medium chain triglycerides. Coconut oil belongs to medium chain triglyceride fats because it's fatty acids consist mostly of medium chain fatty acids. There are two kinds of coconut oil obtained from coconut meat namely coconut oil used for frying, and virgin coconut oil is directly consumable and more suitable in Ketogenic diets.

Key words*:* Virgin coconut oil, triglycerides, ketosis, ketogenic diet, ketone bodies

Abstrak. *Diet ketogenik terdiri dari lemak tinggi, dengan kandungan protein sedang, dan karbohidrat yang rendah, sehingga menyebabkan tubuh menggunakan lemak daripada glukosa untuk menghasilkan energi, yang disebut ketosis. Diet ketogenik biasanya digunakan pada pasien yang mengalami gangguan syaraf yang pada umumnya mengalami epilepsi. Lemak adalah campuran dari berbagai molekul triasilgliserol hasil esterifikasi gliserol dengan tiga asam lemak. Berdasarkan panjang rantai asam lemak di dalam triasilgliserol, lemak dan minyak dibagi menjadi dua golongan yakni trigliserida rantai sedang yang tersusun dari asam lemak rantai pendek dan sedang yang mengandung atom karbon 4 sampai 12, dan trigliserida rantai panjang yang tersusun dari lemak rantai panjang dengan atom karbon 14 sampai 22. Metabolisme dari trigliserida (lemak) rantai sedang berbeda dengan lemak rantai panjang. Diet ketogenik klasik menggunakan lemak rantai panjang sebagai komponen lemak yang bisa menyebabkan efek samping seperti dislipidemia sehingga meningkatkan resiko penyakit kardiovaskular. Efek samping ini dapat dikurangi dengan menggantikan lemak rantai panjang. Minyak kelapa termasuk lemak rantai sedang karena dominan mengandung asam lemak sedang. Ada dua jenis minyak kelapa dari daging buah kelapa yaitu minyak kelapa untuk menggoreng, dan minyak kelapa murni untuk langsung dikonsumsi dan lebih baik dan effektif digunakan di dalam diet ketogenik.*

Kata kunci: *Minyak kelapa murni, lemak, ketosis, diet ketogenik, senyawa keton*

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1. Introduction

Calorie restriction (CR) is a dietary intervention low in calories without malnutrition and known to delay aging process and increase maximal lifespan [1,2]. CR has beneficial effects on brain function, including reducing the incidence of age-related neurodegenerative disease, eliciting antidepressant behaviour and improving memory function in rodents. In adult human a 3-month periode of CR has been shown to improve memory function [3].

CR and during fasting, muscle and liver stores of glycogen are depleted, then fatty acids are metabolized in the liver and converted to ketone bodies called ketogenesis. The ketone bodies produced in ketogenesis namely acetoacetate (AcAc), 3-β-hydroxybutyrate (3HB) not a ketone but a hydroxy fatty acid, and acetone. The levels of ketone bodies depending on their rate of production (ketogenesis) and their utilization (ketolysis) [4]. Ketone bodies are then distributed via the circulation to active tissues, such as muscule or brain and used as energy source. AcAc is the common precursor of the two other circulating ketone bodies, acetone and 3HB. Ketogensis in order to maintain ketone bodies at levels above 2 mM can also be achieved with a specific diet called a ketogenic diet [4,5]

A ketogenic diet consists of high fat, very low carbohydrates, and with moderate to low protein content which forces the body to use fat instead of glucose to produce energy via ketosis (6). Ketosis is a metabolic state in which the body obtains energy from the metabolism of ketone bodies instead of glycolysis, where glucose is the main energy resouce. The term ketogenic comes from the ability of this type of diet to stimulate the production of ketone bodies by the liver from fatty acid beta-oxidation. Those ketone bodies are then released into the blood stream and used as a source of energy by other organs. Ketogenic diets are commonly used in patients suffering from neurological disorders, mostly epilepsy, but also being considered for Alzhemier's disease (AD), parkinson disease (PD). Ketogenic diets also have anticonvulsant effects, leading to a significant decrease in the occurence of seizures in epileptic patients. The type of fat used in the ketogenic diet may affect the ketogenesis [6,7,8].

Fat or oil is a mixture of various triglycerides (TG) or triacylglycerol (TAG) in which glycerol esterified with three identical or different fatty acids to form TAG constitute dietary fats. The structure of fats is diverse based on the types of fatty acid esterified and their positions (Sn-1,2,3) in the TAG molecules[9,10]. The influence of dietary fatty acid chain length, degree of usaturation, geometry of double bonds (*cis* and *trans*), and the positions of fatty acids in the TAG molecules determine the physical and chemical properties of the fats as well as their metabolism in the human body and hence on physiological and pharmacological activities.[11,12]. Therefore, two fats with the same fatty acids compositions can be different in chemical, physical and biochemical properties due to the fatty acids distribution in TAG molecules. These may have implications for the risk of coronary heart disease (CHD) by affecting energy balance, insulin

sensitivity, fasting and postprandial lipids. The distribution of fatty acids in TAG molecules can be changed by interesterification without affecting fatty acids composition of the fats and oils and hence affect the physical, chemical and metabolism.[9,12,13]. Therefore, the type of fat used in the ketogenic diet may result in different physiological effects depending on the fatty acid composition and distribution in the TAG molecules. Based on the fatty acid chain length in the TAG molecules, fats can be devided into two groups namely medium chain triglycerides (MCT) and long chain triglycerides (LCT) oils. Coconut oil is a dietary fat which belongs to MCT oil, hence the use it as fat component in ketogenic diet may result in different effect or more beneficial compared to the other oils.

2. Health Benefits of Coconut Oil

Fatty acid is a monocarboxylic acid containing even number of carbon atom started from 4 to 22 (C:4 – C:22). Based on the chain length, fatty acids is classified in to short (C:4 to C:6), medium (C:8 to C:12), and long (C:14 to C:22) chain fatty acids. Fatty acids are also classified as saturated and unsaturated. Unsaturated fatty acids classified into monounsaturated, di-unsaturated and poly-unsaturated fatty acids. Coconut oil and palm kernel oil (PKO) belong to saturated MCT oil because it's fatty acids consist mostly of medium chain fatty acids (MCFA) (C8:0 to C12:0) and dominated by lauric acid (C12:0).[9,13,14].

Two kinds of coconut oils can be obtained from meat of coconut tree (*Cocos nucifera*), namely coconut oil (copra oil) and virgin coconut oil (VCO). Coconut oil is derived from the dried coconut meat (copra) processed with high temperature and chemical refining. VCO is extracted from fresh milk of mature coconut meat by wet extraction at low temperatur, or by fermentation and enzymatic technique.[11,15,16]. This production method without chemical refining, bleaching and deodorizing,VCO is found to retain the highest levels of biologically active components such as tocotrienols, squalene, tocopherols and phytosterols, α-tocopherol, catechin, gallic, vanilic, and p-coumaric acid. VCO has been shown to enhance antioxidant enzymes activity and inhibit the lipid peroxidation.[11,13,17,18,19,20]. Coconut oil increased the activity of the antioxidant enzyme, so that protective against reactive oxygen species (ROS).[15,21].

Coconut oil and VCO are different from the other common oils. VCO contains the highest proportion of medium chain fatty acids, with MCFA content as high as 75.1 %. Most of other oils are usually composed of long chain fatty acids (LCFA) and hence classified as LCT. Due to the unique property of coconut oil, it has been used in health promotion and also in ailments prevention and medication.[22,23,24,25]. The quality of VCO is determined by MCFA content, especially lauric acid which is influenced by variety and oil extraction process. VCO contains higher antioxidant components such as tocopherol content and total phenolic compounds compared with coconut oil due to different extraction methods, but not fatty acid profile.[26,27,28].

VCO and coconut oil have been traditionally used to enhance the beauty and promote the growth of our tresses, refine and moisturizes our skin conditions as well as being used as ailments for minor ilness such as diarrhea and skin inflammations. VCO is also found to have wound healing activity in rats treated topically.[27,29]. In the human body, triglycerides of VCO are converted into monoglycerides and free fatty acids, which have antibacterial, antifungal, antiviral, hypoglycemic activities. Coconut oil increases absorption of magnesium and calcium compared to LCT, it prevents obesity, and hence, decreases the incidence or prevent diabetes, and induce insulin sensitivity.[11,23,30,31].

Coconut oil and VCO are unique group of oil characterized by the high content of saturated fatty acids (±90%), especially lauric acid (C12:0) as the mayor component at the level of about 50%. Coconut oil also contains about 17.19% for myristic acid (C14:0), 8.80% for palmitic acid (C16:0), 6.76% for caprylic acid and 6.37% for capric acid. Other saturated fatty acids are in the range of 0.50 % caproic acid (C6:0), 3.03% stearic acid (C18:0).The unsaturated fatty acids are relatively low in coconut oil cotaining oleic acid (C18:1) with a content of 5.25-10.54% and 0.79-2.58% for linoleic acid (C18:2). Linolenic acid (C18:3) was found only 0.01%-1.10% [17,18, 22,25,32].

MCTs have different chemical and physiological properties compared with LCTs. In the body, MCT and LCT are differently metabolized by different lipase enzymes active on sn-1 and sn-3 positions in TAG molecules [33]. In the mouth and stomach MCT is hydrolyzed by lingual and gastric lipases into 2-monoacylglycerol (2-MAG) and fatty acids mostly MCFAs which are rapidly absorbed by the enterocytes into the portal vein and then directly enter the liver to be quickly metabolized into energy, hence MCT does not increase blood TG. In addition, MCT does not require bile salts for digestion making them more rapidly absorbed.[15,34,35,36]. LCT is not digested in the mouth and stomach, enter the small intestine which should first be emulsified by bile acid and then hydrolyzed by pancreatic lipase into 2-MAG and free LCFAs, absorbed by the enterocytes and resynthesized into new TGs. The new TGs enter the lymph system as chylomicrons then transported into the heart and circulation, hence, LCT increases blood TG. MCT is absorbed faster than that of LCTs and rapidly metabolized by the liver almost completely (only when the liver's metabolic abilities are exceeded the process is taken over by peripheral tissue) with energy release, without the presence of carnitine (which necessary for the transport of LCFAs through the mitochondrial membrane). This means that MCT is an easy and quick source of energy [10,25,34,35,36,37,38].

Because of its rapid metabolism, MCT oils are beneficial to prevent and treat obesity. MCT oils are also known to be beneficial to improve health condition in general and particularly in lipid profile [39]. The other difference between MCTs and LCTs is the energy yield, for short and medium chain fatty acids is 8.3 kcal/g and for long chain fatty acids is 9.2 kcal/g. MCT oil was

found to be useful for nutritional management of patients with impaired fat digestion. The remaining non-hydrolyzed MCT can be absorbed by intestinal cells.[10,17,25,32,33].

Coconut oil contains high amount of MCFA, which has numerous health benefits. Consumption of food rich in MCFA reduces the level of body fat and heart disease risk.[11,16]. Recently reported that consumption of coconut oil by coronary artery disease subjects does not demonstrate dyslipidemias compared to the sunflower oil as unsaturated oil, and in addition, antioxidant status of subjects comsuming coconut oil is better.[39]. Coconut oil does not increase bad cholesterol low density lipoprotein (LDL) level, but increase good cholesterol high density lipoprotein (HDL) level and therefore decrease LDL/HDL ratio. Whereas soybean oil diet decrease TC and increased LDL fraction, but also decreased HDL and therefore increase LDL: HDL ratio. In fact, the TC/HDL ratio is the strongest indicator of CVD risk than TC and LDL alone. Consuming coconut oil also decreases body mass index (BMI) and waist circumference. Lauric acid in coconut oil prevents various cardiovascular diseases risks such as high blood pressure or atherosclerosis.[17,19,2,40,41,42]. Small amounts of lauric acid may be found in chylomicrons as triglycerides, it is not found in phospholipids, therefore, coconut oil does not contribute to cardiovascular disease and atherosclerosis.[19,32]. Physiological activities and metabolism of MCTs such as VCO may have beneficial effects for health.

3. Virgin Coconut Oil in Ketogenic Diet

Glucose is the main source of energy for cells and organs in our body especially brain. When muscle and liver stores of glycogen are depleted during fasting or CR, then, fatty acids are metabolized and converted to ketone bodies and used as an alternative source of energy. The ketone bodies comprise three compounds: AcAc, 3HB and acetone which can be triggered by ketogenic diet.[4].

Previous study showed that CR is anti-angiogenic, antiinflammatory, and pro-apoptotic in the experimental mouse (CT-2A astrocytoma) and the human (U87-MG malignant glioma) brain tumor.[43]. CR kills tumor cells by decreasing circulating glucose levels since glycolysis needed by tumor cells to survive, and by elevating ketone bodies, which can be used by normal brain cells as an analternative energy to glucose under the natural conditions of CR.[16,24,34,44]. By passing glycolysis, ketone bodies are also effective to treat inherited defects in glucose transporters and pyruvate dehydrogenase, which connects glycolysis with respiration. Ketone bodies are more effective to produce energy than either pyruvate or fatty acids because they have a greater hydrogen/carbon ratio (more reduced) than pyruvate. The transition from glucose to ketone bodies for brain energy metabolism is best under the natural conditions of CR.[44].

The brain is about 2% of body weight but consumes about 20-23 % of whole body weight energy requirements, mainly in the form of glucose, whereas many of our cells can use fat in the absence

of glucose to produce energy (ATP) from fats. However, the brain cannot use fats to generate energy, because fats cannot readily cross the blood-brain barrier (BBB).The water soluble ketone can cross and provide neurons with a very efficient energy source. Neurons can thrive with ketones and some believe this to be a superior energy source especially for individuals with lifestyle induced disease related to impaired glucose metabolism including cognitive deficits.[6,43,45]. It is established that both uptake and metabolism of glucose by the brain deteroirate in AD. [43].

The use of glucose for energy is vital in the brain, but this system is impaired in AD partly due to disruption of the insulin signalling mechanism.[11, 46]. Fats or fatty acids can be used as a non-carbohydrate fuel source by the formation ketone bodies in the body. The BBB is a brain endothelial structure that protects the brain from foreign substances, and more than 98% of all small-molecule drugs do not cross the BBB. Fatty acids cannot pass BBB; thus, the human brain primarily depends on glucose. It was observed that ketone bodies could have an impact on brain disorders.(6,47). Ketones bodies are used for energy production, whereas acetone is a breakdown product of AcAcA and 3HB can cross cell membranes freely, and cross the BBB through proton-linked, monocarboxylic acid transporters. Ketone bodies are absorbed by cells and converted back to acetyl-CoA, which enters the Krebs cycle and oxidized in the mitochondria to produce ATP and also precursors of acetylcholine in neurons. Alternatively, ketone bodies can be converted to acetyl-CoA in the brain to be synthesized into polyunsaturated LCFA [11,43, 45].

Epilepsy is a neurological disorder consisting of recurrent spontaneous seizures, caused by an imbalance between cerebral excitability and inhibition. This imbalance is implicated for a tendency towards uncontrolled excitability [8,47]. AD develops gradually with various types of neurodegenerative disorder, which causes chronic disease in the elders life. AD is a disease that develops over many years, such as diabetes, heart disease and other chronic conditions.[11,48].

Ketogenic diet has been found to be one of the most effective therapies for drug-resistant epilepsy and severe myoclonic epilepsy in infancy, and has been used for many decades, but the mechanism is not fully understood. Recent study has suggested that ketosis enhanced bioenergetics reserves, as well as neuron-specific effects such as modulation of ATP-sensitive potassium channels, enhanced neurotransmission, increased brain-derived neurotrophic factor expression due to glycolytic restriction and reduced neuroinflammation may be involved.[6,11,49]. Based on clinical experiences, ketogenic diets used in the 1990s as alternative in childhood epilepsy patients who were unresponsive to anticonvulsant drug therapies [7]. This therapy was originally designed to mimic the biochemical changes associated with fasting to control seizure activity.[45].

Based on the type of fat used, there are two forms of the KD namely classic or traditional ketogenic diet with LCT and ketogenic diet with MCT. The classic ketogenic diet provides 60–

80% of dietary energy through LCT or LCFAs known as LCTKD developed in 1921.[6,49]. LCTKD contains a 4:1 or 3:1 ratio (by weight) of fat to combined protein and carbohydrates to provide a diet that has an energy distribution of about 8 % protein, 2 % carbohydrate, and 90 % fat. KD can also stimulate gluconeogenesis in human to compensate for the drop in blood glucose levels. The effectiveness of ketogenic diets can be monitored by measuring serum and urine 3HB.[7]. This diet is stringent, with very low carbohydrate content, and hence it is difficult to maintain. In addtion, the fats in LCTKD may increase risk of atherosclerosis and hence may increase the risk of AD. Some studies have shown that this side effect can be reduced by replacing LCT with coconut oil in KD that are rich in MCT, which is known as the MCTKD, and more nutritionally adequate than LCTKD. MCTKD is still effective in treating epilepsy disorders and reduce cardiac risk, because MCTKD has significant effects on lowering the total cholesterol: HDL ratio compared with the LCTKD [6,11].

The MCTKD with VCO (VCOKD) contains less fat, as it contains MCFA (from coconut oil) that can provide a greater amount of ketone bodies per gram of fat and thus allows more carbohydrate and protein in the diet, making the diet more palatable than the classic or LCTKD. [11,49]. By contrast with the LCTKD, only about 45% of dietary energy is provided by MCT and allowing a larger carbohydrate component, and the more rapid metabolism of the shorter fatty acids results in more efficient generation of ketones.[6,50]. To day, there are three ketogenic diets; traditional KD, MCTKD or VCOKD and a combination of the traditional and MCT diets.[47,49]. Recently, other than epilepsy, there has been interest in the potential of the ketogenic diet in the treatment of neurological disorders including AD and Parkinson's disease. MCTKD may not only provide symptomatic benefit, but could also have beneficial disease modifying activity applicable to a broad range of brain disorders related to the death of neurons. KD might have greater efficacy in children than in adults, as younger brains have greater capacity to transport and utilize ketone bodies to produce energy.[7,11,49].

The MCTKD was introduced to surpass the severe restriction of classic KD. The main advantage of MCTs over LCTs is that the MCTs are more efficently absorbed and quickly transported to the liver by albumin. MCT produces more ketones per gram than LCT because of the way it is metabolized. MCT is quickly metabolized by liver mitochondria and, after fatty acid β-oxidation, converted into ketone bodies. On the other hand, LCTs have to be incorporated into chylomicrons and transported into blood circulation. LCTs need carnitine as a carrier to enter the mitochondria and undergo cycles of β-oxidation. Thus, compared with MCTs, LCT metabolism is a slower process and requires more energy expenditure to occur. Because of this, less fat reqiured in MCTKD diet to achieve the desired level of ketosis. Additonally, an enhancement in palatability can be achieved due to a higher content in protein and carbohydrates.[8,51,52].

The most and prominent and universal metabolic alterations found in cancer cells is an increase in the rate of glycolytic metabolism even in the presence of oxygen. Therefore, it was

hypothesized that cancer cells rely on high glucose consumption to maintain redox homeostasis due to increased one electron reductions of O_2 to form O_2^{*-} and H_2O_2 in mitochondria. This metabolism is different from normal cells and increased intertest in targetting mitochondrial oxygen metabolism to selectively sensitize cancer cells to theraphy. In this regard, dietary modification such as KDs that increase mitochondrial oxidative metabolism while decreasing glucose consumption could provide a safe, inexpensive, and effective approch to selectively induce metabolic stress in cancer cells.[7,8]. Therefore, modulation of cellular metabolism by cabohydrate depletion with KD has been hypothesized as a therapheutic strategy to selectively kill cancer cells without affecting normal cells. So that, KD has also been suggested as a co-adjuvant theraphy in cancer and neurological disorders [8]. Studies have indicated that KD reduces tumor growth in animal model of malignant glioma, colon cancer, gastric cancer, and prostat cancer. Although the mechanism by which KD demonstrate anticancer effects when combined with standard radio-chemo-theraphies has not been fully explored, preclinical results have shown the potential effectiveness and safety of using KD in combination with radio-chemotheraphy to enhance responses in mouse cancer model.[7,8].

KD may cause some side effects; lethargy, nausea, and vomitting due to intolerance of the diet, especially in children. The side effects of ketogenic diet in children with epylepsy after prolonged consumption of the diet over a period of 1-6 years. In adults, gastrointestinal discomfort is a common side effect due to the high fat content of the diet. Previous studies have also reported some deficiencies in trace minerals like selenium, copper, and zinc in the serum level of patients on ketogenic diet. The most serious side effects of ketogenic diet can be avoided or corrected by vitamin supllements, assessment of bone function, and use of oral potassium citrate to decrease the risk of kidney stones.(7). Some limitations need to be considered when initiating the MCTKD. Patients who take valproate should not be started on the MCTKD, due to report of liver failure when MCTKD and valproate are combined. KDs in adult humans should only be used under physician supervision, or in the context of a clinical trial [5,50].

4. Conclusions

The KD is a high-fat, adequate protein, low-carbohydrate diet developed to mimick the metabolic effects of fasting. In the condition of inadequate glucose supplies, ketone bodies are produced from fatty-acid metabolism and utilized as the main energy source in the brain. The underlying mechanism of KD action remains unclear; however, research in this field is ongoing major shifts in metabolism appear to underlie the KD's effects. Fats used in KD is usually LCT with very low carbohydrate content, and this diet is stringent, hence it is difficult to maintain. LCT KD may increase risk of atherosclerosis and hence may increase the risk of CVD and AD. This side effect can be reduced by replacing LCT with medium MCT such as coconut oil and VCO in KD being rich in MCFA and known as the MCTKD, which is more nutritionally adequate than LCTKD.

MCTKD is an effective but underutilized epilepsy treatment. As long as health care professionals carefully manage MCTKD, many more patients with epilepsy who are not appropriate for classic KD or LCTKD will benefit from this treatment. MCT such as VCO will not increase blood triglycerides level, has no detrimental effect on lipid profile and may help reduce visceral obesity, both of which are risk factors for CVD. VCO and coconut oil decrease CVD risk by increasing HDL and decreasing LDL/HDL ratio. Ketogenic diet based on VCO can be used in neurodegenerative disease in children and later life adults. Further human studies are necesasy to assure the positive physiological and pharmacological activities of coconut oil.

Conflict of Interest Disclosures

The authors declare no conflict of interests**.**

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