Review Paper:

The Beneficial Effects of VCO in Pharmaceutical and Nutraceutical

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Abstract

Virgin coconut oil (VCO) is considered a functional food oil because it can offer various biological activities that are advantageous for human health. Research conducted on coconut oil's nutritional and clinical aspects has revealed that it consists of 64% medium-chain fatty acid (MCFA). This component has been found to have the potential to both prevent and treat various diseases. VCO is produced from the fresh, ripe flesh of coconuts using mechanical or natural methods, with or without heat. To obtain VCO, there are four different methods: (1) thermal extraction, (2) nonthermal extraction, (3) fermentation technology and (4) enzymatic approach.

Differences in manufacturing methods affect the quality of the VCO produced. The largest content of VCO is lauric acid (C12). In pharmaceutical preparations, VCO is widely used in emulsions as an oil phase, emulsion film and hydrogel matrix in nano-emulgel. VCO is widely used as a functional food to help to overcome health problems, such as being used as supplementation for Covid-19 patients. VCO has shown various pharmacological effects such as antioxidants, anti-inflammatory, neuroprotective, anti-hyperlipidemia, anti-obesity and antibacterial activities. VCO is a functional food oil that can be a component of food items.

Keywords: Virgin coconut oils, nutraceutical, pharmacological activities.

Introduction

The coconut tree (*Cocos nucifera*) is a valuable plantation commodity due to its high economic value, as all parts of the fruit can be processed into various high-value products. The parts of the coconut that have a high economic value such as the fruit flesh, can be used to produce pure coconut oil, also known as Virgin Coconut Oil (VCO), coir, shell, coconut water and coconut pulp[41]. In Indonesia, coconut ranks second in terms of plantation crop production. In 2023, coconut production in Indonesia will reach 2890.9 thousand tons[9]. VCO, with its chemical contents, has a function as a medicine that is rich in nutritional compounds and has a high value in curing diseases. VCO is also known to function as a cosmetic. Based on the beneficial effect of VCO, the market for Indonesian VCO is still wide open for supplying the needs of health and beauty for local and overseas markets[5,34].

In 2023, the worldwide market for virgin coconut oil was valued at USD 2.54 billion. It is expected to increase from USD 2.72 billion in 2024 to USD 5.17 billion in 2032, with a compound annual growth rate (CAGR) of 8.33% during the period from 2024 to 2032. In 2023, the Asia Pacific region held a majority market share of 39.37% in the virgin coconut oil market[16].

VCO showed beneficial effects on human health. Medium-chain triglycerides (MCT) are the main fatty acids in TG which can be broken down and absorbed more easily by certain lipases in the human digestive system compared to long-chain triglycerides. VCO has activity as an antioxidant, can reduce levels of total cholesterol, triglycerides, phospholipids, low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) and can increase high-density lipoprotein (HDL)[33].

Virgin coconut oil (VCO) is a product with a long tradition used in traditional medicine for many years for its ethnopharmacological properties[26]. Virgin coconut oil (VCO) is processed with or without the addition of water, without heating or heating no more than 60°C. VCO is an almost colorless oil, with a characteristic coconut aroma, giving a slightly detectable slightly sour aroma, sweet and salty taste[29]. VCO contains 92% saturated fatty acids consisting of 48% -53% lauric acid (C12), 1.5 – 2.5% oleic acid and other fatty acids such as 8% caprylic acid (C:8) and 7% capric acid (C:10)[15].

The total content of medium-chain fatty acids (MCFAs) in VCO is between 60.5 – 63.6%. Medium-chain fatty acids are saturated or unsaturated fatty acids consisting of 6 to 12 carbon atoms, namely caproic acid (C6), caprylic acid (C8), capric acid (C10) and lauric acid (C12)[28]. This review aims to highlight the different methods of VCO extraction, to identify VCO's physicochemical characteristics and to discover VCO in pharmaceutical and nutraceutical fields.

Techniques of Extraction for VCO: There are four methods to obtain VCO: (1) thermal extraction, (2) nonthermal extraction, (3) fermentation technique and (4) enzymatic technique. Differences in manufacturing methods affect the quality of the VCO produced. In cold extraction, VCO production can be done in various ways without using heating. Mohammed et al[29] employed the chilling and thawing method. The coconut milk was centrifuged for 10

minutes and then cooled at 5 ^{0}C for 24 hours. The upper cream layer was separated and slowly thawed in a water bath at 50 ^{0}C to extract the coconut oil. Other methods for extracting VCO that do not use heat, are ultrasonication and pulsed-electric field processes[32].

Saccharomyces bacteria cerevisiae was used to ferment fresh coconut milk to produce VCO. In this method, a homogeneous mixture of coconut milk and bacteria is left for 36 hours at room temperature until a layer of oil and water is obtained. This bacteria-induced fermentation method produces a VCO yield of 72%[29]. Using enzymatic treatment, papain enzyme was added to the extracted coconut milk to produce VCO. The homogenous solution was allowed to stand at 55 ^{0}C for 3 h, the optimal temperature for papain activity. Then, the mixture was centrifuged to extract the coconut oil. Enzymatic treatment has successfully extracted coconut oil with 0.1% enzyme papain with an oil yield of 62%[29].

In contrast to other methods, the fresh-dry process involved shredding the white coconut meat and drying it in an aerated oven at 35°C for 48 hours. After that, the sample was pressed using a screw to extract the oil. The collected oil was passed through the Whatmann filter paper no. 1 to eliminate any particles or dirt. This method produced an oil yield of 54% lower than other methods (fermentation, enzymatic and cold methods)[29]. This result is in line with the research result of Negi et al[32] where thermal extraction (microwave and OH heating) provided lower yields compared to ultrasonication and pulsed-electric field methods. Similar to this method, VCO can also be obtained from copra (coconut dried at a temperature of 50 ^{0}C), then press the oil using the cold press method at a temperature of 60 ^{0}C[47].

Research conducted by Ndife et al[31] using various methods, namely fermentation, centrifuging, freezing and thawing and the use of solvents, shows that VCO obtained using solvents has the highest oil yield, while the oil yield extracted by fermentation is the lowest and those extracted by freezing and thawing are those that have the highest level of acceptability in terms of appearance, taste, aroma and consistency. The levels of fatty acids in VCO in the four extraction methods used did not show significant differences in levels. The results obtained gave the highest yield of lauric acid at levels of 46.22 – 48.40%. The micronutrient levels in VCO show that the highest levels of vitamin A, vitamin E, Vitamin D, Vitamin K and iron were obtained from the freezing and thawing methods. However, in general, the physicochemical properties and fatty acid composition of all methods provided results that still meet international oil quality standards[31].

Characteristics of Virgin Coconut Oil (VCO): The quality of the pure coconut oil produced must meet the quality requirements of SNI 7381-2022 and APCC 2009, both the physical characteristics of pure coconut oil and the water and free fatty acid content. Based on SNI 7381-2022, the water and free fatty acid content in VCO is a maximum of 0.2% whereas according to APCC 2009, the maximum water content is 0.1% and the maximum free fatty acid content is 0.2%[7,30]. In a previous study, the fatty acid composition of the VCOs from various extraction methods followed the APCC and Codex standards for coconut oil (Table 1).

A previous study that compares the physicochemical properties of VCO developed by newly improved coconut varieties and traditional coconuts produced significantly different variations in free fatty acids, with the highest levels of lauric acid obtained from the hybrid variety CRISL 2013 and the traditional variety Red Kundira[47]. Table 2 presents the physicochemical characteristics of VCO from various extraction methods. The parameters assessed include total free fatty acids, iodine value, peroxidase value, saponification value, moisture content and viscosity. The VCOs were compared to the Codex and APCC standards for VCO and the values were within the limit.

The application of VCO in pharmaceutical dosage form: VCO is widely used in various pharmaceutical dosage forms, such as in emulsions as an oil phase. VCO has been widely used as an oil carrier in various pharmaceutical formulations.

Table 1
Fatty acid composition of virgin coconut oil (VCO) and refined, bleached and deodorized (RDB) coconut oil from various extraction methods

Fatty acid (%)	Extraction methods*				RBD-VCO*	APCC Standard**	Codex Standard***
	Fermentation	Enzymatic	Chilling	Drying			
C8 (caprylic acid)	7.64	7.43	7.5	7.97	7.88	4-10	4.6-10.0
C10 (capric acid)	6.18	6.02	6.01	6.31	6.35	4-8	5.0-8.0
C12 (lauric acid)	47.95	48.68	48.24	48.83	48.74	45-56	45.1-53.2
C14 (myristic acid)	18.58	18.94	18.85	18.7	18.52	16-21	16.8-21.0
C16 (palmitic acid)	9.04	9.08	8.99	8.59	8.68	7.5-10.2	7.5-10.2
C18:0 (stearic acid)	3.16	3.13	3.1	3.27	3.09	2-4	2.0-4.0
C18:1 (oleic acid)	6.07	6.17	6.08	5.36	5.62	4.5-10	5.0-10.0
C18:2 (linoleic acid)	1.38	1.36	1.23	0.97	1.12	0.7-2.5	1.0-2.5

*[29], **[7] and ***[12].

Table 2
Physicochemical properties of virgin coconut oil extracted using different techniques

Physiochemical properties	Extraction methods								RBD-VCO	APCC***	CODEX***
	FVCO*	EVCO*	CVCO*	DVCO*	US-VCO**	PEF-VCO**	MW-VCO**	OH-VCO**			
FFA (as oleic %)	0.2	0.2	0.19	0.16	0.4	0.2	0.2	0.4	0.17	<0.5	Max 0.2
Iodine value (g of I_2/100 g of oil)	6.05	4.33	7.13	4.17	5.83	6.85	4.50	7.10	5.70	4-11	4.1-11
Peroxide value (meq. O_2 /kg)	2.59	2.34	2.19	1.467	0.029	0.029	0.049	0.029	2.18	<5	Max 3
Saponification value (mg of KOH/g of oil)	262.55	259.55	254.10	264.04	255.81	274.88	246.14	264.25	264.38	248-265	250-260
Moisture content (%)	0.15	0.15	0.14	0.12	0.17	0.16	0.15	0.193	-	0.1-0.5	-
Viscosity (cP)	51	49	50	48	32.09	33,19	32.61	32,20	48	-	-

*[29], **[32], ***[7] and ****[12].

The high content of medium-chain fatty acids and antioxidant properties in virgin coconut oil (VCO) has been proven to have health benefits. The process of making VCO, which is carried out using the cold method, causes VCO to still have various contents that are beneficial for health compared to coconut oil, which is made by heating, causing high levels of unsaponified components such as polyphenols and α-tocopherol. VCO has been used in nanoemulsion preparations at concentrations ranging from 10 to 20%[23].

The amount of oil contained in the nanoemulsion significantly influences the particle size and zeta potential[11]. VCO has been widely used as an oil phase in oil-in-water emulsion systems. The study investigated the use of a D-optimal mixture design to create a nanoemulsion of Centella asiatica extract with VCO as the oil phase, to improve its bioavailability in the brain. The optimal composition for the VCO-based nanoemulsion was found to be 80% water (w/v) and 10% VCO (w/v), resulting in a smaller particle size.

Nevertheless, the particle size increased as the percentage of water and VCO increased. This indicates that the proportions of water and VCO need to be adjusted precisely to produce a VCO-based nanoemulsion with a reduced particle size[24].

VCO as the oil phase in noni fruit extract nanoemulsion provides optimal results at a composition of 4.5% VCO, Cremophor RH 40 as a surfactant and propylene glycol as a cosurfactant showing the smallest droplet size (1.1–1.85 μm), with good stability over 5 days[21]. The various effects on the formation of extra virgin coconut oil-in-water microemulsion and their physicochemical properties can be attributed to the use of surfactants with different hydrophilic-lipophilic balance (HLB)[40]. The inhibitory effect on the growth of *Glomerella cingulata* and its antifungal activity was influenced by the use of VCO in cinnamaldehyde emulsions. VCO's contribution in decreasing the maximum growth rate of the fungus was slightly superior to that of oleic acid[36].

A promising biomaterial for use in biomedical applications is emulsion film which is created by combining polymers and VCO. Emulsion films can be created by combining chitosan and VCO or by adding VCO to the ideal ratios of corn starch, sodium alginate and gum arabic[44,50]. CHT/VCO-based emulsion films could absorb 4.5 times their weight in water and they were classified as superabsorbent materials. The amount of VCO added to the stable emulsion film preparation can alter this behavior. Because of their superabsorbent qualities, the emulsion films that have been produced here, have the necessary attributes to be employed as topical patches for wound treatment or as drug delivery vehicles where the release of the active chemical may be controlled[44].

The films that were formed of corn starch/sodium alginate/gum arabic composite and their properties were greatly impacted by the VCO content of the emulsions. Increasing the VCO concentration resulted in a more uniformly distributed droplet size but also diminished emulsion stability over an 8-hour storage period owing to floating[50].

The use of VCO in the development of new oral delivery systems contributes to the expansion of research on the utilization of fiber structures in dietary supplement and drug delivery applications. VCO successfully loaded into polyvinylpyrrolidone (PVP) using the rotary force spinning (RFS) method. PVP/VCO fiber showed an amorphous pattern and thermally stability[38].

The application of VCO in topical preparations has been widely developed including use of VCO as a base in a hydrogel matrix in nano-emulgel preparations with the

active substance palm-pressed fiber oil (PPFO). This formulation produces nano-emulgel with particle size in nanometers. It showed good stability with negative zeta potential in a 3-month accelerated stability study[27].

The role of VCO as a nutraceutical: The term nutraceutical comes from "nutrition". Nutraceutical can be defined as, "a food (or a part of food) that provides medical or health benefits, including the prevention and or treatment of a disease". Nutraceuticals include functional foods (such as vitamin-enriched products), nutritional supplements, sports drinks and medically formulated foods[39].

The VCO diet decreased the levels of triacylglycerol (TAG) while increasing the levels of high-density lipoprotein cholesterol (HDL-C) in the rats, demonstrating hypolipidemic effects. The most important results of this study include discovering potential cellular markers that could impact both nutritional metabolism and the reprogramming of immune cells by VCO and the potential for VCO to affect immune response in the spleen and to promote overall health. Additionally, more research is needed to understand the effect of VCO on the communication between intracellular signaling molecules and the role of certain types of immune cells in immunomodulation in the lymphoid organs[20]. Other studies related to the hypolipidemic effect of VCO have also been conducted.

VCO as a nutraceutical was also used as a dietary intervention for dyslipidemia in diabetes mellitus patients. This study evaluated the effect of VCO on people with DM and dyslipidemia. A total of 136 participants finished the study. The group that received VCO intervention for 30 days, demonstrated improved lipid parameters compared to the control group. This was evident in the reduction of total cholesterol, triglyceride and LDL levels, as well as an increase in HDL levels. The noted impact of VCO on lipid levels in diabetic patients indicates that VCO can effectively improve diabetic complications like cardiovascular disease, arteriosclerosis and coronary artery disease. This is attributed to its high polyphenol content, which is its active component[29,42].

In 2020, a clinical trial demonstrated that virgin coconut oil (VCO) can rapidly improve symptoms of COVID-19 and helps to normalize the concentration of C-reactive protein (CRP) in potential and suspected cases of the virus. The main goal of this current research was to confirm those findings and to assess the impact of VCO on COVID-19 patients in a 28-day randomized, single-blind trial involving 76 confirmed adults with SARS-CoV-2 RT-PCR where VCO was administered as an additional therapy for COVID-19. After 14 days of intervention, there was a substantial decline in CRP measurements, with the mean CRP level normalized to ≤ 5 mg/dL in COVID-19 patients who were given VCO mixed with meals, indicating quicker recovery. By contrast, individuals in the control group experienced a reduction in symptoms on day 23 and returned to normal CRP levels by day 25. This second research supports using VCO as a beneficial additional treatment for COVID-19 patients with mild to moderate symptoms[3,4]. VCO's high lauric acid content is widely known. Conversely, monolaurin suppresses inflammatory cytokines which can modify the immune system. A dietary supplement containing a blend of VCO (95%) and rice bran oil (5%) in the capsule is designed to boost immunity[22,37]. The antiviral and anti-inflammatory characteristics of VCO, which originate from the VCO metabolites lauric acid and monolaurin, are responsible for these advantageous outcomes.

Research has shown that lauric acid and monolaurin can disrupt the late stage of the viral replicative cycle, can break down the virus envelope in vitro and can stop viral proteins from binding, all of which can cause viruses to become inactive[4,19,22,45,46]. A study on early virgin coconut oil (VCO) supplementation's effects on the electrical activity of the adult rat brain and its lipid peroxidation was conducted by Alves et al[2]. Studies both *in vivo* and *in vitro* have demonstrated the neuroprotective benefits of VCO. The CSD propagation velocity of adult rats was lowered by VCO supplementation throughout the key stage of brain development and this impact was unaffected by either environmental enrichment (EE) in the juvenile phase or overnutrition imposed during lactation[1,2].

How does VCO function pharmacologically?

VCO has been reported to have several pharmacological effects such as antioxidants, anti-inflammatory, anti-hyperlipidemia, anti-obesity and antibacterial activities. The total phenolic content (TPC) and antioxidant activity in VCO were influenced by the extraction method used. In the chilling and thawing method, a higher TPC value was obtained, namely 68.12 mg GAE/100 mL oil compared to fermentation, enzymatic and drying methods. Meanwhile, the highest antioxidant activity was obtained from fermented VCO with an IC50 value of 205.15 mg/mL[29]. The results of the total phenolic compound showed that the traditional varieties (Red dwarf) contained higher amounts of phenolic compounds (82.69 mg GAE/kg) compared to the selected hybrid cultivars, CRISL 2013 oil extract (21.44 mg GAE/kg)[47].

The total phenol content in VCO is also influenced by the effect of drying. The wet extraction method, namely fermentation of VCO, produces higher TPC values than the dry method. This is because the drying process can cause damage to the phenolic compound components. The TPC value in this fermentation method is comparable to the IC50 value. The higher is the phenol content, the higher is the antioxidant activity[17].

The effects of VCO on neuronal and anti-inflammatory factors in the mesenteric lymph nodes (MLN) and thymus have been studied. Dietary VCO (8% and 16%) may decrease oxidative stress and inflammatory mediators

through intracellular signaling pathways while upregulating neuroprotective factors to control immunological responses[25]. Furthermore, supplementing with virgin coconut oil was able to reverse the inflammatory infiltration around the bronchial tubes, the thickening of the epithelial cells and the increased muscle thickness and contractility by reducing oxidative stress and interacting with the nitric oxide (NO) pathway. Animals with lung inflammation showed a greater contraction of the trachea in response to ovalbumin administration and also exhibited an increased contractile response to carbachol (CCh) and histamine. However, this response was prevented by the addition of coconut oil to their diet[46].

An *in vitro* study was carried out to investigate VCO's anti-inflammatory properties using ELISA kits for TNF-α, IFN-ϒ, IL-8, IL-6 and IL-5. Tumor necrosis factors (TNF-a) and Interleukins (IL) are cytokines with proinflammatory properties that cause inflammation, fever, tissue damage and cell death. An important initiator cytokine of inflammatory responses is TNF. VCO exhibited a 42.66 – 62.34% decrease in anti-inflammatory markers. VCO has anti-inflammatory properties that help to reduce inflammatory markers and to improve skin barrier function, protecting the skin[14,25].

An *in vivo* study showed that VCO was able to lower blood TG levels, performing equally in conventional treatment with simvastatin. The research was conducted using rats that were given a high-fat diet and then intervened with simvastatin, VCO and a combination of VCO-simvastatin. The specific dosage and duration of VCO therapy will effectively reduce triglyceride levels in the blood as much as simvastatin. VCO does not show any effectiveness when used in combination with simvastatin[10].

The anti-adiposity effects of VCO were studied, focusing on the liver health and biochemical parameters of obese rats. The study's findings demonstrated that VCO enhanced hormonal parameters, lowered accumulation of liver fat, hepatic cholesterol and triglyceride levels, raised the excretion of cholesterol from the feces and decreased the excretion of triglycerides from the feces. Coconut oils may have a significant role in liver homeostasis because of their polyphenols, vitamin E, phytosterols and compounds with anti-inflammatory and antioxidant activities. Since fat is mostly oxidized in the liver, MCFA's rapid oxidation is linked to decreased fat formation, which helps to explain the obese rats' low levels of fat, cholesterol and hepatic TG[13].

VCO incorporated in emulgel formulation for the treatment of acne was found to be successful in inhibiting the growth of propionibacterium acnes bacteria[18]. It was reported that lauric acid (LA) (C12), a saturated fatty acid found in VCO, has antibacterial properties. VCO can hinder the growth of *S. aureus* by targeting the bacterial cell walls and enhancing the function of the phagocytic immune cells. At a concentration of 200 µL, VCO could effectively enhance the macrophage cells' capacity to phagocytose *S. aureus*. The medium-chain fatty acids found in VCO could potentially improve the phagocytic function. The essential fatty acids found in VCO are considered to contribute to enhance the macrophage cell's ability to phagocytose[48]. VCO obtained from fermentation and cold press process was tested for its antibacterial effect against *Aggregatibacter actinomycetemcomitans* and *Porphyromonas gingivalis*, which are two common types of Gram-negative bacteria associated with periodontal diseases.

VCO derived from the cold press process showed inhibition against bacteria at concentrations of 25% and 50%. The test results at 50% concentration, VCO from the cold press process gave higher results although not significantly different from the fermentation process[8]. Saturated acids make up 92% of the content of coconut oil, of which 50% is lauric acid. A variety of microorganisms are susceptible to the antimicrobial effects of monolaurin and monoglycerides of lauric acid. Few investigations have revealed that lauric acid's antibacterial activity stems from its capacity to destroy bacterial cell membranes[6,35,43,49].

The supplementation of virgin coconut oil demonstrates potential as a functional food and to add benefits in treating chronic diseases. Using coconut oil in its different forms can help to promote a stronger and healthier future.

Conclusion

VCO is made using cold, hot extraction, fermentation and enzymatic methods. VCO production using various methods affects the physicochemical properties. VCO is widely used as a functional food. Apart from that, VCO has various pharmacological activities such as antioxidants, anti-inflammatory, neuroprotective, anti-hyperlipidemia, anti-obesity and antibacterial activities. Based on the nutritional and health benefits of coconut oil, this should be a concern for industrial utilization and development.

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