Antioxidant, Antibacterial, Antiviral and Antifungal properties of Virgin Coconut Oil (VCO)

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Abstract

Coconut can be the source for five types of food products: coconut water, coconut milk, sugar, oil, and meat. Medical uses of coconut have been known in India since ancient times. Many coconut parts have medicinal properties. It has antiseptic, anthelmintic, antitodal, diuretic, hemostat, aphrodisiac, astringent, bactericidal, depurative, pediculicide. It is used as a folk remedy for abscesses, alopecia, amenorrhea, asthma, blennorrhagia, bronchitis, constipation, cough, debility, dropsy, dysentery, bruises, burns, dysmenorrhea, earache, phthisis, pregnancy, rash, erysipelas, fever, flu, gingivitis, gonorrhoea, cachexia, calculus, colds, hematemesis, hemoptysis, jaundice, menorrhagia, nausea, scabies, scurvy, sore throat, stomachache, swelling, syphilis, toothache, tuberculosis, tumors, typhoid, venereal diseases, and wounds. It is also believed to be anti-blennorrhagia, antibronchitis, febrifugal, and anti-gingivitis. VCO has been brought up as a possible adjuvant therapy in the treatment of COVID-19, and several countries are conducting trials in this area. As highly relevant as this potential application is within the context of the current global COVID-19 pandemic, it is just as important to continue assessment of VCO for its myriad antibacterial, antiviral, antifungal, and anti-inflammatory capabilities in potential adjuvant therapies for a wide range of diseases. This paper aims to provide a comprehensive overview of these capabilities as well as clinical trials in the existing literature that have assessed VCO's many therapeutic properties.

Keywords: Coconut, Virgin Coconut Oil (VCO), Antioxidant, Antibacterial, Antiviral, Antifungal

Introduction

The coconut plant has found use in medicine, culinary and other fields since ancient times. Indian mythology explains the creation of the palm with its crown of leafy fronds to the sage Vishwamitra, to prop up his friend when he was thrown out of heaven [1,2]. Human beings seem to have no role in the spread of coconut to various places as these can float for very long periods, and then sprout when they lodge on the shore. This was dramatically demonstrated when coconuts were found growing on an island created by volcanic activity in Krakatoa in 1929-30 [3]. In India, this was considered a mythological tree that would grant all desires. The fossil found indicates that the coconut plant evolved as far as 20 million years ago. Coconut can be the source for five types of food products: coconut water, coconut milk, sugar, oil, and meat. If the Coconut fruit is unopened, its water remains sterile. As the nut matures, its water diminishes considerably, and its taste is not that good anymore. Its white part is edible and can be used fresh or dried. Sprouting seeds may be eaten just like celeries. The source of coconut oil is the copra or the kernel of the coconut fruit. Coconut can also be used in cakes, pies, and other cooked foods. It contains glycerin and is often used in making soaps, shampoos, shaving creams, hydraulic fluid, rubber, plastics, ice cream.

Medical uses of coconut have been known in India since ancient times [4,5].

Many coconut parts have medicinal properties. It has antiseptic, anthelmintic, antidotal, diuretic, hemostat, aphrodisiac, astringent, bactericidal, depurative, pediculicide. It is used as a folk remedy for abscesses, alopecia, amenorrhea, asthma, blennorrhagia, bronchitis, constipation, cough, debility, dropsy, dysentery, bruises, burns, dysmenorrhea, earache, phthisis, pregnancy, rash, erysipelas, fever, flu, gingivitis, gonorrhea, cachexia, calculus, colds, hematemesis, hemoptysis, jaundice, meningitis, nausea, scabies, scurvy, sore throat, stomachache, swelling, syphilis, toothache, tuberculosis, tumors, typhoid, venereal diseases, and wounds [6,7]. It is also believed to be anti-blennorrhagia, anti-bronchitis, febrifugal, and anti-gingivitis. Coconut flowers are edible. They are given to newlyweds as an aphrodisiac or can be mixed with curd in the diabetic patient's diet [8]. Ibn Batutta, a scholar, mentioned that people living in Maldives isles gain considerable erotic potency from fish and coconut and he has confirmed this by his own experience [9,10]. In the literature, it has been mentioned that little coconuts are used in children to treat diarrhea and mouth sores. The coconuts of the bigger size of 71-76 cm are full of refreshing, sweet water that can help to treat the inflammation of the liver, kidneys, and bladder. They can be very refreshing during hot summers [11,12].

Coconut oil is high in saturated fatty acids more than any other non-hydrogenated oil. It can have a long shelf life. Coconut oil contains lauric acid, which helps to raise both HDL and LDL cholesterol levels. If used in reasonable amounts to replacing other oils in the diet, it might have a favorable effect on lipid profiles. Still, it is not yet clear whether it will reduce the risk of cardiovascular events. Coconut water is commonly used as a beverage and as a solution for treating dehydration related to diarrhea or exercise. It is also tried for high blood pressure and to improve exercise performance [13]. Coconut byproducts are defatted, and they contain a high percentage of dietary fiber. It can be used to treat diabetes, bladder stones, and weight loss [13]. Coconut oil is found to be helpful to ease the pain during teething if rubbed on the gums of babies. In the Philippines, often coconut oil has been used as a muscle relaxant and to treat arthralgias. Jamaicans believed coconut oil to be valuable as cardio-protective and drank it as a tonic whenever sick [14].

Coconut products such as coconut milk have long been used to help treat gallstones, urinary issues, and as a remedy for burn wounds [15], and have also shown to be of help in antihypertensive and cardioprotective measures [16,17] as well as in diarrhea and gastrointestinal problems [18]. It has even been considered in terms of neuroprotective capability in Alzheimer’s disease [19]. Coconut oil has also been utilized as a skin moisturizer, to promote hair growth, and to treat various infections of the skin [18,20]. Coconut oil has been demonstrated to be safe for use as topical and ingested applications [16,21].

Virgin coconut oil (VCO) is made up of medium-chain fatty acids as compared to butter and other oils that have long-chain fatty acids, and this component is thought to contribute to its health benefits [17,18]. Also, VCO has been shown to possess a range of biological activities including antimicrobial, antioxidant, antiviral, antifungal, and anticancer properties [16,17,20].

Studies have demonstrated that VCO can alter gene expression in inflammatory responses and suppress pro-inflammatory cytokines as well as enhance protective barriers in the skin [17,20].

VCO has been brought up as a possible adjuvant therapy in the treatment of COVID-19, and several countries are conducting trials in this area [22,23] (see below for a description of one such trial in Indonesia). As highly relevant as this potential application is within the context of the current global COVID-19 pandemic, it is just as important to continue the assessment of VCO for its myriad antibacterial, antiviral, antifungal, and anti-inflammatory capabilities in potential adjuvant therapies for a wide range of diseases. This paper aims to provide a comprehensive overview of these capabilities as well as clinical trials in the existing literature that have assessed VCO’s many therapeutic properties.

Currently, there is an ongoing randomized clinical trial assessing the use of VCO in hospitalized COVID-19 patients in Indonesia [23]. Patients who were diagnosed with COVID-19 in four hospitals were separated into two groups, with one group receiving the standard therapy regimen as well as 15 mL of VCO twice a day for 14 days and the other group (the control) receiving the standard therapy regimen with 15 mL of placebo twice a day for 14 days. There were 60 patients enrolled, and all patients were monitored for a total of four weeks using PCR of nasopharyngeal or oropharyngeal swabs. The study was concluded at the end of December 2020 and results are pending.
Mechanism of Action of VCO and Discussion

Antioxidant Properties of VCO

The beneficial antioxidant effects of VCO have been studied and include effects on several antioxidant pathways in the body. The antioxidant activity of specific compounds and extracts of natural products (such as coconut oil) is typically measured through both chemical and automated assays and technologies; this includes analyzing the scavenging properties of various free radicals/reactive oxygen species as well as looking at chelation and reducing properties [24]. Reactive oxygen species and oxidative DNA damage to cells (including damage to lipids, nucleic acids, and proteins) play crucial roles in chronic diseases, including cardiovascular diseases, cancers, and neurological disorders [25]. Preventing the accumulation of these toxic compounds and inhibiting DNA damage are extremely important potentials in prevention and therapy for such diseases [25]. One significant consideration in determining antioxidant capacity is the total phenolic content, used frequently to assess natural extracts [24] (the phenolic compounds in VCO are discussed later in this section).

Studies looking at the extracted individual protein fractions from coconut products have found that the protein fractions show not only high nutritional value but also strong antioxidant properties [26,27]. Most of the fractions were able to protect cell DNA from oxidative damage, and they exhibited capabilities for superoxide radical scavenging, reducing, and ion chelating [26,27]. Several of the protein fractions, specifically prolamine, glutelin-1, and glutelin-2, showed increased ability to scavenge radicals, thought to be due to a high aromatic amino acid content, enabling these to act as hydrogen donors [26]; the aromatic amino acid content could also contribute to the higher reducing power of all these protein fractions, especially prolamine [26]. The same study showed that prolamine and globulin displayed protection against DNA damage; this was most likely due to their strong chelating ability, possibly due to high sulfur amino acid content, as well as their chelating ability of Fe2+ specifically, which is an antioxidative mechanism [26]. A study of VCO’s effects on rat brains and corresponding antioxidant activity showed that VCO increased antioxidant levels including superoxide dismutase (an enzyme that breaks down toxic oxygen species) while decreasing levels of oxidative stress [27].

Numerous studies have shown that polyphenolic compounds have antioxidant properties; the characterization of polyphenols and their properties has gained significant interest in recent years [27,29,30,41]. Polyphenols can scavenge free radicals and chelate metals, resulting in LDL-cholesterol oxidation inhibition, which can help prevent atherosclerosis and resultant heart disease [24]. Polyphenolic compounds have also been shown to prevent DNA damage by inhibiting oxidative stress in cells, and they have shown potential in preventing or treating cancers [24]. The amount of polyphenols found in coconut products appears to vary depending on the type of preparation of the coconut, such as dry, water, or oil form [26,27,29-31]. Studies conducted on the polyphenol compounds extricated from VCO have shown that VCO increases enzymes that participate in antioxidant pathways [28-31]. These polyphenols increase the activity of superoxide dismutase and glutathione reductase, enzymes that play vital roles in preventing oxidative cell damage [30,31].

There have been a very limited number of clinical trials that have looked specifically at the antioxidant properties of VCO and its applications in medicine.

A clinical trial assessed the use of VCO about anti-inflammatory markers in multiple sclerosis patients [32]. Fifty-one patients who had a previous diagnosis of multiple sclerosis were divided into two groups: one group had 60 mL of VCO (taken as 30 mL with breakfast and 30 mL with lunch) added to their Mediterranean-style diet, while the other group (the control) took a placebo with the same diet. The study took place over four months. The results showed a significant decrease in levels of interleukin 6 (IL-6), an inflammatory biomarker; however, a decrease was seen in both the intervention group and the control group. A decrease in anxiety was seen in the intervention group as well.

A study involving nine patients assessed inflammatory response and gene expression in nasal mucosa after being exposed to ozone and then given antioxidant oils, including coconut oil, in an aerosolized state [33]. Their data showed that pretreatment with the oils as compared to the control showed significantly decreased inflammatory cell counts in patients, and even showed decreases in these cells compared to baseline before ozone exposure.

According to one study done in rats, after 45 days of coconut oil (comparing to copra oil) feeding the rats, several lipid parameters and lipoprotein levels were assessed. Polyphenol fraction was isolated from the oils and its effect on in vitro LDL oxidation was assessed. It reduced triglycerides, LDL, and VLDL cholesterol levels, total cholesterol, phospholipids, and increased HDL cholesterol in serum and tissues. The Polyphenol fraction of virgin coconut oil can prevent in vitro LDL oxidation with reduced
carbonyl formation. The potential beneficiary effect of virgin coconut oil is because it can lower the lipid levels in serum and tissues and help LDL oxidation by physiological oxidants. This may be attributed to the biologically active polyphenol components present in the coconut oil [34].

Oxidative stress has been studied to be involved in the physiopathology of diabetes mellitus. The antioxidant properties of VCO might have a beneficial effect in ameliorating diabetes. According to another study, VCO has a hypoglycemic action because it can enhance insulin secretion and ameliorate oxidative stress-induced in type I (alloxan-induced diabetic) rats [35]. The antioxidative effect of VCO on oxidative stress, testosterone and gonadotropic hormones in alcohol-induced testicular injury were assessed in another study. Many studies have shown that excessive ethanol ingestion induces hypoandrogenism and hypogonadism in males with low testosterone levels [36,37]. Research in animals has demonstrated an association between both acute and chronic alcohol consumption and low testosterone levels [38,39]. This study report resulted that VCO lowered alcohol-induced oxidative stress by reducing MDA levels and improved the effect of alcohol on serum testosterone level but didn’t affect serum FSH and LH levels [40].

Another study compared the lipid profile and antioxidant enzymes in diabetic and healthy subjects that consumed two different types of oil as a cooking medium. Triacylglycerols, LDL, and VLDL cholesterol levels were high in the diabetic subjects compared to the controls. Total glutathione and glutathione peroxidase values showed a significant decrease in diabetic subjects as compared to the controls, while superoxide dismutase values showed a significant difference between coconut oil consuming groups. Though lipid profile parameters and oxidative stress were high in Type 2 diabetic subjects compared to controls, no pronounced changes for these parameters were observed between the subgroups (when coconut oil was compared to sunflower oil) [41].

No matter the existing concerns on its high saturated fatty acids and the risk of heart disease, coconut oil is recommended in neurodegenerative diseases. The lack of effective treatment options against these disorders has somehow made coconut oil a potentially sought-after option. As part of the efforts in gaining a deeper understanding of its potential neuroprotective properties, this chapter reviews both the preclinical and the clinical evidence of the beneficial effect of coconut oil against various neurogenerative [42]. Also, this other study is assessed the antioxidant and hepatoprotective effect of Virgin coconut oil supplementation against hepatotoxicity and oxidative damage via improving antioxidant defense system in rats. Their findings may have beneficial application in the management of hepatotoxicity associated with MTX cancer chemotherapy [43]. VCO has also affects on exercise-induced and chronic cold restraint stress. According to this study, the serum antioxidant SOD enzyme level was increased, and lipid peroxidation was significantly reduced in VCO-treated mice post-forced swim test. Furthermore, the oxidation and 5-HT levels, which were higher in the untreated stress control group mice, were significantly reduced in the diazepam- and VCO-treated mice [44].

**Antibacterial properties of VCO**

VCO has been shown to form holes in the walls of staphylococcus aureus [45]. However, several studies show that VCO alone has limited use as an antibacterial [46,47]. It is only when VCO is separated into its constituents as free fatty acids namely lauric acid (or its triglyceride GML), capric, and caprylic acid that it has several mechanisms by which it can fight bacteria. Hydrolyzed VCO especially using lipo-enzymes (ie. using Candida rugosa lipase (CRL) instead of using altered pH for hydrolysis) acts against gram-negative bacteria like salmonella enteritidis, Escherichia coli, and gram-positive bacteria like staphylococcus aureus [48], Bacillus subtilis [46], and bacillus cereus [49]. Staphylococcus aureus can outsmart our antibiotics by producing the exoprotein Beta-lactamase (thus acquiring Beta-lactam antibiotic resistance). Monolaurin (GML) has been shown to inhibit the transcription of TSST-1 and anti-hemolysin (effectively inhibiting virulence), and while allowing beta-lactamase to be constitutively synthesized it prevents induction of beta-lactamase synthesis (thus inhibiting antibiotic resistance) [50]. The surface of the bacterial cell membrane participates in receiving signals that turn on the transcription of virulence factors and antibiotic resistance genes. Gram-negative cell membranes are thicker as they are made of a thick layer of lipopolysaccharide and lipophilic FFAs get incorporated into it easily. Gram-positive cell membranes are a thinner fat layer, however, monolaurin being a non-ionic surfactant with a polar side as well as a hydrophobic side can damage and lyse even these cell membranes. Bacterial cells produce exoproteins using membrane-associated steps. Monolaurin affects this step (where external metabolites activate signal transduction receptors on the cell membrane which in turn switch on the exoprotein genes) by damaging the cell membrane [50]. Another mechanism of action is to just block biofilm formation from proceeding, if that is the modus operandi of the bacteria, by being a surfactant on
the vulnerable substratum like catheter/stent/prosthetic using “the adhesion force” [51,52] and preventing bacteria from laying down the initial lipid-rich biofilm. GML can also suppress the growth of Vancomycin-Resistant *E. Faecalis* if introduced as surfactant onto an agar plate treated with Vancomycin [53] by inhibiting signal transduction through GML’s interaction with the cell membrane. Cell membrane destruction by these lipids is the mechanism by which both Chlamydia and Neisseria are inactivated [54,55].

Though in several traditional medical systems, the oil, milk, and flesh of coconut (*Cocos Nucifera*) are used as a pangea, the research backing, using allopathy’s rigorous scientific method, which is required to make it as ubiquitous a treatment as it should probably be in the allopathic medical system is yet insufficient. Virgin coconut oil (VCO) is composed of medium-chain-fatty-acid: lauric (12-C) acid (48%) and smaller but significant proportions of short-chain-fatty-acids: caprylic (8-C) and capric acid (10-C) amongst others [56]. The lipolysis of VCO begins in the mouth, continues in the stomach and gets completed in the small intestine [57]. Monolaurin (GML/ glycerol monolaurate) and Monocaprin are among VCO’s metabolites. While ample studies have shown the effectiveness of these byproducts in thwarting the activity of a variety of bacteria [54], the mechanism by which these fatty-acyl compounds accomplish the feat is yet to be definitively elucidated.

Studies have shown monolaurin, (its hydrolyzed version) lauric acid and caprylic acid to be effective against several gram-positive bacteria and gram-negative bacteria [58]. Studies have been conducted using these short and medium-chain saturated fatty acids concerning the treatment of human dermal infection [5,9,60], promotion of healthy urogenital microflora, and healthy phenotype induction in obese women [61] decreasing oral plaque formation [62], minimizing bacterial growth in semi-processed refrigerated food [63] to combat mastitis in cows and dairy goats [45,64], to fight nosocomial infections [62] and to replace the antibiotic growth promoters used in poultry farming [66]. To tide over the emerging antibiotic resistance trend among bacteria, incorporating these antibacterial properties of VCO’s components into medical practice is the need of the hour.

The antibacterial activity of the FFAs was measured using:

1. Disc Diffusion method (measuring the growth inhibition radius around the antibiotic (controls like beta-lactam antibiotics and test discs with lauric acid/ GML, caprylic acid, and capric acid) saturated paper discs which were placed on the surface of the bacterial colony inoculated Petri-dishes) [49] and

2. Serial Dilution method for MIC (in this method test tubes filled with bacterial colony inoculated agar growth media are incubated at controlled temperatures with serial dilutions of antibiotic- in this case of short and medium-chain fatty acids of VCO- the first in the series being the most dilute. The minimum inhibitory concentration of fatty acid would be the test tube with the growth medium cleared from its turbidity and comparable to the control which would be treated with a clinically relevant antibiotic [45].

Staphylococcus aureus can outsmart our antibiotics by producing the exoprotein Beta-lactamase (that can destroy the beta-lactam rings of antibiotics). The nonionic surfactant Monolaurin (GML) has been shown to stop the transcription of TSST-1 and anti-hemolysin, and while allowing beta-lactamase to be constitutively synthesized it prevents induction of beta-lactamase synthesis [50]. The inability of bacteria to form virulent exoproteins is due to the destruction of receptors (in the lipoprotein cell membrane) (aka altered membrane permeability) [64] which were supposed to receive transfusable signals that would turn on exoprotein genes [50].

Like fighting fire with fire, lipids such as lauric acid and monolaurin can interfere with the formation of lipid-containing Extracellular Polymeric Substances (EPS) which is the life source of biofilms. In the early stages of biofilm formation, the biofilm is lipid-rich. There are pockets of lipid-rich bacteria-encasing biofilm that prevents antibiotics from wiping out the nosocomial bacteria colonizing prosthetic devices with biofilms (Biofilms were viewed using phase-contrast microscopy of the subject material that was suture-associated biofilm). The surgeons doing the study also measured the biofilm biomass. Since GML and Lauric acid already are effectively antibacterial against planktonic bacteria they decided to use GML (which is 10 times more effective against biofilm formation than lauric acid due to the presence of glycerol) as the (naturally occurring) surfactant that would treat the silk sutures on which they were cultivating adherent and biofilm-producing gram-positive bacteria: Staphylococcus Aureus and Enterococcus Faecalis. With a significance value of P<.05 they proved their hypothesis that surfactant can inhibit biofilm formation at 100 mcg/ml GML [51].

Capric and Caprylic acids being shortest among coconut oil’s fatty acids are least hydrophobic and hence most useful in treating milk to prevent its contamination with
Lauric acid, which approximately 6% of it is further metabolized into monoglyceride [70,71].

There are 3 proposed mechanisms of action for why coconut oil works against microbial growth: 1) Disintegration of the lipid membrane; 2) inhibit maturation of pathogens; and 3) prevents binding of pathogens to host cell membrane [70,72]. Hierholzer and Kabara [73] experimented with monolaurin alone and monolaurin with tert-butyl hydroxyanisole (BHA), methylparaben, or sorbic acid in vitro to test virucidal activity against 14 human RNA and DNA enveloped viruses in cell culture. Human enveloped viruses used, RNA viruses [Influenza virus, pneumovirus, paramyxovirus, morbillivirus (rubeola virus)], coronavirus (avian infectious bronchitis virus), and DNA viruses (Herpesvirus 1 & 6). When the 1% concentration was added to the reaction mixture, after 1 hour at 23°C, all viruses were reduced in infectivity by >99.9%. The combination of monolaurin with BHA was the most virucidal as it tested to remove all measurable infectivity of viruses. It was important to note that all compounds also disintegrated the virus envelope. Destruction of lipids and phospholipids in the viral envelope is the key factor in the virucidal activity of monolaurin [73,74].

Hornung et al. [75] conducted a study using rhabdovirus vesicular stomatitis virus (VSV) to assess whether lauric acid, a major component of coconut oil may inhibit the maturation of the virus. VSV is an enveloped, negative-stranded RNA virus encoding five functional proteins; two of which make up the viral RNA polymerase and the other three are structural proteins. The M protein that binds to cellular membranes, allows the virus to exit the host cells by interacting with the viral G protein and nucleocapsid, known as the budding of the virus and commonly seen in enveloped viruses [75]. The study showed that the infected cells treated with medium-chain lengths of monocarboxylic acid had better antiviral potential than those treated with short or longer chain lengths. The medium-chain lengths of monocarboxylic acid also enhanced levels of triacylglycerols by ninefold and stopped the release of infectious virus particles [75].

Thormar et al. [76] conducted an in vitro study to assess the microbicidal activity of monocaprin against herpes simplex virus type 2 (HSV-2) and human immunodeficiency virus type 1 (HIV-1). The virus suspension in the culture medium was mixed with the gel formulations of monocaprin and incubated at 1 and 5 minutes. The gel was also mixed with human semen to assess the effect on leukocytes. Researchers noted greater than 100,000-fold inhibition.
of HSV-2 and by greater than 10,000-fold inactivation of HIV-1 in semen at 1 minute. Thormar et al. [77] conducted another trial where they proved lauric and capric acids are capable of the destructing lipid layer of virus ten times harder than long-chain fatty acids. Tayag et al. [78] also conducted a study to assess the viral load of HIV viruses in patients using monolaurin at 2.4 g and 7.2 g doses and 50 mL of coconut oil. There were 15 patients in each group and documented virus presence at baseline, 3 months, and 6 months, respectively. In this study, researchers discovered a significant reduction in viral load of at least 3 patients from the coconut oil group and 2 patients from the 2.4 g monolaurin group.

Widhiarta [79] conducted a study with 40 HIV subject with CD4+ T lymphocyte count > 200 cell/μL. These subjects were divided into two groups: VCO (VCO supplementation 3 × 15 ml/day for 6 weeks) and non-VCO group (without VCO supplementation), both groups followed for 6 weeks. In addition to basic demographics, CD4+ T lymphocyte counts were followed for 6 weeks. At 6 weeks, the researchers discovered an increase of CD4+ T lymphocyte concentration in HIV patients of the VCO group, which is used to assess an indicator for HIV disease progression, as the higher counts mean stronger immunity. Dayrit [80] conducted an HIV-AIDS trial in the Philippines using coconut oil (45 mL daily) and monolaurin (95% purity, 800 mg daily) with 15 patients aged 22 to 38 years. These patients were followed for 6 months and showed higher CD4 and CD8 counts after 6 months, with one fatality.

SARS-CoV-2 is an enveloped virus with lipid membrane coating. As per Ramesh (2020), the mechanism of action for why lauric acid or its derivative monolaurin blocks SARS-CoV-2 entry into the host cell using S glycoprotein on the cell is not yet known. However, any disruption of the viral protein-membrane may help prevent viral infection [73]. Liu et al. [81] demonstrated the anti-inflammatory properties of monolaurin in acute respiratory syndrome (ARDS) by reducing pro-inflammatory cytokines such as IL-6. Zhang et al. [82] further contributed this effect to the disruption of viral lipid in the T-lymphocytes.

The Philippine General Hospital conducted a trial involving 80 moderates to severe COVID-19 hospitalized patients. Patients were divided into two groups: VCO and standard of care (SOC) [73]. The primary endpoint of the study is to measure time to resolution of symptoms and the secondary endpoint was to assess time to first receiving ventilation or admitted to intensive care, white blood cell count, IL-6, ferritin, CRP, immunoglobulin, CD4+ counts at baseline, at one week and two weeks, and negative test results for COVID. The study results are not published in their entirety; however, researchers have reported VCO decreased the coronavirus count by 60 to 90% for mild to moderate cases of COVID-19 [83]. As of December 26, 2020, there is only one other active clinical trial taking place in Indonesia assessing the role of VCO as a potential adjuvant therapy in COVID-19 patients [84]. This is a randomized, interventional, pilot trials aiming to recruit 60 participants who are 18 years or older with COVID-19. The trial will recruit from June 1, 2020, to December 31, 2020. The primary endpoint of the trial will assess the severity and duration of clinical symptoms at Day 14 in patients divided into VCO and placebo groups.

**Antifungal properties of VCO**

One of VCO’s component fatty acids, namely, Lauric acid can be used to inhibit or kill several plant fungi (Rhizoctonia solani, Blumeria graminis, Pythium ultimum) [85] and against the food spoiling fungus, Aspergillus niger [86]. However, the fungus that most affects humans is the opportunistic pathogen Candida albicans. *C. Albicans* is found as a commensal on the skin, in the oral and vaginal cavities, in the vascular system, and in the GIT. If robust Candida albicans colonies exist in the GIT, at-risk patients often experience the conversion of *C. Albicans* into the pathogenic form that can progress from oral thrush and candidiasis (mucocutaneous) to Candidemia (systemic) [87]. Both the unicellular and hyphal forms of *C. albicans* (increased mortality (P<.001) can cause nosocomial biofilm-associated infections. Other species of Candida like C. parapsilosis, C. glabrata, and C. tropicalis are also responsible for nosocomial infections [88]. VCO is rich in medium-chain saturated fatty acids, which are amphiphilic just like the macrolide antifungal drugs [89], is the most promising of natural antifungal treatments. While VCO fatty acids too would get sequestered inside the biofilm matrix-like their synthetic counterparts and must (probably) be aided by beta-1,3 glucanase treatment [90], our interest is in the amazing ability of coconut oil in the diet to reduce colonization by *C. Albicans* [87]. The decreased presence of commensal candida colonies, using coconut oil (MCFA) diet, will decrease the risk of pathogenic conversion of the same in immunocompromised and hospitalized patients.

**Dietary Coconut Oil for Reducing Candida Colonisation:** By observing *C. Albicans* genes found in the cecal contents of murine models fed with coconut oil (that provided a modified environment for the gut microbiota) and comparing them to the *C. Albicans* genes in the control mice (fed with 3 other diets that considered all probable confounding factors), Gunsalus et al. [87]
proved that dietary coconut oil actively inhibits *C. albicans* colonization in the gut. When long-chain fatty acid (LCFA) diet was replaced by Medium-chain fatty acid (MCFA) diet, *C. Albicans* (which can survive purely on lipids) decreased fatty acid utilization and utilized glucose (which is in short supply in Candida's normal distal gut habitat), MCFA fed mice showed cecal *C. albicans* with decreased expression of several genes. Particularly, fatty acid beta-oxidation (POT1, POX1-3) genes, carnitine acetyl-transferase (CTN1) genes, genes required to synthesize the sugar, ribose (an essential nucleic acid precursor) by inhibiting expression of glyoxylate cycle's genes (ICL1 and MLS1).

*(Glyoxylate cycle utilizes acetyl-CoA to form sugar rather than ATP). MCFA fed mice showed *C. albicans* with increased expression of glycolytic genes and decreased gluconeogenesis [87].

**Capric Acid (C-10:0) for preventing Nosocomial Fungal Infection:** Coconut oil and the probiotic *S. boulardii*, have an active molecule in common, which is Capric acid (C-10:0) [91]. Treated with capric acid, *C. albicans* decreases transcription of HWP1 by 8 times thus decreasing the encoding of wall proteins of the hypha involved in adhesion and biofilm formation. INO1 gene expression was reduced, thus decreasing the synthesis of phospholipomannan (PLM), a glycolipid on its cell surface (however these PLM molecules can induce protective antibody formation, so while virulence does decrease, the immune response also decreases [92]. Finally, CSH1 gene expression was also decreased consistently with observed inhibition of adhesion and biofilm formation when *C. albicans* is treated with capric acid [91].

**Lauric Acid (C-12:0) to support other antifungals:** While capric acid causes the most rapid and effective killing of all 3 Candida strains, Lauric acid (C-12:0) was the most active at lower concentration and lower incubation time [93]. Capric acid and Caprylic acid at low concentration has been proved to inhibit mycelial and yeast-form growth of *C. albicans* at very low concentrations and can be used to support anti-candida treatment [94].

**Caprylic acid (C-8:0) and synergistic elimination of fungus:** Caprylic acid (C-8:0) alone can't successfully eradicate *C. albicans* however in combination with other essential oil-derived compounds like Carvacrol and thymol it can eliminate all *C. albicans* pathogens. Caprylic acid disrupts fungal cell membranes (>83.1% of cells) which facilitates entry of antifungals into the cytoplasm and all 3, damage efflux pumps (>95% of cells) causing their accumulation within cells and leading to cell death [95].

**Monoglycerides to Kill Fungus:** Monoglycerides such as Monolaurin, Monomiristine, and Monocaprin have proven antifungal properties as described through multiple studies, a few of which we have brought to your attention. It is assumed that like their synthetic counterparts, these natural antifungals also utilize their amphiphilic nature to interact with the outer structures of fungi. Ergosterol is the fungal wall, interact with the acyl lipophilic part of monoglycerides through Van der Waals forces, thereafter lysing and leading to cell death. The 2 hydroxyl groups form hydrogen bonds with other cell wall components like glucans and chitins which are polar and assist cell membrane lysis [89].

Ogbulu et al. [96] conducted an in vitro comparative study of antimicrobial properties of coconut oil on Candida species in Ibadan, Nigeria. The study was done to characterize Candida species and determine the effectiveness of virgin Coconut oil as an antifungal agent on these species. Around 52 Candida species were isolated from clinical specimens in Medical Microbiology Laboratory, University College Hospital, Ibadan, Nigeria [96]. An agar-well diffusion technique was used to study the susceptibility of isolated Candida species to the virgin Coconut oil and Fluconazole. The most common Candida species which was isolated was Candida albicans, other less common were Candida glabrata, Candida tropicalis, Candida parapsilosis, Candida stellatoidea, and Candida krusei. Ogbolu et al. [96] found that of all the Candida species Candida albicans had the highest susceptibility to coconut oil, which was 100%, with a minimum inhibitory concentration (MIA) of 25% (1:4 dilution) . On the other hand, Fluconazole did show 100% susceptibility but at a MIC of 64 micrograms/mL (1:2 dilution) . In their study, *C. krusei* showed the highest resistance to Coconut oil. On whole, Coconut oil was active against Candida species at 100% concentration as compared to the Fluconazole. They concluded that Coconut oil should be used as an antifungal to treat fungal infections given the emerging drug-resistant Candida species [96].

Shino et al. [97] conducted an in vitro study to compare the antifungal activity of 0.2% Chlorhexidine, Coconut Oil, Lactobacillus (probiotic) on Candida albicans in comparison with Ketoconazole. The Candida species were isolated in children with Early Childhood Caries (ECC) . Swab samples using sterile cotton swabs were collected from tooth surfaces from children with ECC of 3 to 6 years. The swabs were streaked on Sabouraud dextrose agar (HI Media) plates, it was then incubated in a 5% CO₂ enriched
atmosphere at 37°C for 24 hours [94]. Disc Diffusion Method was used to determine the susceptibility of Candida isolates to each of the mentioned agents. The results showed the mean zone of inhibition for Chlorhexidine was 21.8 mm, whereas for Coconut oil it was 16.8 mm, for Probiotic it was 13.5 mm, and for Ketoconazole it was 22.3 mm [97]. Statistical analysis showed that the difference between the groups was not statistically significant as it had the Chi-square value of 7.42 and P-value of 0.06. Hence, Shino et al. [97] concluded that Chlorhexidine and Coconut oil have shown significant antifungal activity comparable to Ketoconazole.

Krishnamoorthy et al. [98] conducted an evaluative in-vitro study that tested the tensile strength and growth of Candida albicans on Viscogel tissue conditioner when incorporated with Coconut oil. This study compared its efficacy with other antifungal agents. About 50 samples (n=10) of Viscogel tissue conditioners were fabricated (based on ASTM standard) [3]. These were classified into 5 groups: i) 10% w/w Coconut oil, ii) 30% w/w Tea Tree Oil, iii) 5% w/w Fluconazole, iv) w/w Silver Nanoparticles, and v) Plain Tissue Conditioner [98]. These 50 samples were then compared and studied for their tensile strengths. Next, to test the antifungal activity a total of 60 samples (n=15) were fabricated and further divided into three subgroups (n=5), ie. 24-h, 3-days, and 5-day period, then these inoculated in Sabouraud Dextrose Agar plate to observe the growth of C. Albicans. Krishnamoorthy et al. [98] used One-way ANOVA and post hoc Tukey honestly significant difference test for statistical analysis. Based on the above-described study design Krishnamoorthy et al. found their results to show mean tensile strength of 20.06 for 10% w/w Coconut oil as compared to 17.81 mean tensile strength of plain tissue conditioner [98]. Moreover, they also found similar results for 10% w/w Coconut oil incorporated into Viscogel tissue conditioner which showed a significant reduction in the colonization of C. Albicans, add it also increases the tensile strength of the tissue conditioner.

**Conclusion**

This paper aims to provide a comprehensive overview of these capabilities as well as clinical trials in the existing literature that have assessed VCO’s many therapeutic properties. Further clinical trials are warranted to effectively assess the antioxidant, antibacterial, antiviral and antifungal capabilities of VCO and to provide a complete picture of the many potential applications of VCO in adjuvants and therapies.

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