A critical appraisal on the antimicrobial, oral protective, and anti-diabetic functions of coconut and its derivatives

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Received: 8 January 2022; Accepted: 30 March 2022; Published: 28 April 2022

OPEN ACCESS

REVIEW ARTICLE

Abstract

The coconut palm is aptly described as the "tree of life" because of its myriad of uses and diversified value added products. Coconut and its derivatives are considered to be an emerging functional food. It is also called a "miracle food". In recent years, there have been conflicting reports regarding the consumption of coconut oil and its health benefits. In this backdrop, our article systematically analyses the antimicrobial, oral protective, and anti-diabetic effects of coconut products in light of the recent scientific literature. Numerous scientific reports have highlighted that the coconut oil has antimicrobial properties improving oral hygiene. Although its anti-obesity and hypoglycemic effects are backed by emerging scientific literature, many questions remain unanswered. In general, consumption of coconut oil has many beneficial effects; nevertheless, long-term clinical trials are warranted. Indeed, the exploration of coconut phytochemicals, clinical trials, and epidemiological studies unleash the true therapeutic prospects of coconut and its derivatives. At this juncture, we suggest shifting our research focus from the fatty acid composition of coconut oil towards characterization of other phytochemicals such as polyphenols, phytosterols, etc., conduct of clinical trials and epidemiological studies to unleash the true potential of coconut products.

Keywords: coconut oil; fatty acids; lauric acid; phytochemicals; polyphenols

Introduction

Coconut palm (*Cocos nucifera* L.) is one of the major plantation crops grown in many parts of the world; it acts as a symbol of national and international integration (Manikantan *et al*., 2018). Each and every part of the palm is useful in one way or another. Coconut has been used as a source for health and nourishment since time immemorial. The kernel, or endosperm, is the part of the coconut fruit or nut that has economic relevance. The development of the nuts continues for 11–12 months. The inflorescence sap, tender coconuts, mature coconuts, etc., are used for culinary purposes, traditional medicinal preparations, etc. Coconut kernels contain carbohydrates

ISSN 1757-837X online, DOI 10.15586/qas.v14i2.1040

(10–20%), fat (27–35%), and protein (3–4%),with moisture content between 40 and 50% (Beegum *et al.*, 2021). Coconut oil has been recognized for its healing properties by Ayurvedic and other traditional medicines for over 4,000 years. The oil is acknowledged for its antimicrobial properties, anti-inflammatory properties, antioxidant properties, anti-cancerous properties, etc. Many oleo chemicals have been extracted from coconut oil, which have wide applications in various sectors. The coconut endosperm is processed either wet (VCO: virgin coconut oil) or dry (copra oil/coconut oil) for the extraction of oil. It is dried to less than 6% moisture content to get copra, which is then ground, steamed, and expelled by a wedge press, screw press, or hydraulic press to extract coconut oil (Manikantan *et al*., 2018). On the other hand, VCO is processed from the fresh kernel by mechanical or natural means, through the application of physical methods such as cold pressing, expeller-pressing, centrifugal force, heating,or by natural means without undergoing chemical refining (Beegum *et al*., 2019). It is widely popular for its multipurpose applications such as cooking oil, cosmetic uses (Pandiselvam *et al*., 2019), and functional and nutraceutical applications (Ramesh *et al*., 2020). If coconut oil is believed to be one of nature's healthiest cooking oils, VCO is considered as the purest form of coconut oil. The oils derived from coconut have great potential as an anti-microbial agent and are good for oral hygiene, while other products, including coconut water, coconut inflorescence sap, coconut shell, husk, etc., have anti-diabetic effects. Coconut oil has been shown in studies to be effective in treating novel SARS-Coronavirus-2 (Angeles-Agdeppa *et al*., 2021; Ramesh *et al*., 2021a). Even though it is very difficult to differentiate the VCO from coconut oil, studies have shown that VCO has a lower diglyceride (1.55 w/w% than RCO at 4.1 w/w%) and high vitamin E, phenolics, and antioxidant activity (Ramesh *et al*., 2020). Coconut oil is rich in saturated fatty acids (SFAs), especially medium chain fatty acids (MCFAs). The MCFAs consist of SFAs with 6–12 carbon chains (Dayrit, 2014). The major MCFA of oils from coconut are lauric acid (47.0–50.0%), caprylic acid (8.00–9.00%), capric acid (5.00–7.0%), and caproic acid (0.80–0.95%) (Nasir *et al*., 2018). In addition, MCFA gets absorbed and rapidly converted to energy (Los-Rycharska *et al*., 2016) as it is easily transported across the mitochondrial membrane without any carrier molecule and hence is rapidly metabolized in the liver (Wang *et al*., 2018). MCFAs are generally absorbed through portal veins, whereas long chain fatty acids (LCFAs) enter the lymphatic system (Dayrit, 2014). Due to its high content of SFAs, it is more resistant to oxidation and polymerization than unsaturated oils such as sunflower oil and olive oil. In addition, studies have shown the similarities between the MCFA of coconut oil and that of human breast milk (Joshi *et al*., 2020). α-tocopherol, which is the most biologically active form of vitamin E, is high in coconut oil (40–44% of total tocopherol content) than in palm oil (Mansor *et al*., 2012). Maonolaurin, a derivative of lauric acid, is mainly responsible for the functional and therapeutic effects of coconut. Furthermore, VCO is widely preferred owing to its phenolic and antioxidant potential. Due to all these functional compounds, oils derived from coconut have been proven to be antioxidants (Illam *et al*., 2017), anti-inflammatory (Vysakh *et al*., 2014), immunomodulatory (Verma *et al*., 2019), anti-carcinogenic (Lappano *et al*., 2017), anti-diabetic (Rohman*et al*., 2019), anti-hyperlipidemic (Srivastava*et al*., 2013), antimicrobial (Joshi *et al*., 2020), oral protective (Peedikayil *et al*., 2015), neuroprotective (Ramesh *et al*., 2021a), cardioprotective (Shetty *et al*., 2021), and anti-ulcerogenic (Meng *et al*., 2019). In this context, this comprehensive review attempts to present the therapeutic effects of coconut in terms of its role as an anti-microbial agent, oral protective function, and as a source for anti-diabetic agent based on available and recent scientific evidence and plausible mechanisms of action. Based on the review, a concise summary has also been given under each section.

Coconut as an Antimicrobial Agent

Antibacterial effect

The lauric acid present in coconut kernel and the extracted oil is proven to have antimicrobial effects. The human body metabolizes lauric acid, converting it to monolaurin, a monoglyceride (Ramesh *et al*., 2021a). Monolaurin is found to be an active antimicrobial agent. Even though the exact mechanisms by which coconut oil and its active bio-ingredients inactivate the microbes remain unknown, two model theories have been put forth to elucidate the inactivation mechanisms: (i) by membrane disintegration and (ii) by preventing the maturation of pathogens (Figures 1A–C). Lauric acid mimics the structure of the peptidoglycan present in the bacterial cell wall. When VCO comes into contact with the bacterial cell, the lauric acid present in the oil covers the whole surface area of the cell, slowly penetrating inside. This process alters the fluidity of the cell membrane, leading to impaired permeability and eventually rupturing the cell wall, affecting the cell metabolism and causing cell death. This feature was clearly visible under a scanning electron microscope (SEM) when *Staphylococcus aureus* strains were treated with 0.1% lauric acid (Widianingrum *et al*., 2019). Similar results were also observed by Shilling *et al*. (2013) when VCO and its MCFAs (lauric acid, capric, and caprylic acids) were screened for antimicrobial activity against *Clostridium difficile.* The transmission electron microscopic (TEM) image showed 100% alteration in the ultrastructure of the cell, as evidenced by a disorganized cytoplasm and ruptured lipid layers. Anzaku *et al*. (2017) extracted lauric acid from coconut

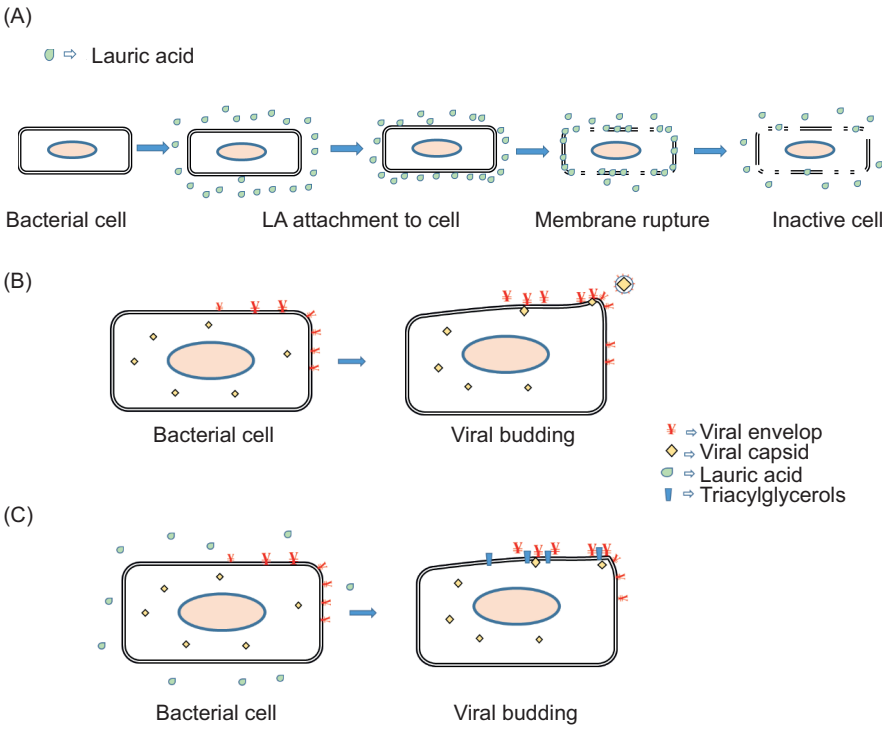

Figure 1. Anti-bacterial inactivation by lauric acid (A), Viral inhibition by lauric acid: viral budding in the absence (B) and in the presence of lauric acid (C).

oil by the freezing method and evaluated its antibacterial properties against clinical isolates of both Gram-positive and negative bacteria such as *S. aureus, Streptococcus pneumonia, Mycobacterium tuberculosis*, *E. coli,* and *Salmonella* spp. by the Bauer–Kirby disc diffusion assay. The test showed that lauric acid has high antimicrobial activity against the Gram-positive strains of *S. aureus* and *S. pneumonia*, both giving an inhibition zone of 1 mm even at 1:100,000 dilutions. At higher dilutions, lauric acid was effective against Gram-negative species only at higher dilutions; at a 1:10 dilution, the zone of inhibition for *E. coli*, *Salmonella* spp., and *M. tuberculosis* was 8 mm, whereas *S. aureus* and *S. pneumoniae* had a 15 mm inhibition zone. *E. coli* and *Salmonella* spp. showed resistance to lauric acid above 1:10,000 dilutions. Adding to that, a study showed that VCO could successfully inhibit the growth of *S. aureus* at concentrations as low as 200 µL (Widianingrum *et al*., 2019). SEM clearly indicated that the *S. aureus* inactivation was mainly due to cell wall damage followed by leakage of cytoplasmic fluid. Lauric acid was also effective against clinical isolates of *Lactobacillus* spp. (Abbas *et al*., 2017). The free fatty acids (FFA) derived by the hydrolysis of MCFAs of VCO were also studied for their antimicrobial properties by Mena *et al*. (2020). The addition of 2% of FFA to the culture media successfully inactivated *E. coli* and *S. aureus.* Nonetheless, incorporation of VCO showed no inhibitory effect on *C. difficile,* but 1.2% of lipolyzed VCO inhibited 99.9% of its growth. Shilling and colleagues (2013) and Oyi *et al*. (2016) formulated a coconut oil–based cream and studied its inactivation efficacy on a skin model. The standardized cream formula successfully inhibited the growth of *Pseudomonas aeruginosa*, *E. coli*, *P. vulgaris* (clinical isolate), and *B. subtilis* on the skin surface.

Apart from coconut oil, the coconut kernel, or endosperm, has also exhibited antibacterial effects. Dabesor *et al*. (2017) reported the effectiveness of ethanolic and aqueous extracts of coconut kernel against *Bacillus cereus*, *Klebsiella pneumonia*, *S. aureus*, and *E. coli*. Specifically, the ethanolic extract of coconut kernel had high antibacterial activity against *Bacillus cereus*, *Klebsiella pneumonia*, and *S. aureus* compared to the aqueous extract. The aqueous extracts showed higher inhibition activity against *E. coli*. The differences in antibacterial properties of various extracts were caused by differences in antibacterial agents, such as alkaloids, oxalate tannins, phytate, and glycosides, present in the final extract. Extracts from other parts of the coconut, such as coconut shell, coconut husk, and coconut roots, have also shown significant antibacterial activities (Esquenazi *et al*., 2002; Prakash *et al*., 2018; Uy *et al*., 2019). Aqueous leaf extract of coconut was utilized to mediate a silver nanoparticle synthesis (Uddin *et al*., 2020). The nanoparticles thus produced showed remarkable antibacterial properties against *S. typhimurium*, *C. freundii*, *E. coli*, and *P. aeruginosa*. A comparatively low inhibition of Gram-positive bacterial strains of *S. aureus* and *B. subtilis* was

also observed and was attributed to the thick and rigid peptidoglycan layer on its cell wall, which prevents the penetration of nano-particles. Tables 1 and 2 show a consolidated report of the antibacterial and antifungal effects of the coconut and its derivatives.

Antiviral effect

Another widely accepted theory on microbial inactivation,which is applicable to viruses,is that the coconut oil prevents the maturation of pathogens and precludes the pathogens' binding to the host cell. Lauric acid treatment can increase the production of triacylglycerols in the host cell, which in turn penetrates the plasma membrane and alters its membrane fluidity. This alteration in membrane lipid composition severely affects the reproduction of those viruses which are dependent on the host plasma membrane for the development of their envelopes (Hornung *et al*., 1994). Lauric acid is converted to monolaurin inside the human body, which is responsible for disrupting the phospholipid layers in the membranes of the enveloped viruses. It has an effect on the virus assembly and maturation phases of the infection cycle even though the viral RNA and protein synthesis remain unimpeded (Hornung *et al*., 1994; Ramesh *et al*., 2021a). Lauric acid inhibited the production of vesicular stomatitis virus by several orders of magnitude. Bartolotta *et al*. (2000) also reported similar results when arenavirus was inhibited by lauric acid. Lauric acid inhibits the binding of the viral glycoproteins and helps in further inhibition of growth. The anti-viral activity of coconut oil and its derivatives against different RNA and DNA viruses was also studied (Table 3). Hornung *et al*. (1994)

Table 1. Antibacterial activities of coconut.

Compound	Target organism	Features	Reference
Coconut kernel extract	*B. cereus*, *K. pneumonia*, *S. aureus*, and *E. coli*	The ethanoic extract of coconut kernel had higher inhibition of *B. cereus*, *K. pneumonia*, *S. aureus* where aqueous extract was more effective against *E. coli*.	Dabesor *et al*. (2017)
MCFA	*S. mutans*	The efficacy against *S. mutans* biofilm by 80% VCO mousse was comparable with positive control	Firdaus *et al*. (2019)
Lauric acid	*S. aureus* and *E. coli*	Lauric acid was ineffective against Gram negative *E. coli.*	Ezigbo *et al*. (2017)
Lauric acid	*S. pneumonia, M. tuberculosis*, *E. coli*, *S. aureus*, and *Salmonella* spp.	Lauric acid was effective in inhibiting both Gram-negative and Gram-positive bacteria at high concentrations.	Anzaku *et al*. (2017)
VCO/Lauric acid	*S. aureus*	VCO inhibited the bacterial growth by cell wall disruption	Widianingrum *et al*. (2019)
Lauric acid	*S. aureus*, *Streptococcus* spp., and *Lactobacillus* spp.	Lauric acid showed excellent antibacterial property whereas VCO showed resistance	Abbas *et al*. (2017)
Coconut oil	*Pseudomonas aeruginosa*, *E. coli*, *P. vulgaris* (clinical isolate) and *B. subtilis*	The standardized coconut oil–based cream formulation effectively inhibited the growth of all tested bacterial strains	Oyi *et al*. (2016)
Coconut oil	*S. mutans* and *Lactobacilli*	Coconut oil showed 89.3% reduction on *S. mutans* but showed no effect on *Lactobacillus*	El-Sayed *et al*. (2017)
VCO, lauric acid, capric acid, and caprylic acid	*C. difficle*	Lauric acid: 1000μM, Capric acid: 2000 μM, and Caprylic acid: 10,000 μM showed over 99.9% reduction	Shilling *et al*. (2013)
VCO, Lauric acid, and monolaurin	*S. aureus*	VCO showed nil inhibition against *S. aureus*, whereas MIC for LA and monolaurium were 1.6 and 0.1 mg/mL, respectively	Tangwatcharin and Khopaibool (2012)
Coconut leaf	*S. typhimurium, C. freundii, E. coli, P. aeruginosa*, *S. aureus*, and *B. subtilis*	The leaf extract was used to prepare silver nano particles which were efficient in inhibiting bacterial growth	Uddin *et al*. (2020)
FFA from VCO	*E. coli* and *S. aureus*	A zone inhibition diameter of 12.2 and 14.2 mm were observed for *E. coli* and *S. aureus*, respectively, with 2% FFA addition	Mena *et al*. (2020)
Coconut shell extract	*E. coli, S. enterica, S. flexneri, S. aureus*, and *S. pyogenes*	The inactivation efficiency varied with respect to the extraction solvent used	Prakash *et al*. (2018)
Coconut root extract	*K. pneumoniae, B. subtilis*, and *S. aureus*	The sensitivity was in the order of *K. pneumoniae* and *B. subtilis* > *S. aureus*	Uy *et al*. (2019)
Coconut milk kefir	*S. typhi, S. aureus, and E. Coli*	Anti-microbial activity was *S. typhi* < *S. aureus* < *E. Coli*	Lakshmi *et al*. (2017)

Table 2. Anti-fungal activity of coconut.

Compound	Targeted organism	Observations	Reference
Lauric acid	*C. albicans* and *A. flavus*	Addition of 1.2g and 4g of lauric acid successfully inactivated the fungal strain	Ezigbo *et al*. (2017)
Coconut oil	*C. albicans* and *A. niger*	*C. albicans* was found to be more resistant to coconut-based cream than *A. niger*	Oyi *et al*. (2016)
Coconut oil	*C. albicans*	87.5% reduction observed after 2 h treatment with coconut oil	El-Sayed *et al*. (2017)
Coconut root extract	*C. albicans* and *A. niger*	The extract significantly reduced the growth of *C. albicans* and but was ineffective against *A. niger*	Uy *et al*. (2019)
Coconut milk kefir	*A. niger* and *S. cerevisiae*	*A. niger* was more susceptible *to* coconut milk kefir than *S. cerevisiae*	Lakshmi *et al*. (2017)
Tender coconut water extract	*C. albicans*	1000 µg/mL of tender coconut water extract effectively inhibited the growth of *C. albicans*	Cholan *et al*. (2017)

Table 3. Anti-viral activity of coconut.

Compound	Targeted organism	Observations	Reference
Lauric acid	VSV, HSV-l, SV40, and retro virus MoMuLV	Lauric acid was effective against VSV and MoMuLV viruses	Hornung *et al*. (1994)
Husk fiber extract	HSV-1-ACVr	Greater than 99.9% of inhibition was observed with maximum non-cytotoxic concentration (MNTC) for both cell lines	Esquenazi *et al*. (2002)
Coconut oil	HIV	A reduced viral load was observed in more than 50% of test subjects	Dayrit (2000)

studied the inhibitory effect of lauric acid on vesicular stomatitis viruses, Herpes Simplex Virus (HSV-l), Simian Virus 40 (SV40), and the retrovirus MoMuLV. Lauric acid inhibited the VSV in a dose-dependent manner and the inhibition was reversible, indicating that the antiviral properties were lost when lauric acid was removed from the medium. The addition of 40 g/mL of lauric acid successfully reduced the VSV viral progeny by 98%. Other SCFAs (C6, C8) and LCFAs (C16, C18) were also capable of inactivating VSV. MoMuLV, which buds from the host plasma membrane, was also inhibited to the magnitude of 2. However, HSV-l and SV40 were not affected by lauric acid since HSV-l buds in the nuclear membrane and SV40, even though it buds in the plasma membrane, is a non-enveloped virus. These results clearly indicate that the inactivation of viral particles occurs mainly because the viral particle maturation is impeded in the presence of lauric acid due to the altered lipid composition of the host plasma membrane. Replication of Junin virus (JUNV IV4454), of *Arenaviridae* causing Argentine hemorrhagic fever, was also inhibited by lauric acid. Inactivation of various JUNV strains (IV4454, XJ, XJC13, and C167) in different host cells such as CV1 (monkey kidney line cells) and PH (human foreskin cell) lines was successful. Lauric acid did not interfere with the infectivity of the virus, nor did it induce a state of cellular defense against the virus infection. Lauric acid induced the production of triacylglycerol in the host cell, which modified the glycoproteins in the plasma membrane. This reduced the viral glycoprotein insertion at the cell surface and thus virus multiplication. Coconut oil has also shown antiviral effects against the HIV, as consumption of the oil showed a reduced viral load for more than 50% of test subjects infected by the virus (Dayrit, 2000). Also, catechin-rich crude extract from coconut husk fiber exhibited inhibitory action against acyclovir-resistant Herpes simplex virus type 1 (HSV-1-ACVr) (Esquenazi *et al*., 2002). The percentage of viral inhibition was always greater than 99.9% when used with the maximum nontoxic concentration of host cells: human larynx carcinoma cell line (HEp-2) and kidney epithelial cells (Vero). In a project entitled,"Virgin Coconut Oil and Omega-3a Adjunctive Therapy for Hospitalized Patients with COVID-19," the Philippine Council for Health Research and Development (PCHRD) and the Department of Science and Technology (DOST) have explored the possibility of administering VCO to treat SARS-CoV-2. Thus, VCO-based adjunct therapy to treat or reduce the impact of COVID-19 was proposed based on its positive effect of normalizing the C-Reactive protein level in COVID-19-infected patients (Angeles-Agdeppa *et al*., 2021). A concise review presents the antiviral properties of coconut oil with regard to SARS-CoV-2 with proven mechanisms of action (Ramesh *et al*., 2021b).

Antifungal effect

Coconut and its products have also been proven to possess antifungal properties. The antifungal activity of a coconut oil–based cream was tested in skin inoculation tests on *Aspergillus niger* (clinical isolates) and

Candida albicans (Oyi *et al*., 2016). When the microbes were directly inoculated in the cream, they inhibited the growth of *C. albicans*,and no visible growth was found until 28 days. The clinical isolates of *A. niger* were more resistant to the cream and showed visible growth after the seventh day of exposure. The inhibitory action of the cream was increased when cetrimide was used to preserve the cream, as it inhibited the microbial growth for up to 28 days. Application of this cream preserved with cetrimide on skin successfully inactivated both the fungal strains, and no viable cells were observed. Coconut oil also showed a high inhibitory effect against *C. albicans*. *C. albicans* exposed for 2 h to coconut oil exhibited 87.5% reduction in the total colony forming unit (CFU) count (El-Sayed *et al*., 2017). Lauric acid isolated from coconut oil was highly effective against fungal strains of *A. flavus* and *C. albicans*, and the addition of 1.2 g and 4 g of lauric acid in the culture dish completely inactivated these microorganisms (Ezigbo and Mbaegbu, 2017).

Numerous research and clinical studies have been undertaken on the antimicrobial effects of coconut oil and its derivatives. It has been proven that coconut oil has a high inhibitory effect against many bacteria, fungi, and viruses owing to its high lauric acid content. In addition to coconut oil and VCO, the coconut kernel has been reported to have antibacterial activity due to the lauric acid content.

Coconut Oil for Oral Hygiene

The human oral cavity harbors more than 700 diverse microorganisms or microbiota, including bacteria, fungi, and viruses (Shanbhag, 2017; Xiao *et al*., 2020). The most common oral diseases are periodontal/gum/gingiva (gingivitis and periodontitis) and tooth decay from dental caries (Gbinigie *et al*., 2016; Li *et al*., 2000). Oil pulling has been a folklore practice for oral hygiene since time immemorial. It is nothing but acquiring systemic benefits by swishing about a table spoon of oil in the oral cavity on an empty stomach for a period of 15–20 min before spitting it out (Gbinigie *et al*., 2016; Shanbhag, 2017). Oil pulling helps to remove the plaque-building bacteria that cause diseases such as bad breath, dental caries, periodontitis, and gingivitis, as it removes the tartar coating on the teeth and gums (gingiva). It prevents bacterial co-aggregation and plaque formation (Peedikayil *et al*., 2015). Oils from coconut and sesame are mostly preferred for oil pulling (Sezgina *et al*., 2019) owing to their varied mechanisms of action (Figure 2). A general view is that oil acts like a cleanser while swishing around the teeth and gums, pulling out bacteria and other debris (Mythri, 2017). Saponification of oil and the formation of a soap-like substance with saliva, which has a neutral to alkaline pH, could explain the antimicrobial action. A soapy layer formed as a result of the emulsification of

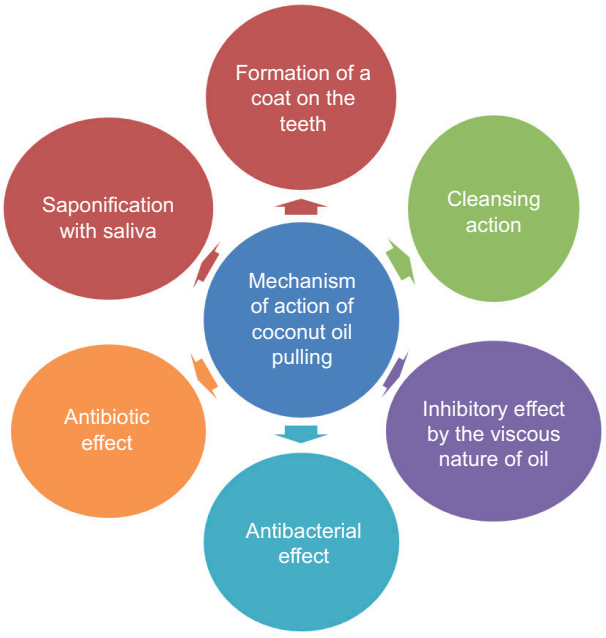

Figure 2. Multiple mechanisms of action of coconut oil in overall oral health.

oil in the mouth hinders the adhesion of bacteria/plaque on the tooth surface and thereby removes worn out squamous cells and enhances oral hygiene (Asokan *et al*., 2011; Hebbar *et al*., 2010; Naseem *et al*., 2017). Besides, the viscosity of coconut oil inhibits plaque and adhesion of bacteria (Asokan *et al*., 2011) and is an alternate mechanism attributed to the antibiotic effect of coconut oil (Asokan *et al*., 2011; Naseem *et al*., 2017). Also, monolauric and monocapric acids in coconut oil penetrate cell membranes and kill pathogens (Saher *et al*., 2018). Due to its antimicrobial property, coconut oil has been found to be effective against a wide range of microorganisms. The antimicrobial property of coconut oil was first recorded during 1979, which was mainly attributed to its lauric acid content. Lauric acid has antimicrobial and anti-inflammatory activity. Clinical studies on the effects of oil pulling using coconut oil are furnished in Table 4.

Dental caries, or tooth decay, is another common disease and a major tooth loss factor. It is caused by lengthened demineralization, mainly calcium of the tooth surface due to dissolution by acids formed by the action of the plaque bacteria, especially by Streptococcus *mutans* and *Streptococcus sanguis.* In addition, 530 million children have dental caries in the world (WHO, 2020). Rahamat *et al*. (2019) evaluated the potential of coconut products, namely, coconut oil, coconut milk, VCO, and coconut water, in the remineralization of the enamel subsurface. VCO had the highest percentage of calcium, followed by milk and water. Nevertheless, following the 14 days of remineralization treatment, all the enamel of the different

Table 4. Coconut oil and oral health.

Sl.No.	Study model	Treatment	Inferences	Reference(s)
1	Coconut oil pulling/oil swishing on plaque formation and plaque-induced gingivitis	Oil pulling as an oral hygiene routine for 30 days in adolescents	Reduction in plaque formation and gingivitis due to high saponification value, anti-inflammatory and emollient effects, respectively	Peedikayil *et al*. (2015)
2.	Oil pulling against oral microorganisms in biofilm models	Oil pulling with different vegetable oils on biofilm models formed by *Streptococcus mutans*, *Lactobacillus casei*, and *Candida albicans* on salivary-coated microtiter plates	Coconut oil showed antimicrobial activity against *S. mutans and C. Albicans*	Thaweboon *et al*. (2011)
3	Coconut oil pulling on plaque-induced gingivitis	Coconut oil pulling treatment against plaque-induced gingivitis for 30 days in patients agedabove 70 years	Coconut oil pulling when used as an adjunctive oral hygiene is effectively decreasing plaque formation and subsequent plaque-induced gingivitis	Chalke *et al*. (2017)
4	Coconut oil pulling against *Streptococcus mutans*	Coconut oil pulling treatment against *Streptococus mutans* for a day	45% reduction in *S. Mutans* population *after* oil pulling with coconut oil	Pavithran *et al*. (2017)
5	Comparison of the effect of oil pulling using coconut oil and sesame oil against plaque-induced gingivitis	Oil pulling with coconut oil, sesame oil, and normal tooth brushing as a measure against plaque-induced gingivitis	Coconut oil effectively reduced the severity of gingivitis than sesame oil	Kaliamoorthy *et al*. (2018)
6	Coconut oil pulling on *Streptococcus mutans* count in saliva in comparison with chlorhexidine mouthwash	Analysis of saliva samples rinsed with coconut oil pulling, chlorhexidine, and distilled water for 2 weeks	Coconut oil showed similar effect to that of Chlorhexidine treatment suggesting the effectiveness of coconut oil pulling therapy as a preventive measure to maintain oral hygiene	Kaushik *et al*. (2016)
7	Coconut oil pulling on supragingival plaque growth	Coconut oil pulling therapy compared with chlorhexidine gluconate in a 4-day plaque regrowth model	Plaque regrowth inhibitory activity of coconut oil pulling therapy revealed oil pulling as a promising alternative to chlorhexidine gluconate rinse causing less staining	Sezgina *et al*. (2019)
8	Oil pulling with virgin coconut oil and palm oil on gingival health and plaque microorganisms	Comparison of oil pulling with virgin coconut oil and palm oil as an adjunct to routine oral hygiene care for 28 days	Both the oils showed similar effects on gingival health and plaque microorganisms	Srithanyarat *et al*. (2018)
9	Virgin coconut oil mouthwash on plaque index	Effect of VCO mouthwash against plaque causing bacteria for 4 days	VCO mouth wash showed significant reduction of plaque index	Saputra *et al*. (2017)
10	Coconut oil against plaque-induced gingivitis	Coconut oil pulling as an adjunct to the oral hygiene procedure for 6 weeks	Coconut oil pulling as an adjuvant to oral hygiene imparted promising oral health effect by reducing plaque-induced gingivitis	Menaka *et al*. (2020)
11	Coconut oil for people with poor hygiene	Effect of oil pulling with coconut oil	Promising effect of coconut oil	Reddy *et al*. (2021)

treatment groups showed an increase in total calcium content. Moreover, coconut oil had a significant influence on the color of teeth in comparison to olive oil or lemon juice (Saravanan *et al*., 2018). The decay in tooth treated with coconut oil has improved the appearance. Hegde *et al*. (2019) documented the radioprotective-action of VCO and also the tissue properties of enamel. Interestingly, topical applications of VCO during radiation treatment have preserved the tissue integrity of teeth.

Research studies on coconut oil and oral hygiene suggest that the former has oral protective effects with various mechanisms of action. Oil pulling with coconut oil is highly effective for oral hygiene. Besides, coconut oil and its derivatives are effective for the treatment of tooth decay, improvement of tooth color in comparison to olive oil or lemon juice. Moreover, the radioprotective action of VCO has been shown to improve the tissue integrity of teeth after being exposed to radiation. Many clinical studies have been reported along similar lines. Even the pharmaceutical sprays for mouth, nose, and throat using coconut oil attained popularity during the COVID-19 pandemic. It is safely concluded that coconut oil and its derivatives serve as an important means for oral hygiene.

Antidiabetic Effects of Coconut

As diabetes is a global health disorder, large-scale investigations are being carried out to develop appropriate drugs that cause hypoglycemia (Ma and Shi, 2021; Zhang *et al*., 2021). In this context, plant-based antidiabetic products are gaining popularity for various reasons, such as ease of availability, lower costs, and fewer side effects. The various products of coconut, including kernel, coconut oil, coconut water, inflorescence, husk, etc., are utilized for culinary purposes and are also used as traditional medicine for treating several ailments. Owing to its multifaceted properties, the coconut palm is well accepted in Indian medicine and culture. Coconut oil, coconut inflorescence sap, coconut water, coconut kernel, etc., are being used against diabetes-related ailments.

Coconut oil

VCO extracted using fermentation methods (F-VCO) could reduce the blood glucose level in alloxan-induced diabetic rats (Maidin and Ahmad, 2015). The role of antioxidants in improving insulin response and reducing insulin resistance is already recognized (Aisuodionoe *et al*., 2018; Djurasevic *et al*., 2019). Narayankutty *et al.* (2016) found that F-VCO prevents the development of insulin resistance in rats fed with a high fructose diet and provides protection against renal dysfunction in diabetic rats. Phenolic compounds contribute to F-VCO's anti-diabetic activity and render protective functions against renal dysfunction by inhibiting ROS, which causes the death of beta cells (Ekici *et al*., 2014; Tang *et al*., 2020). Similar effects were reported for the cold extracted VCO as it enhances insulin secretion, fights against the induced oxidative stress, and bestows hypoglycemic action in diabetic rats (El-Shemy, 2018; Iranloye *et al*., 2013; Rohman *et al*., 2019). VCO extracted using the hot process has higher polyphenols and antioxidant properties, which in turn have high hypoglycemic and insulinotropic properties compared to the VCO obtained from cold processes. Also, VCO extracted using both methods inhibited lipoprotein oxidation with hypolipidemic effects (Siddalingaswamy *et al*., 2011).Rahmawati *et al*. (2020) reported that the MCFAs in VCO are responsible for lowering the blood glucose level as they are directly absorbed into cells and then into the mitochondria, and thus, with the increase in metabolism, cells work more efficiently to form new cells and replace damaged cells more quickly. Recently, Shetty *et al.* (2022) have advocated that dose-dependent dietary VCO supplementation could be an effective strategy to reduce obesity and reduce the risks of cardiovascular diseases, based on their studies in Wistar rat models.

Co-administration of vitamin D and coconut oil registered stronger and synergistic antihyperglycemic effects by decreasing the blood glucose level, increasing the C-peptide, and playing a constructive role in the recovery of the structure and functions of the damaged liver, pancreas, and testes in diabetic rats than each alone (El-Desouki *et al*., 2019; Nabila *et al*., 2019). Coconut products (virgin and filtered coconut oils, coconut water, and coconut milk) administered to streptozotocin (STZ)-induced diabetic rats recorded significant reversal in the levels of serum glucose, glycated hemoglobin (HbA1c), triglycerides, total cholesterol, low-density lipoprotein cholesterol (LDL-cholesterol), serum and kidney creatinine, total protein, urine glucose, urea, albumin, and creatinine levels (Alatawi and Alshubaily, 2021).

Coconut inflorescence sap

In Indian traditional medicine (Renjith *et al*., 2013), coconut inflorescence is used for the treatment of diarrhea, dyspepsia, dysentery, diabetes, and hemoptysis. Biochemically, coconut inflorescence comprises diverse polyphenols, amino acids, phenolics, dietary fibers, proteins, and flavonoids (Hebbar *et al*., 2018) that contribute to its antioxidant property (Pandiselvam *et al*., 2020a, 2021; Renjth and Rajamohan, 2012a). Glucose homeostasis and antioxidant levels in diabetic rats were improved by administering a diet based on a young coconut inflorescence (20% w/w) (Renjith and Rajamohan, 2012a). Also, the presence of phenolics, flavonoids, and other phytoconstituents in the extracts of the young coconut inflorescence could act collectively or independently, providing protective effects against alloxan-induced pancreatic cytotoxicity and hyperglycemia. In addition, inflorescence-treated rats exhibited lowered blood glucose levels, improved antioxidant activity, and improvement in rejuvenating the population of residual betacells (Renjith and Rajamohan, 2012b). Coconut inflorescence sap affects the key enzymes of carbohydrate metabolism in the liver. Methanolic extracts of coconut inflorescence showed a drop in blood glucose and elevated insulin levels in male Sprague Dawley rats compared to nondiabetic rats. In addition, the levels of cellular damage marker enzymes (serum alkaline phosphatase, alanine aminotransferase, and serum aspartate aminotransferase) were significantly reduced in the treated rats. Free radicals formed are considerably scavenged by the extracts due to their rich antioxidant potential (Tayebeh *et al*., 2021; Zieliska-Dawidziak, 2021). These findings confirm the nontoxic and antihyperglycemic nature of coconut inflorescence extracts (Renjith *et al*., 2013). Study on the antidiabetic activity of coconut inflorescence extract alone and along with metformin in STZ-induced diabetic rats resulted in reduced plasma glucose levels on 7, 14, 21, and 28 days (Kaur *et al*., 2020). Histopathological investigation of pancreatic tissue showed that treatment with coconut inflorescence extract per se and in combination

with metformin recouped the damaged architecture of pancreas. Coconut inflorescence sap is rich in antioxidants, vitamins, and amino acids (Aalbersberg *et al*., 1997; Hebbar *et al*., 2015). As it has a lower glycemic index (GI 35) than table cane sugar (GI 60) (Srikaeo and Thongta, 2015; Trinidad *et al*., 2010), it is considered suitable for consumption by diabetic (Jenkins *et al*., 2002; Rajamohan and Archana, 2018). Inulin, a fiber present in coconut sugar, may reduce glucose absorption (Hebbar *et al*., 2018, 2022; Trinidad *et al*., 2010; Vayalil, 2012).

Coconut water

Coconut water (CW) is considered nature's gift as it is a pure and healthy beverage enriched with bioactive compounds (vitamins, proteins, minerals, phytohormones, amino acids, etc.) that make it a functional/nutraceutical food (Pandiselvam *et al*., 2020b, 2022; Preetha *et al*., 2021; Prithviraj *et al*., 2021, 2022; Rajamohan and Archana, 2018; Yong *et al*., 2009). Mature coconut water possesses hypoglycemic activity and shows its antioxidant potential in diabetic experimental rats (Preetha *et al*., 2012). Similarly, administration of lyophilized matured coconut water (LMCW) resulted in reduced levels of glycated hemoglobin (HbA1c) and blood glucose in addition to an increased level of plasma insulin. A significant reduction of hepatic marker enzymes along with the improved levels of blood urea, serum creatinine, albumin, and albumin/globulin ratio were found in LMCW administered to alloxan-induced diabetic rats. Furthermore, considerable reversals in the level of nitric oxide synthase in the liver and plasma L-arginine were documented. The presence of a high concentration of L-arginine (5.85%), a precursor of nitric oxide, could reduce hyperglycemia by enhancing insulin secretion in diabetic rats. In addition, the anti-diabetic effects of LMCW were on par with those of a recognized anti-diabetic drug, glibenclamide (Preetha *et al*., 2013). Uddin *et al*. (2019) confirmed the antidiabetic effects of CW in diabetic rabbits, manifested as a reduction in a number of factors, *viz*. frequent urination, weight loss, sluggish physical activity, blood glucose, cholesterol, low-density lipoprotein, and triglycerides. Ehsayed *et al*. (2020) analyzed the effects of coconut water on biological parameters, liver function, and its architecture in STZ-induced hypoglycemic rats and validated its effectiveness in attenuating oxidative stress *via* the upregulation of the biochemical mechanisms conferring high antioxidant status. Hence, coconut water could be considered as a drink with significant anti-diabetic potential and as a nutraceutical or functional food in the treatment of diabetics.

Anti-retinopathy effects of matured CW were proven in STZ-induced diabetic Sprague Dawley (SD) rats (Zhang*et al*., 2020). Administration of CW in diabetic rats ensured the enlarged number of neurons in the ganglion cell layer (GCL), thickness of the retinal nuclear layer (RNL), and total retina thickness (TRT), compared to glibenclamide, an anti-diabetic drug. In addition, the levels of a proinflammatory mediator, interleukin-6 (IL-6), and an adhesive factor, intercellular adhesion molecule-1 (ICAM-1), in the retina were considerably reduced in diabetic rats. It was attributed to the effect of CW in inhibiting the early adhesion of white blood cells, reducing retina inflammatory damages and to advance the microcirculation, and alleviate and setback the succession of diabetic retinopathy. In CW-treated diabetic rats, the oxidative stress marker, malondialdehyde (MDA), level is reduced and serum levels of superoxide dismutase (SOD), and glutathione peroxidase (GSHPx) levels are increased. These are the biochemical and functional features underlying the protective effects of coconut water against the oxidative stress that leads to damage of the retina.

Tender coconut water (TCW) is a healthy and nutritious drink rich in antioxidants, minerals (Cu, Zn, Mn, and Mg), and amino acids (L-arginine, vitamin C, selenium), which play a major role in the peroxidation of lipids (Nova *et al*., 2020). L-Arginine, one of the main constituents of TCW, could considerably lower the free radicals and also aid in the regeneration of pancreatic β-cells. TCW could also rectify insulin insensitivity and possess antihypertensive effects (Mohamad *et al*., 2017). Administration of TCW in STZ-induced diabetic pregnant Wistar rats exhibited increased insulin plasma levels and reduced blood glucose against the control rats. Also, TCW can prevent lipid peroxidation by decreasing MDA levels and supplementing the concentration ofavailable minerals (Cu, Zn, and Mn), which in turn increases the activity of the antioxidant enzyme, superoxide dismutase (SOD) (Nova *et al*., 2020).

Coconut kernel

Fresh coconut contains almost all the vitamins, minerals, phytohormones, phenolic compounds, fiber, and proteins (Rajamohan and Archana, 2018). In test rats, coconut mesocarp juice extract (CMJE) significantly reduced blood glucose, serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, uric acid, and lipid levels, and increased glucose tolerance as well as glucose homeostasis (Das *et al*., 2021). Coconut kernel protein is rich in globulins (70–80%), which have good digestive and biological value (Rajamohan and Archana, 2018). The functional properties of coconut kernel protein are attributed to the presence of a higher amount of L-arginine (Salil *et al*, 2011). Salil *et al*. (2011) discovered that the coconut kernel has anti-diabetic properties. Similarly, kernel fiber has hypocholesterolemic

and hypoglycemic (Manoj *et al*., 2001; Sindhurani and Rajamohan, 2000) effects in addition to other health benefits.

Coconut husk

Despite its multipurpose utilities, the medicinal properties, especially the antidiabetic properties of the coconut husk (exocarp and mesocarp), are less explored. Coconut husk extract is known to have significant and rapid hypoglycemic effects in alloxan-induced diabetes in male Wistar rats (Victor and Jeroh, 2012). Histopathological observations in coconut husk extract treated rats showed an increased islet volume density and beta cell percentage, which might be attributed to the positive effect of the extract on the regeneration of ß cells and potentiating insulin secretion from surviving ß cells of the islets of Langerhans. Nevertheless, two of the test rats succumbed due to rapid hypoglycemia induced by coconut husk extract. Hence, administration of this extract requires caution, mandating regular monitoring of blood glucose levels. Hence, coconut husk extract has huge potential to be used as an adjuvant in the management of diabetes mellitus (Victor and Jeroh, 2012).

The use of coconut and its byproducts in the management of diabetes reveals that it has several beneficial effects, such as lower levels of blood glucose, lower levels of liver and cellular damaging enzymes, increased insulin response, recovery of the function and architecture of liver cells, increased body weight, regeneration and improvement of pancreatic cells, scavenging free radical formation, upregulation of antioxidant levels, and so on. Therefore, it can be suggested that coconut by products could be employed for the treatment of diabetes directly or could be used as amendments (Figure 3). The dietary consumption of coconut products appears to impart antidiabetic health effects. Hence, coconut derivatives can be used as an anti-diabetic component in food products. Earlier studies proved the beneficial effects of coconut products were as efficient as other artificial antidiabetic

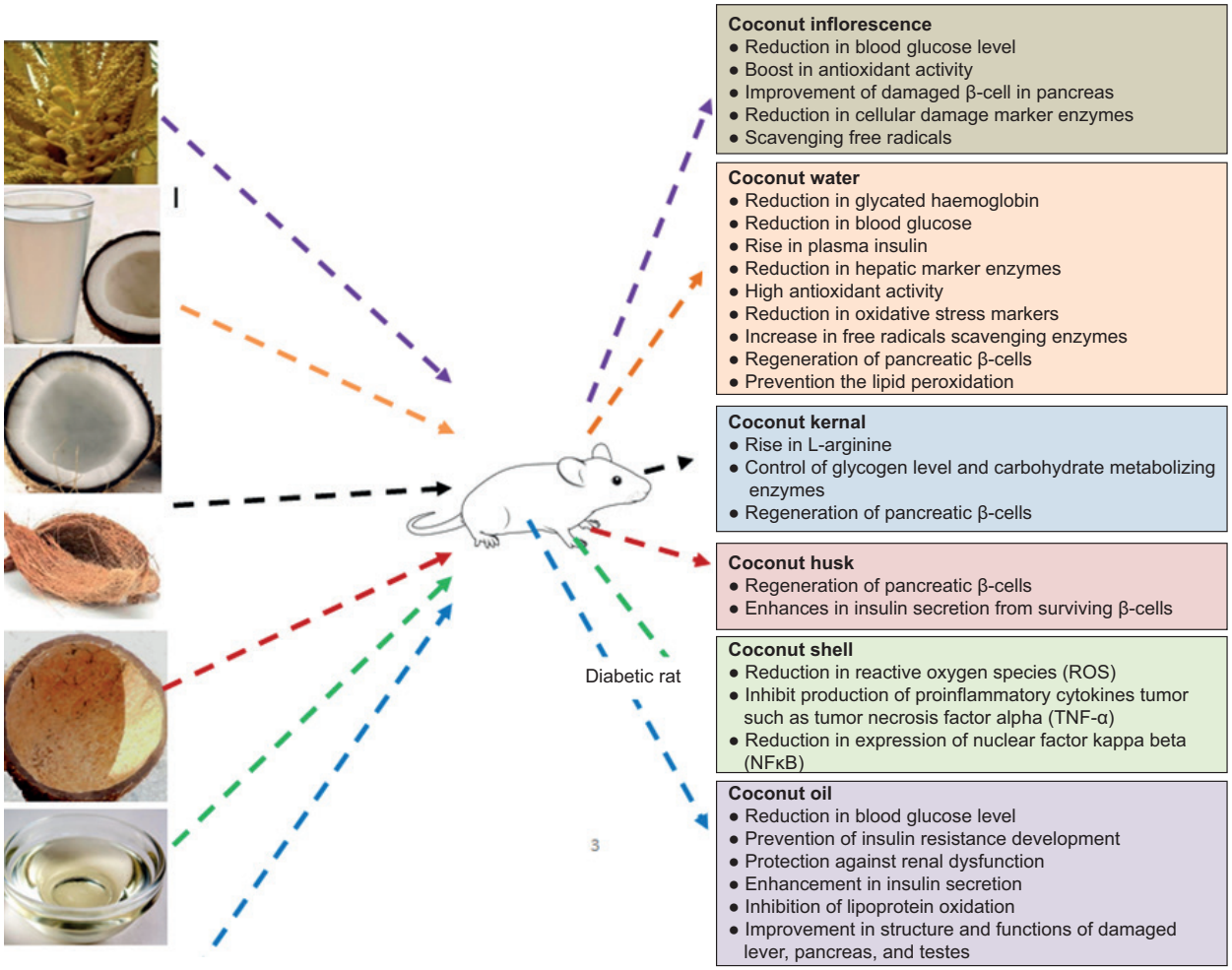

Figure 3. Antidiabetic effect of coconut and its derivatives.

drugs in controlling the parameters of diabetes. Further research into the potential of these coconut derivatives in the pharmaceutical industry as a replacement for synthetic antidiabetic drugs is required.

Conclusion

Coconut and its diversified value-added products have proven to possess abundant health benefits. It was a part of ancient medicine in the tropics. Recently, coconut and its derivatives have attained greater significance in the mainstream media, the digital world, and medical practitioners have endorsed its health benefits, recognizing coconut oil as a highly valuable and healthy oil. Besides being antimicrobial in nature due to lauric acid content, coconut and its derivatives have other potential health benefits, including maintaining heart health, managing diabetes, improving oral hygiene, preventing other diseases, etc. Among the several health benefits of coconut oil, cardio-protectant and neuroprotective effects assume greater significance because the currently available therapeutic models to treat cardiac and neuro-associated ailments are fraught with many side effects. Hence, the consumption of coconuts and their derivatives on a regular basis needs to be encouraged and popularized as a functional food. Nonetheless, literature pertaining to the health promotion effects of coconut oil still remains inconclusive with regard to its anti-obesity and anti-diabetic effects. Generally, these studies warrant large-scale clinical trials, complete control over the dietary intake during the period of study, and the dietary history of the subjects. As stated above, coconut oil alone could not be attributed to the satiety feeling observed in the subjects who have undergone the trials. In addition, the epidemiological studies attributing the health benefits of coconut oil and its derivatives have to consider the holistic view of diet in the study regions to arrive at a meaningful conclusion.

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