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MINI REVIEW

Bioactive monolaurin as an antimicrobial and its potential to improve the immune system and against COVID-19: a review

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Abstract

Monolaurin is monoacylglycerol which is a bioactive lipid since it can affect the human biological systems. This review discusses the bioactive properties of monolaurin, especially its role as an antibacterial, immune system enhancement, and its ability as an antiviral so that it has the potential to fight against various viral attacks. Monolaurin can act as an antibacterial in inhibiting the growth of several pathogenic bacteria, especially gram-positive bacteria. Monolaurin is known to be able to enhance the immune system through modulation of various immune systems, controlling pro-inflammatory cytokines, activating and attracting leukocytes to the site of infection. Monolaurin can also act as an antiviral, especially against enveloped viruses, such as Maedi-visna virus, vesicular stomatitis, herpes simplex-1, measles, HIV, cytomegalovirus, influenza, and corona. Monolaurin inhibits the virus through the mechanism of the disintegration of the viral membrane, prevents binding of the viral protein to the host-cell membrane, inhibits the process of assembling the viral RNA, and the process of virus maturation in the replication cycle. Therefore monolaurin has the potential for human consumption to boost the immune system and ward off various virus attacks, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the cause of COVID-19 which became a pandemic in the world.

1. Introduction

Glycerol monolaurate (GML) or known as monolaurin is an ester of glycerol and a lauric acid that acts as an emulsifier or non-ionic surfactant with important applications in the food and pharmaceutical industries. Monolaurin like other monoacylglycerols (MAGs), is known to have no irritating effect and it can be used as a food additive classified as generally recognized as safe (GRAS) for human consumption (Feltes *et al*., 2013; Subroto, 2020). Besides, monolaurin can affect the biological system so that it is known as bioactive lipids. Medium-chain fatty acids, including monolaurin, can reduce serum cholesterol and prevent cardiovascular disease (Eyres *et al*., 2016). It increases the high-density lipoprotein (HDL) (German and Dillard, 2004). It also shows the most easily oxidized by the metabolic system and does not cause obesity or fat accumulation (DeLany *et. al*., 2000).

Monolaurin has anti-atherogenic, antioxidant, and anti-diabetic properties by *in vitro* and *in vivo* testing in cells (Lieberman *et al*., 2006; Masmeijer *et al*., 2020). Monolaurin can inhibit the increase in blood TAG after eating. Monolaurin and other MAGs can regulate the increase in insulin levels, so that blood sugar is controlled, thus preventing diabetes and obesity due to hyperglycemia (Cho *et al*., 2010; Feltes *et al*., 2013). Monolaurin prevents obesity mainly through the mechanism of regulating the metabolism of glycerophospholipids and modulating the gut microbiota (Zhao *et al*., 2020).

Monolaurin is known to be able to inhibit various pathogenic bacteria, even in the form of vegetative cells and bacterial spores, including *Clostridium botulinum* and *Bacillus cereus* (Dayrit, 2014; Schlievert *et al*., 2018). Monolaurin also has a wide spectrum of activities against various fungi and viruses. Monolaurin can increase the organism's defense against virus attacks, which has the potential to produce immunological reactions initiated by antigens (Pereira *et al*., 2004). The role of monolaurin, especially in the pharmaceutical and food fields continues to be developed considering various studies have shown that monolaurin is good for health, especially in inhibiting the pathogenic bacteria,

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enhancing the immune system, and fighting various viral attacks. COVID-19, which attacks humans almost all over the world caused by SARS-CoV-2 demands various studies to overcome it. Therefore this review provides some insight into the characteristics of monolaurin, which could potentially be an alternative against COVID -19.

2. General characteristics of monolaurin

Monolaurin is a type of monoacylglycerol (MAG) from lauric acid. Monolaurin can be produced from oils that contain lots of lauric acid such as palm kernel oil and coconut oil. These oils contain about 50% of lauric acid, so they are known as lauric oil (O'Brien, 2009; Dayrit, 2014; Boateng *et al*., 2016). Lauric acid is also found in some foods that are produced with the addition of lauric oils such as shortening and cocoa butter substitute. Synthesis and production of monolaurin are the same as other monoacylglycerols, namely through partial esterification of lauric acid with glycerol, partial hydrolysis of lauric oil, and glycerolysis of lauric oil with glycerol both chemically and enzymatically (Nandi *et al*., 2004; Subroto *et al*., 2020). The synthesis methods of monolaurin can be seen in Table 1. Glycerolysis is the most effective method because of the abundance and cheapness of glycerin which is a derivative of biodiesel production that can be used as a substrate after purification (Feltes *et al*., 2013; Subroto *et al*., 2019). Monolaurin can be consumed directly or applied to a variety of food and pharmaceutical products since it provides beneficial effects and is safe for consumption (Lieberman *et al*., 2006; Marten *et al*., 2006).

Monolaurin is a non-ionic molecule that has hydrophilic and hydrophobic groups. With these characteristics, MAG shows great emulsifying properties, can be widely applied to food, cosmetics, chemicals, and the pharmaceutical industries (Chen *et al*., 2014; Subroto, 2020). Monolaurin is a multifunctional compound with properties as an emulsifier, improves physicochemical, bioactive properties, and can act as an antimicrobial (Lieberman *et al*., 2006). Monolaurin can be used in a variety of food and pharmaceutical industries because it has quite high antimicrobial activity. Monolaurin has been reported to increase shelf life in various foods. Yu *et al*. (2017) reported that monolaurin can extend the shelf life of grass carp fillets through a coating process with chitosan and monolaurin, which monolaurin was able to hamper the bacterial growth and maintain sensory properties. Monolaurin applications also showed improvements in the quality of physicochemical and functional properties of the products (Dayrit, 2014; Zhao *et al*., 2019).

3. Monolaurin is an antimicrobial

Monolaurin and lauric acid are very active against pathogenic bacteria (gram-positive and gram-negative), various fungi, and viruses (Silalahi *et al*., 2014; Nasir *et al*., 2018). Monolaurin and its derivatives act as antimicrobials through several mechanisms, namely (i) destruction of lipid-coated bacterial and viral cell membranes by physicochemical processes, (ii) disturbances the signal transduction and transcription in cellular, and (iii) stabilization of the host-cells membrane (human cells). The availability of some of these mechanisms might be one reason why bacteria cannot develop resistance to the action of monolaurin (Dayrit, 2014). However, the studies that measure how much monolaurin is metabolized from certain amounts of certain types of oil are still limited. The role of monolaurin as an antimicrobial for various types of bacteria can be seen in Table 2.

Monolaurin is proven to effectively block and inhibit exotoxin production by various gram-positive pathogenic bacteria (Projan *et al*., 2012). Monolaurin inhibits effectively against vegetative cells of *Bacillus cereus*. The studies have also shown that monolaurin can inhibit the activity of *Listeria monocytogenes, Bacillus stearothermophilus* and *Bacillus subtilis* (Cotton and Marshall, 1997). The mechanism of monolaurin in inhibiting the synthesis of *Staphylococcus* and other exoprotein poisons is proven to occur at the transcription stage. Furthermore, monolaurin can interfere with signal transduction in its activity to inhibit the induction of β-lactamase. Monolaurin is effectively able to inhibit

Table 1. The synthesis methods of monolaurin

Synthesis methods	Materials and catalysts	References
Esterification	Glycerol and lauric acid, using p-toluenesulfonic acid (pTSA)	Nitbani *et al.* (2018)
	Glycerol and lauric acid, using sulfated zirconia	Abdullah *et al.* (2016)
	Glycerol and lauric acid, using Lipozyme (IM-20)	Pereira *et al.* (2004)
Hydrolysis and esterification	Coconut acid oil using *Candida rugosa lipase and Rhizomucor miehei* lipase	Nandi *et al.* (2004)
Hydrolysis	Virgin coconut oil, using lipozyme and NaOH	Silalahi *et al.* (2014)
	Coconut oil, using KOH	Sangadah *et al.* (2018)
Glycerolysis	Coconut oil and glycerol, using Novozyme 435	Zha *et al.* (2014)
	Coconut oil and glycerol, using *Carica papaya lipase*	Pinyaphong *et al.* (2012)
	Virgin coconut oil and glycerol	Ponphaiboon *et al.* (2018)

Table 2. The role of monolaurin as an antimicrobial

Microbial type	Formulation	References
Staphylococcus aureus	Monolaurin (4000 µg/mL) diluted in BHIB	Zare *et al*. (2014)
	GML 182 mM diluted in chloroform for biofilm	Hess *et al*. (2015)
	GML 0.25 mM in Broth and Biofilm Cultures	Schlievert and Peterson, (2012)
	GML microemulsions	Zhang *et al.* (2007), Zhang *et al*. (2009)
	Combination monolaurin with essential oils	Preuss, Echard, Dadgar *et al*. (2005)
	Monolaurin 100 µg/mL in ethanol	Schlievert *et al*. (1992)
Staphylococcus epidermidis	1-monolaurin (1000–1953 µg/mL)	Krislee *et al*. (2019)
Escherichia coli	Microemulsions contained 1 g/mL of monolaurin	Petra *et al*. (2014)
	Monolaurin (128 µg/mL) diluted in BHIB	Zare *et al*. (2014)
	GML microemulsions	Zhang *et al*. (2009)
	Monolaurin microemulsion	Fu *et al*. (2009)
	Microemulsion contained 8% GML	Fu *et al*. (2006)
Bacillus and *Clostridium* spores	50,000 g/mL monolaurin gel was effective to kill the spores	Schlievert *et al*. (2018)
Bacillus anthracis	15-20 µg/mL monolaurin in absolute ethanol	Vetter and Schlievert. (2005)
Bacillus subtilis	Microemulsion contained 8% GML	Fu *et al*. (2006)
	Microemulsions contained 1 g/mL of monolaurin	Petra *et al*. (2014)
	GML microemulsions	Zhang *et al*. (2008)
	Monolaurin microemulsion	Fu *et al*. (2009)
Bacillus licheniformis	Combination monolaurin with nisin	Mansour *et al*. (1999)
Bacillus cereus	Microemulsions contained 1 g/mL of monolaurin	Petra *et al*. (2014)
	Monolaurin (25 µg/mL) dissolved in ethanol	Cotton and Marshall (1997)
Candida and *Gardnerella vaginalis*	GML gels (500 µg/mL)	Strandberg *et al*. (2010)
Candida albicans	Monolaurin (62.5-250 µM and 12.5 mmol/L)	Seleem *et al*. (2016), Seleem *et al.* (2018)
Enterococcus faecalis	GML 182 mM diluted in chloroform for biofilm	Hess *et al*. (2015)
	Microemulsions contained 100 mg/mL of monolaurin	Petra *et al*. (2014)
Pseudomonas aeruginosa	GML (62.5 µg/mL) and GML Nanocapsules (15.62 µg/mL)	Lopes *et al*. (2019)
	Microemulsions contained 1.9 g/mL of monolaurin	Petra *et al*. (2014)
Listeria monocytogenes	GML combined with organic acids	Oh and Marshall (2006)
	Monolaurin combined with lactic acid and nisin	Tokarskyy and Marshall (2008)
Mycobacterium terrae	Combination monolaurin with essential oils	Preuss, Echard, Enig *et al*. (2005)
Helicobacter pylori	Monolaurin 0.5 mM in Iso-Sensitest broth	Sun *et al*. (2003)
	Monolaurin 1.25 mM in ethanol	Bergsson and Thormar (2002)
Salmonella enterica	Microemulsions contained 1 g/mL of monolaurin	Petra *et al*. (2014)
Micrococcus luteus	Microemulsions contained 100 mg/mL of monolaurin	Petra *et al*. (2014)
Stenotrophomonas	GML microemulsions	Feng *et al*. (2009)

tumor necrosis factor-α, growth of *Staphylococcus aureus,* and exotoxins produced (Lin *et al*., 2009). Monolaurin hampers the expression of the virulence factor *S. aureus* and induction of vancomycin resistance of *Enterococcus faecalis*. Monolaurin acts by inhibiting signal transduction (Ruzin and Novick, 2000).

Murhadi (2009) reported that the concentration of the minimum inhibitory of lauric acid against *S. aureus* was below 1.0 mg/mL. This shows that monolaurin is very active as an antibacterial compound. Other studies also reported that the addition of 150 mg of monolaurin per liter decreases the growth and toxin production by *S. aureus* (Preuss, Echard, Dadgar *et al*., 2005). The study reported by Zare *et al*. (2014) showed the ability of monolaurin with a concentration of 128 µg/mL inhibits *S. aureus* but did not inhibit *E. coli* significantly. Hess *et al*. (2015) applied 182 mM monolaurin dissolved in chloroform as a surfactant for biofilms, the results showed that monolaurin was able to inhibit *S. aureus* and *E. faecalis*. Besides, the use of laurate in the form of monolaurin is more effective in inhibiting pathogenic bacteria than in the form of lauric acid. Similar results were reported by Schlievert and Peterson (2012) who found that monolaurin at a concentration of 0.25 mM in broth and biofilm cultures was able to inhibit *S. aureus, Streptococcus pyogenes,* and *Haemophilus influenzae*. The antibacterial spectrum of monolaurin becomes more extensive when the system in an acidic pH.

Monolaurin has a broad spectrum as antibacterial. Widiyarti *et al*. (2010) reported that the antibacterial properties of monolaurin affect other pathogenic bacteria, such as *L. monocytogenes, Streptococcus*

agalactiae, Hemophilus influenzae, and *Helicobacter pylory*. Monolaurin is also effective in inhibiting the vegetative cells of *B. cereus* (Cotton and Marshall, 1997; Affandi, 2017). 1-monolaurin (1-1.9 mg/mL) was reported to be effective in inhibiting *Staphylococcus epidermidis* on biofilms (Krislee *et al*., 2019). Monolaurin 15-20 µg/mL in ethanol was even reported to inhibit *Bacillus anthracis,* which is a pathogenic bacterium that causes anthrax disease (Vetter and Schlievert, 2005). Monolaurin in human milk was also reported to be able to effectively inhibit *Escherichia coli, Clostridium perfringens, B. subtilis, S. aureus* and *E. faecalis* compared to cow's milk or formula milk (Schlievert *et al*., 2019).

Monolaurin has good emulsion capacity and stability. Therefore, monolaurin has been widely used in the form of emulsions, especially microemulsions. Monolaurin microemulsion has been proven to be effective in inhibiting various types of pathogenic bacteria. Zhang *et al*. (2009) reported that GML microemulsion by combining with propionic acid and tween 80 was proven to be effective in inhibiting *S. aureus* and *E. coli* in less than 1 hour. Whereas Zhang *et al*. (2008) reported that GML microemulsion was effective in inhibiting *B. subtilis*. GML also shows a synergistic effect when combined with antimicrobial salt such as sodium lactate, so GML can potentially be widely used as an antimicrobial by combining several other types of antimicrobials. The use of monolaurin as an antibacterial in the form of microemulsion was also reported by Petra *et al*. (2014) who found that microemulsion containing 1.9 g/L was proven effective in killing gram-positive pathogenic bacteria such as *Bacillus cereus, S. aureus*, *E. faecalis, Micrococcus luteus and B. subtilis;* and gram-negative bacteria such as *Pseudomonas aeruginosa, E. coli, Citrobacter freundii, Salmonella enterica* and *Serracia marcescens*. The results also showed that monolaurin was more effective as an antibacterial compared to monoacylglycerol from other medium-chain fatty acids such as capric (C10:0), undecanoic (C11:0), and myristic (C14:0). The application of monolaurin as an antimicrobial has also been developed in the form of nanocapsules as an anti-biofilm whose results show that monolaurin nanocapsules were effective against *P. aeruginosa* (Lopes *et al*., 2019).

The inhibition mechanism of bacterial growth by monolaurin is related to the disruption of cytoplasmic membrane permeability of these bacteria. Several studies have shown that monolaurin is more effective to inhibit gram-positive bacteria, such as *L. monocytogenes*, compared to gram-negative bacteria such as *S. enteridis* or *E. coli*. When the use of monolaurin is combined with other types of antibacterial agents, such as EDTA, this can increase its ability to inhibit these gram-positive bacteria (Affandi, 2017). Monolaurin has been proven both through in vivo and in vitro testing to have potential antifungal activities, including *Candida albicans* and to modulate the host-cells pro-inflammatory response (Seleem *et al*., 2016; Seleem *et al.,* 2018). The advantage of monolaurin is that high doses do not cause the side effects of metabolic dysfunction or inflammation of the metabolic system (Mo *et al*., 2019). Another advantage is that in vivo and in vitro tests show that monolaurin can inhibit the bacteria that cause vaginal infections such as *Candida vaginalis* and *Gardnerella vaginalis*, but does not inhibit beneficial bacteria such as *Lactobacillus* (Strandberg *et al*., 2010).

4. Monolaurin for enhancing the immune system

Monolaurin can play a role in improving the human immune system. Schlievert *et al*. (2019) reported that monolaurin greatly contributes to anti-inflammatory activity in human milk. Human milk contains monolaurin about 3 mg/mL. When the monolaurin is eliminated, the anti-inflammatory and antimicrobial human milk activity is also lost. The addition of monolaurin restores anti-inflammatory and antimicrobial human milk activity. Masmeijer *et al*. (2020) reported that glycerol esters of medium-chain fatty acids, including monolaurin, were able to produce immune-modulating effects in experimental animals, namely veal calves. The enhancement of the immune system through an increase in fast and strong inflammatory reactions by increased production of pro-inflammatory cytokines, then activate and attract leukocytes to the site of infection with limited ROS production, so that tissue damage occurs is less.

Monolaurin can enhance the immune system through the mechanism of modulating T-cell lymphocyte production and controlling immune cell proliferation. Witcher *et al*. (1996) reported that monolaurin can improve the immune system through increased T-cell lymphocyte production. Monolaurin is also able to enhance the immune system by stimulating splenocyte proliferation and inducing T-cell proliferation. However, at high concentrations (> 5 µg/mL), monolaurin can control T-cell lymphocyte proliferation. Induction of T-cell proliferation is optimal when pure monolaurin is used at a concentration of 0.1 µg/mL. Monolaurin inhibits the effects of the mitogenic toxin-1 syndrome shock on T-cells but does not hamper lipopolysaccharide -induced B cell stimulation. This shows that monolaurin specifically affects T-cell populations. Monolaurin can exert the effect of T-cell proliferation along the phospholipid inositol signal transduction pathway.

Monolaurin also plays a role in changing LAT, PLC-γ, and the formation of AKT groups induced by TCR PI3K -AKT. This mechanism is supported by the presence of calcium which affects human T-cell signalling and function, thereby reducing cytokine production (Zhang *et al*., 2016).

Both studies in vivo and in vitro show that monolaurin can play a role in hampering the production of pro-inflammatory cytokines (IL-1 α, IL-1β, IL-2, IL-6, IL-8, MIP-3α, TNF- α, and IFN-γ) (Witcher *et al*., 1996; Li *et al*., 2009; Zhang *et al*., 2016). In other studies Silva *et al. (*2018) through *in vitro* testing showed that monolaurin could modulate the metabolite production and host immune response when inoculated with *Aggregatibacter actinomycetemcomitans*. In the fibroblasts layer (HGF-1), the genes IL-6, IL-18, TNF, and IL-1α showed decreased expression, whereas, in keratinocytes, the genes increased expression (except IL-1α) when given monolaurin treatment. Besides, metabolites in the form of pyruvic acid and glycerol increase significantly when monolaurin is added to 50 μM. Monolaurin can also play a role in controlling the activity and function of human T-cells through the binding of human serum albumin (HAS). Monolaurin controlled or rearranged the formation of PLC-γ1, LAT, and phosphorylation of AKT and then controlled cytokine production in cells (Zhang and Houtman, 2016).

5. Monolaurin as an antiviral

Lauric acid has greater antiviral properties than other fatty acids. Lauric acid inhibits the virus through an inhibitory mechanism at the end of the maturation stage of the replication cycle (Bartolotta *et al*., 2001). Laurate in the form of monolaurin is more biologically active than free lauric acid to kill bacteria and viruses. While in the form of diacylglycerols and lauric acid triacylglycerols are not active against microorganisms (Lieberman *et al*., 2006). The antiviral mechanism of monolaurin is by dissolving lipids and phospholipids, which make up the outer part of microorganisms or viruses which then causes disintegration of the outer membrane. Damage to the outer membrane of the virus causes the virus to rupture and die. Other researchers report that the antiviral mechanism is that monolaurin interferes with the signal transduction of organisms and through interference in the process of assembling viral RNA and the process of virus maturation or propagation (Projan *et al*., 1994; Arora *et al*., 2011). In general, the recommended dosage of monolaurin for adults is 1-3 grams, while for children (aged 3-10 years) it is recommended around 30 mg as much as 1-3 times a day. However, consumption of monolaurin at higher doses is still permitted because monolaurin has "GRAS" status and non-toxic to humans (Lieberman *et al*., 2006). Monolaurin can inhibit various types of viruses. Some monolaurin studies as antiviral can be seen in Table 3.

Monolaurin has been reported to have the ability to fight various types of viruses, especially enveloped viruses, including various influenza viruses. Hilmarsson *et al*. (2007) reported that monoacylglycerols with medium-chain fatty acids such as monocaprylin, monocaprin, and monolaurin have good virucidal effects against influenza viruses such as HPIV2 and RSV. The virucidal activity becomes more effective if the pH is lowered to around 4.2. The results of this study increase the potential of medium-chain monoacylglycerols for pharmaceutical preparations in counteracting respiratory viral infections caused by RSV and HPIV2 viruses, and possibly for other paramyxo and myxoviruses. Arora *et al*. (2011) reported that monolaurin which is mostly derived from coconut oil has the potential as an alternative treatment and to prevent the pandemic of the Novel H1N1 virus or swine flu virus that once attacked in several countries in the world.

Monolaurin was also reported to be able to destroy

Table 3. The role of monolaurin as an antiviral

Virus type	Formulation	References
HIV-1 and SIV	GML (5%) was dissolved in K-Y gel	Li *et al*. (2009)
	GML 5% in gel	Haase *et al*. (2015)
	GML 40 μg/mL	Welch *et al*. (2020)
respiratory syncytial virus (RSV) and human parainfluenza virus type 2 (HPIV2)	Monolaurin in lower pH (4.2)	Hilmarsson *et al*. (2007)
	1% monolaurin (Lauricidin) in 5% ethanol	Hierholzer (1982)
Avian Influenza VIRUS	VCO sebesar 10 mL/kg pakan	Yuniwarti *et al*. (2012)
herpes simplex virus types 1 and 2 (HSV-1 and HSV-2)	Monolaurin in lower pH (4.2)	Hilmarsson *et al*. (2005)
	1% monolaurin (Lauricidin) in 5% ethanol	Hierholzer (1982)
Mump virus	GML 80 μg/mL	Welch *et al.* (2020)
	1% monolaurin (Lauricidin) in 5% ethanol	Hierholzer (1982)
Yellow fever virus (YFV)	GML 80 μg/mL	Welch *et al*. (2020)
Zika virus	GML 80 μg/mL	Welch *et al*. (2020)
coronavirus 229E	1% monolaurin (Lauricidin) in 5% ethanol	Hierholzer (1982)

the herpes virus and HIV-1, and reduce the risk of transmission of the virus in infants of pregnant women infected by HIV (Lieberman *et al.*, 2006; Hilmarsson *et al*., 2007; Li *et al*., 2009). Li *et al*. (2009) using as much as 5% monolaurin dissolved in K-Y gel and then applied vaginally to monkeys that have been infected with SIV. The results of his research showed that monolaurin was proven to protect against SIV virus infection when applied vaginally. Besides, monolaurin is also able to inhibit the production of various pro-inflammatory cytokines8 and MIP-3α. Vaginal use of monolaurin also plays a role through an indirect mechanism as a protection against microbicides containing anti-retroviral (ARV) agents, thereby increasing monolaurin antiviral activity (Haase *et al*., 2015). Welch *et al*. (2020) conducted a study of the activity of virucidal monolaurin on several types of viruses, including HIV-1. The results showed that monolaurin at a concentration of 40 μg/mL effectively inhibited HIV-1 replication and was able to maintain the viability of vaginal microflora, especially the *Lactobacillus* group. The study was also carried out using an analog of monolaurin, which is in the form of reutericyclin compounds secreted by *Lactobacillus*, the results showed that reutericyclin was also able to inhibit replication of HIV-1. In the efficacy study of monolaurin against HIV-1 using the rhesus macaque model, the use of 5% monolaurin is very safe and does not affect microflora especially vaginal *Lactobacilli* (Schlievert *et al*., 2008). Kirtane *et al*. (2017) also reported that monolaurin added to vaginal cream up to 35% was proven to be safe without side effects and was effective in controlling microbes in the vagina.

Monolaurin has also been shown to be able to destroy herpes simplex virus types 1 and 2 (HSV-1 and HSV-2). Hilmarsson *et al*. (2005) reported that monolaurin has virucidal activities effectively against HSV-1 and HSV-2, especially at low pH (pH 4.2). Virucidal activities of monolaurin are higher than monoacylglycerol from long-chain fatty acids such as myristate, palmitate, and oleate, but not significantly different from monocaprin. Other studies show that monolaurin has a broad spectrum inhibiting various other types of viruses, especially the group of enveloped viruses (Hierholzer, 1982; Welch *et al*., 2020). Welch *et al*. (2020) also reported that the use of monolaurin to concentrations of 80 μg/mL effectively inhibited the replication of enveloped viruses such as mump virus, yellow fever virus, and Zika virus. The ability of monolaurin to inhibit the replication of various types of viruses shows that monolaurin has great potential to be used for medical and pharmaceutical purposes in preventing or preventing virus attacks, including SARS-CoV-2 which is a group of enveloped viruses which is now becoming a pandemic in almost all countries in the world.

6. Prospective of monolaurin against SARS-CoV-2

Monolaurin has been known to have antiviral activity for various types of viruses, including parainfluenza virus and respiratory syncytial virus. This makes monolaurin interesting to learn more about its ability as an antiviral in counteracting the virus that is currently a pandemic in almost all countries in the world, namely SARS-CoV-2, which is the cause of COVID-19. SARS-CoV-2 is a virus that attacks the respiratory tract; its characteristics are closely related to the SARS virus which had become a pandemic in 2003 (Kang *et al*., 2020; Zhou *et al*., 2020). This virus has almost the same characteristics, which include a group of enveloped viruses, where the virus membrane is composed of phospholipids, and the core of the virus is composed of the RNA genome. Previous research has reported that monolaurin compounds can inhibit various types of viruses from groups of enveloped viruses including viruses that infect the respiratory tract such as HPIV, RSV, and coronavirus 229E (Hierholzer, 1982; Hilmarsson *et al*., 2007). Monolaurin is proven to be able to inhibit viruses like this through the disintegration mechanism of the viral membrane, preventing the binding of the virus to the host-cell membrane, or the mechanism of inhibiting RNA synthesis and viral maturation.

Monolaurin is known to have active properties as an antimicrobial and antiviral, which is more effective than other monoacylglycerols. Monolaurin is monoacylglycerol in which the head (glycerol) is polar or hydrophilic while the acyl/tail (laurate) is non-polar or hydrophobic. It is this non-polar tail that has the potential to interact and destroy the outer membrane of SARS-CoV-2 composed of lipid components (phospholipids). The nature of monolaurin is similar to amphilitic soaps which are proven to be very effective at killing SARS-CoV-2 through the destruction of viral membranes. Previous studies have reported that monolaurin and its derivatives such as lauric acid and sodium lauryl sulfate are effective in destroying the membrane of enveloped viruses (Thormar *et al*., 1987; Piret *et al*., 2005). The characteristic of monolaurin, which is capable of destroying the outside of enveloped viruses, also has the potential to prevent the attachment of the virus to host-cells, thereby reducing virus infectivity. The studies have shown that lauric acid hampers vesicular stomatitis of the virus by inhibiting the binding of the virus to host-cells (Hornung *et al*., 1994). The mechanism through which interference with decreasing viral attachment with host-cells is known to be an effective method in reducing the infectivity of SARS-CoV-2 (Baglivo *et al*., 2020).

Monolaurin can also fight viruses by inhibiting viral maturation. The research conducted by Bartolotta *et al*. (2001) showed that lauric acid was able to inhibit the Junin virus (JUNV) by inhibiting the final maturation stage in the replication cycle. As it is known that JUNV is an enveloped virus similar to SARS-CoV-2, the outer membrane is composed of lipid bilayers that are shaped like nails.

Clinical research on monolaurin against SARS-CoV-2 is still limited, but various studies have proven that monolaurin has a good antiviral ability, especially in the enveloped viruses group. Besides, various studies have shown that consumption of lauric oil as a source of monolaurin provides good health effects. Therefore a more in-depth study is needed relating to the clinical test of monolaurin potential in counteracting COVID-19 both through the mechanism of enhancing the immune system and the mechanism of inhibiting the synthesis/ propagation of viral RNA.

7. Conclusion

Monolaurin is a bioactive lipid from medium-chain fatty acids that have been proven safe for consumption, has a broad spectrum as an antibacterial, boosts the immune system, and acts as an antiviral. The recommended dosage of monolaurin for adults is 1-3 grams, while for children is 30 mg as much as 1-3 times a day from coconut oil, palm kernel oil, or supplements as a source of monolaurin. Its ability to kill various types of viruses, especially enveloped viruses such as influenza viruses and coronavirus 229E, makes monolaurin potentially able to ward off SARS-CoV-2 which is the cause of the COVID-19 pandemic. However, further clinical tests are needed to determine the accuracy of efficacy and effectiveness.

Conflict of interest

The author declared no conflict of interest.

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