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The effect of coriander seed extract on reducing triacylglycerol synthesis and lipid droplets in the liver of obese rats induced by high-fat diet

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Abstract

Obesity is a serious health problem that is often caused by consuming a high-fat diet (HFD) and exacerbated by a sedentary lifestyle. Non-alcoholic fatty liver disease (NAFLD), a condition where triacylglycerol (TAG) is accumulated in the liver as lipid droplets, could be found as a complication associated with obesity. The main objective of this study was to analyze the effect of coriander seed ethanolic extract (CE) treatment on liver TAG synthesis and lipid droplets in HFD-induced obese rats. A total of twenty-five Wistar rats were divided into the following five groups: control group, control-CE group, HFD-CE group, obese group, and obese-CE group. Obesity induction was conducted for the first 12 weeks followed by CE treatment for the second 12 weeks and then the rats were sacrificed, and the liver organ was collected. We measured the TAG level, the level of peroxisome proliferator-activated receptor gamma (PPAR-γ) protein, the relative mRNA expression of PLIN2 and DGAT2, also histology analysis of lipid droplets in the liver. The results of this study demonstrated that the TAG levels in the liver of the obese group were associated with the increase in DGAT2 and PLIN2 mRNA expression compared to the control group. The histology section also showed a large amount of lipid droplets in the obese group. The results also showed that the CE treatment, either in the HFD-CE or the obese-CE group, generated the reduction of liver TAG levels, mRNA expression of DGAT2 and PLIN2, and lipid droplets in the liver compared to the control group. In conclusion, the results showed that CE treatment in obese or HFD-induced rats could suppress lipid droplets in the liver by decreasing triacylglycerol synthesis.

1. Introduction

Obesity is one of the metabolic disorders and is considered a major risk factor for chronic degenerative diseases such as type 2 diabetes mellitus, non-alcoholic fatty liver disease (NAFLD), hyperlipidemia, cardiovascular diseases, hypertension, chronic kidney disease, obstructive sleep apnea, osteoarthritis, and malignancies (Willis *et al*., 2021; Yang *et al*., 2022). Some factors that lead to obesity are a sedentary lifestyle, overnutrition, socioeconomic status, and other environmental and genetic conditions. In obesity, adipocyte hypertrophy occurs which will stimulate inflammatory signals through various pathways, including increased expression of pro-inflammatory adipocytokines and stress on the endoplasmic reticulum. Increasing levels of pro-inflammatory cytokines cause oxidative stress conditions which is the basis for the pathogenesis of other diseases associated with obesity (Ellulu *et al*., 2017; Ghowsi *et al*., 2021; Yang *et al*., 2022).

The liver plays a crucial role in maintaining lipid homeostasis in the body through intricate biochemical processes and signaling pathways. Hepatocytes, the main parenchymal cells of the liver, are pivotal in controlling various aspects of lipid metabolism, including TAG metabolism. The fatty acids in the liver can come from the diet and endogenous sources (synthesis in the liver). Under normal daily circumstances, the liver processes significant amounts of fatty acids, but it stores only a small proportion of these fatty acids (less than 5%) in the form of TAG (Alves-Bezerra and Cohen, 2018). In obesity, fatty acid metabolism in the liver is disrupted, which can lead to the accumulation of TAG in hepatocytes, ultimately causing a clinical condition

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known as non-alcoholic fatty liver disease (NAFLD) (Polyzos *et al*., 2019).

Fatty acids (FA) in the blood are taken up by hepatocytes through FA binding protein (FABPpm), FA translocase (FAT)/CD36, caveolin-1, and very long chain acyl-CoA synthetase (ACSVL/FA transport protein), that located on the cell membrane (Lehner and Quiroga, 2016). However, FA can also be produced by hepatocytes through the de novo FA biosynthesis pathway. In the liver, these FA are used for TAG synthesis by binding FA to glycerol molecules. Synthesis of TAG in the liver is mostly via the glycerol 3-phosphate (G3P) pathway, contributing more than 90% of the total synthesis of TAG. TAG synthesis consists of several steps: firstly, the esterification of long-chain acyl -CoA to G3P produces lysophosphatidic acid (LPA); secondly, LPA is then acylated to form phosphatidic acid (PA) and followed by dephosphorylation of PA to form diacylglycerol, which serves as the precursor molecule for TAG synthesis; finally, diglyceride acyltransferase (DGAT) catalyzes diacylglycerol acylation to form TAG (Coleman and Lee, 2004). There are two isoforms of DGAT: DGAT1 (luminal activity) which contributes to TAG synthesis which is packaged into VLDL and DGAT2 (cytosol activity) which contributes to TAG which is stored in lipid droplets (Jackson, 2019).

Perilipins are proteins that play an important role in the formation of lipid droplets (LD). The predominant hepatocellular LD protein is a member of the perilipin protein superfamily (PLIN1–5). PLIN1, also known as Perilipin A which is expressed in the LD of adipocytes, plays a key role in regulating lipolysis (the breakdown of stored triglycerides) in adipose tissue. However, PLIN2 and PLIN3 are associated with LD in hepatocytes and are involved in the regulation of lipid storage and mobilization within the liver. Overexpression of PLIN2 in rat liver stellate cells leads to an increase in lipid accumulation within LD, while PLIN2 knockout mice exhibit a significant reduction (around 60%) in hepatic triglyceride (TG) content (Itabe *et al*., 2017). This suggests that PLIN2 is involved in regulating lipid storage in hepatic stellate cells. Another study revealed that PLIN2 knockout mice are resistant to diet-induced obesity, fatty liver disease, and alcohol-induced steatosis. This resistance indicates that PLIN2 is a crucial factor responsible for lipid accumulation, especially in the liver (McManaman *et al*., 2013; Faulkner *et al*., 2020).

Peroxisome proliferator-activated receptor gamma (PPAR-γ) is a type II nuclear receptor, and it plays a critical role in the transcriptional regulation of various cellular processes, including adipocyte differentiation and lipid storage. Some studies reported that PPAR-γ expression is elevated in the rat livers that develop fatty liver (steatosis) and it is also upregulated in the livers of obese patients with NAFLD (Huang *et al*., 2019; Skat-Rørdam *et al*., 2019). PPAR-γ signaling in hepatocytes contributes to alcohol-induced liver injury by promoting fatty liver and inflammation (Zhang *et al*., 2016). PPAR-γ is also involved in upregulating several proteins that play important roles in various aspects of lipid metabolism, including lipid uptake, triacylglycerol storage, and the formation of lipid droplets (Wang *et al*., 2020).

Coriander (*Coriandrum sativum* L.) is a popular herb and spice used in many cuisines around the world, including Indonesian cuisine. It also has been proven to have various health benefits because of contains rich polyphenol. Previous studies reported that coriander seeds have recognized linalool as the main active compound and have important biological activities, such as antioxidant, anticancer, anti-diabetic, and anti-inflammatory (Scandar *et al*., 2023). Numerous studies have been conducted to explore the potential of herbal plants in treating obesity. A systematic review reported that there are 10 potential plants for the management of obesity, especially in the inhibition of pancreatic lipase activity (Hasim *et al*., 2023). Several previous studies have revealed that some herbs extract including coriander can reduce TAG and cholesterol levels in the rat blood. However, studies to analyze the effects of coriander seed extract on the expression of TAG synthesis enzymes and lipid accumulation in liver tissue are still limited. So, in this study, we used coriander as a herbal plant and aimed to reveal the effect of coriander seed extract on TAG synthesis and lipid droplet accumulation in the liver of obese rats.

2. Materials and methods

2.1 Experimental design

This *in vivo* experimental study used an animal model. Twenty-five male Wistar rats at 8 weeks of age and weighing 150-200 g were divided randomly into 5 groups: rats with normal diet as control group (n = 5), rats with normal diet and CE treatment as control-CE group (n = 5), rats with high-fat diet (HFD) and CE treatment as HFD-CE group (n = 5), obese rats induced by HFD as obese group (n = 5), obese rats induced by HFD with CE treatment as obese-CE group (n = 5). The caring of experimental animals in this study was carried out for 24 weeks, consisting of the first 12 weeks for obesity induction and the second 12 weeks for CE treatment. The flowchart of animal model treatment in this study can be seen in Figure 1.

Rats in the control group were given a normal diet for 24 weeks. Rats in the control-CE group were given a

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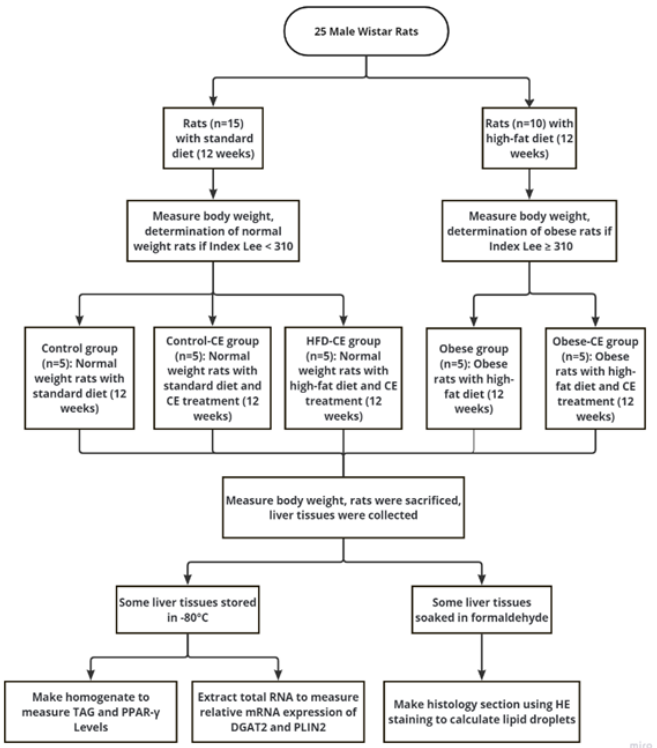

Figure 1. Flowchart of the animal model treatment.

normal diet for 24 weeks and they got CE treatment in the second 12 weeks. Rats in the HFD-CE group were given a normal diet for the first 12 weeks and then they were given HFD and CE treatment for the second 12 weeks. Rats in the obese group were given HFD for 24 weeks. Rats in the obese-CE group were given HFD for 24 weeks and they got CE treatment for the second 12 weeks. After CE treatment, all rats were sacrificed and the liver organs were collected. All experimental procedures were approved by the Health Research Ethics Committee Faculty of Medicine University of Indonesia with ethical approval No. KET-77 /LN2.FI/ETIK/ PPM.00.022022.

2.2 Composition of the standard and high-fat diet

The standard diet contains 64.4% of carbohydrates, 22% of protein, and 13.6% of fat from total calories. However, the high-fat diet used in this study contained 32.2% of carbohydrates, 20% of protein, and 47.8% of fat (Wang *et al.*, 2013). Table 1 shows the composition of standard and high-fat diets that were given to experimental rats. The high-fat diet was formulated by combining the standard diet with the addition of some fats, sugars and proteins.

2.3 Coriander seed extract preparation

The coriander seed used in this study was obtained from The Indonesian Spice and Medicinal Crops Research Institute (ISMCRI), Bogor, Indonesia. The coriander seed ethanolic extract was produced by grinding and then continuing with the process of

Table 1. Nutritional composition of standard and high-fat diet (g/100 g).

Content	Standard diet	High-fat diet
Standard chow (g)	100	60
Beef Tallow (g)	-	15
Egg Yolk Powder (g)	-	13
Casein (g)	-	10
Sugar (g)	-	2
Energy composition		
Protein (kJ %)	22	20
Carbohydrate (kJ %)	64.4	32.2
Starch	64.4	30.5
Sugar	-	1.7
Fat (kJ %)	13.6	47.8
Saturated	3.4	20.9
Monosaturated	3.2	21.9
Polyunsaturated (n6)	7	5
Density (kJ/g)	13.8	19.3

macerating the finely ground coriander seeds with ethanol solvent and incubating for 24 hrs. It was filtered and evaporated using an evaporator machine to obtain ethanol extract of coriander seeds. Coriander extract was given orally (100 mg/BW) to experimental rats every day for twelve weeks, starting from week 13th to week 24th (Mima *et al.*, 2020; Hardiany *et al.*, 2024).

2.4 Measurement of triacylglycerol and peroxisome proliferator-activated receptor gamma levels in liver tissues

The liver homogenate was used as a sample for measuring TAG and PPAR-γ levels. Liver tissue was weighed 100 mg and then created a homogenate in PBS 0.01 M pH 7.4 in a ratio of 1:9. The liver tissue was crushed with a homogenizer until evenly crushed. The homogenate was centrifuged at 10,000×*g* for 10 mins at 4℃ and then the supernatant was transferred to a new tube and was used for measurement of TAG and PPAR-γ levels. The triacylglycerol level was measured using a Triglyceride (TG) Colorimetric Assay Kit (Elabscience®). The level was divided by total protein concentration and reported as mg/g protein. Measurement of PPAR-γ protein level using sandwich-ELISA method, Peroxisome Proliferator-Activated Receptor Gamma ELISA Kit (Elabscience®). This assay was carried out according to the instruction manual from the factory and was done duplication for each sample. PPAR-γ level was divided by total protein concentration and presented as ng/mg protein.

2.5 Measurement of DGAT2 and PLIN2 mRNA expression in liver tissues

In performing the relative mRNA expression using quantitative real-time PCR, total RNA was used as the

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sample. Total RNA was extracted using the Quick RNA Miniprep kit (Zymo Research®). Approximately 50 mg of liver tissues were weighed, and the extraction steps were according to the kit manual. Total RNA concentration and purity were measured using nanodrop at A230, 260, and 280 nm. Quantitative real-time polymerase chain reaction (qRT-PCR) was used to analyze the expression of these genes. The Q3200 Real-Time PCR machine (Biogener®) was used with SensiFAST SYBR No-ROX One-Step Kit (Bioline®) for the one-step qRT-PCR reaction in this experiment. Analysis of gene expression levels was performed using the Livak 2-ΔΔCT formula (Livak and Schmittgen, 2001). The total RNA amount in qRT-PCR was 100 ng per reaction. The housekeeping gene was 18s RNA in this analysis. The primer sequences of each gene are listed in Table 2.

2.6 Lipid droplets analysis in liver tissues

Histology analysis of liver tissues was conducted using HE staining. Fresh liver tissue was soaked in buffer-neutral-formalin/BNF 10%. Paraffin blocks were cut using a microtome with a thickness of 3-5 µm and the slide stained using hematoxylin-eosin dye. Microscopic observation was carried out in 5 fields of view for each sample with 40× magnification. Analysis of the histologic section was conducted using the ImageJ application to determine the number and area of lipid vacuoles that represent lipid droplets in liver tissues. The results of the lipid droplet area were summed and divided by the total area (Munika *et al.*, 2024).

2.7 Statistical analysis

The data distribution was evaluated using the Saphiro-Wilk test. The significant difference for all parameters among the group was conducted using the One-Way ANOVA test and continued to LSD post-hoc test. The data was displayed as a bar graph (mean ± SD) if the data was homogenous and a table (median, min-max) if the data was not homogenous. Data were analyzed using IBM SPSS statistics software version 27.0.

3. Results

The liver TAG level (Figure 2a) was significantly different among the five groups (One-Way ANOVA, p = 0.013). After LSD post-hoc test, there was a significant increase in liver TAG level among the HFD-CE (172.367±16.827, p = 0.023) and obese group (182.215±16.361, p = 0.007) when compared to the control group (126.673±7.004). The highest TAG levels were found in the obese group. In the obese-CE group, the liver TAG level was decreased (146.894±9.037) when compared to the obese group but not significant (p = 0.061) and not significant also when compared to the control group (p = 0.293). There was also no difference in liver TAG level between the control-CE (126.004±10.387) and the control group (126.673±7.004).

The result of PPAR-γ levels (Figure 2b) in rat liver tissues showed an insignificant difference among the five groups (One-Way ANOVA, p = 0.704). The level of PPAR-γ in the control (0.0179±0.0036), control-CE (0.0184±0.0019), and obese group (0.0169±0.0019) did not differ much. However, there was a tendency of PPAR-γ to decrease in the rat group that received coriander extract such as the HFD-CE group (0.0141±0.0030) and obese-CE group (0.0144±0.0035).

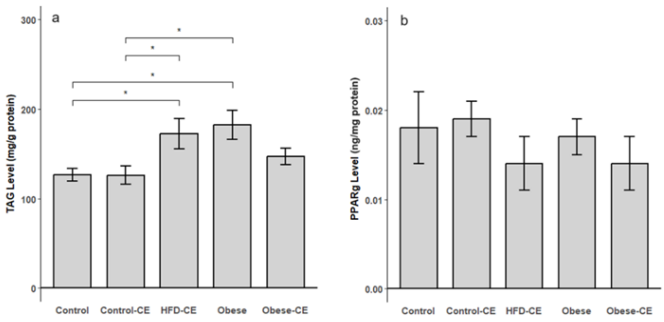

Figure 2. Level of (a) TAG (mg/g protein) and (b) PPARγ (ng/mg protein) in rat liver tissues in the group: Control (normoweight with normal diet), Control-CE (normoweight normal diet with CE treatment), HFD-CE (normoweight with high-fat diet and CE treatment), Obese (obese with high-fat diet) and Obese-CE (obese with high-fat diet and CE treatment). Statistical analysis using One-Way Anova test, post-hoc LSD with significance *p<0.05 and **p<0.001.

The result of DGAT2 mRNA relative expression is shown in Figure 3a. A significant difference in DGAT2 mRNA expression among five groups (One-Way ANOVA, p = 0.001) was observed. There was a significant increase of DGAT2 mRNA expression in the obese group (3.191±0.861) when compared to control (p = 0.003) and control-CE (p = 0.000). The mRNA expression of DGAT2 was significantly decreased in HFD-CE (0.488±0.168) and obese-CE group (0.338±0.083) when compared to the obese group (p = 0.000 and p = 0.000, respectively). Though there was a

Table 2. Primer sequences of DGAT2, PLIN2 and 18sRNA.

Gene	Primer Forward	Primer Reverse	PCR Products
DGAT-2	5'-GCACTGACTGCTGGCTGATA-3'	5'-CATGGGGATGGTATCCAAAG-3'	204 bp
PLIN-2	5'-GCTCTCCTGTTCGGCATCTC-3'	5'-TGCCATCTCACACACTGACC-3'	188 bp
18s RNA	5'-CGCGGTTCTATTTTGTTGGT-3'	5'-AGTCGGCATCGTTTATGGTC-3'	219 bp

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decrease in DGAT2 mRNA expression in the control-CE group (0.667±0.333), it was not statistically different (p = 0.575) when compared to the control group (1.031±0.122).

The relative mRNA expression of PLIN2 is shown in Figure 3b. A significant difference in PLIN2 mRNA expression was observed among the five groups (One-Way ANOVA, p = 0.000). There was a significant decrease of PLIN2 mRNA expression in HFD-CE (0.429±0.119) when compared to control (p = 0.010), control-CE (p = 0.023), and obese group (p = 0.001). There was also a significant decrease of PLIN2 mRNA expression in the obese-CE group (0.135±0.056) when compared to the control (p = 0.000), control-CE (p = 0.001), and obese group (p = 0.000). Although there was an increasing mRNA expression of PLIN2 in the obese group (1.207±0.222), it was insignificant when compared to the control group (p = 0.506). There was no difference in PLIN2 mRNA expression between control (1.056±0.158) and control-CE group (0.949±0.164).

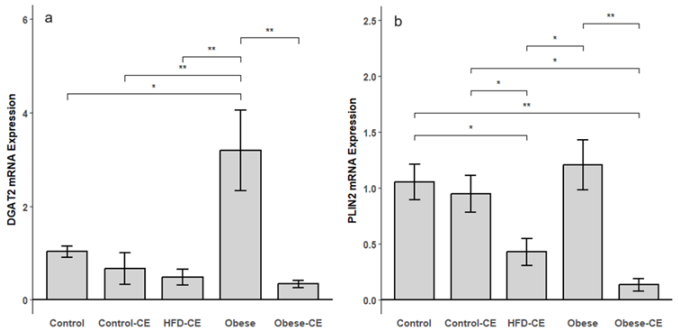

Figure 3. Relative mRNA expression of (a) DGAT2 and (b) PLIN2 in rat liver tissues in the group: Control (normoweight with normal diet), Control-CE (normoweight normal diet with CE treatment), HFD-CE (normoweight with high-fat diet and CE treatment), Obese (obese with high-fat diet) and Obese-CE (obese with high-fat diet and CE treatment). Statistical analysis using One-Way Anova test, post-hoc LSD with significance *p<0.05 and **p<0.001.

The liver histology was analyzed to evaluate the lipid droplets in this tissue. Figure 4 shows the histologic section of the liver represents five groups in this study. In the control and control-CE groups, there were very little of lipid droplets in the liver tissues. In the obese group, there was an increase in lipid droplets in the liver tissues. However, in the rats with coriander extract treatment (HFD-CE and Obese-CE group), the lipid droplets were reduced compared to the obese group. Calculations of lipid droplet amounts in liver tissues using ImageJ software were presented in Table 3. Because the data were not normally distributed, the Kruskal-Wallis test was used for further analysis. It was found that there was a significant difference in lipid droplet amounts among the five groups (p = 0.000). The significance of lipid droplets amount between the experiment group and control group was presented in Table 3.

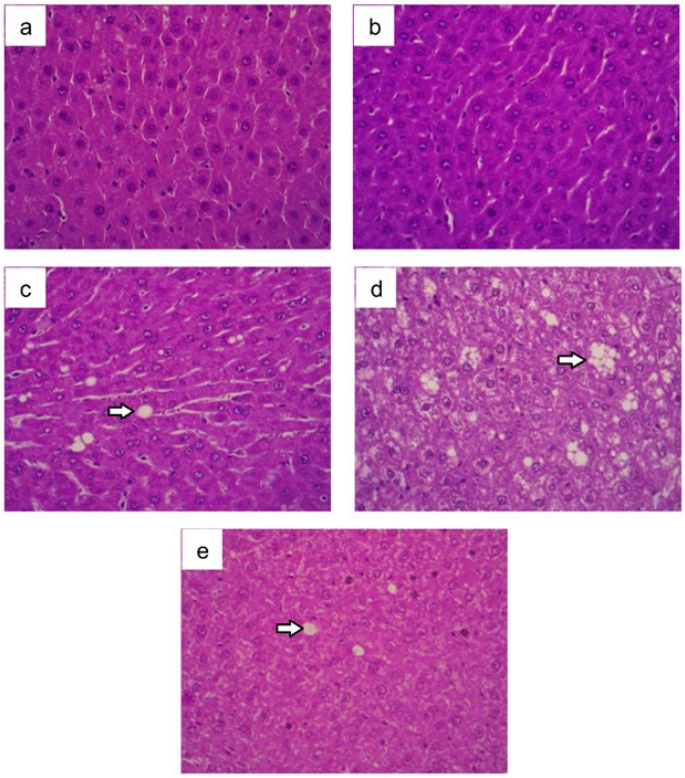

Figure 4. Histological image of lipid droplets in liver tissue with 40× magnification HE staining at group (a) Control (normoweight with normal diet), (b) Control-CE (normoweight with normal diet and CE treatment), (c) HFD-CE (normoweight with high-fat diet and CE treatment), (d) Obese (obese with high-fat diet) and (e) Obese-CE (obese with high-fat diet and CE treatment). The arrow points to lipid droplets.

Table 3. Lipid droplets calculation in rat liver tissues using ImageJ software.

Group	N	Median of lipid droplet amount (Min-Max)	P-value (vs control group, Mann-Whitney U test)
Control	5	0.0140 (0.000-0.039)	-
Control-CE	5	0.0005 (0.000-0.004)	0.249
HFD-CE	5	0.1092 (0.046-0.227)	0.006
Obese	5	0.3310 (0.190-0.557)	0.006
Obese-CE	5	0.0438 (0.007-0.128)	0.271

4. Discussion

This study proved that twelve-week HFD treatment caused obesity in male rats and resulted in an increase in liver TAG levels. A study on the body weight measurement of the rats according to the Index Lee calculation formula showed that all of the rats that received HFD in twelve weeks had the highest Index Lee average (≥310) (Hardiany *et al.*, 2022). In another study on the obesity induced by HFD in rats, the time required for rats to develop obesity ranged from 8 days to 27

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weeks (Dias *et al*., 2021). The other study noted that around the seventh week of HFD induction, there was a significant increase in weight gain and changes in their metabolic characteristics. A longer intervention period of HFD, specifically from 10 to 12 weeks, was necessary for the consolidation of the phenotypic and metabolic characteristics of obesity in the rats (Savetsky *et al*., 2015; Matias *et al*., 2018). Fat composition in this study was around 47.8% in the diet and concurred with other studies that used around 41-60% of fat in the diet to induce obesity (Dias *et al*., 2021).

Liver TAG level was increased in the obese group, and other studies proved that obese subject has a high accumulation of fat in liver tissues and become an independent risk factor for incidents of NAFLD (Xing *et al*., 2021). The administration of CE both in obese and HFD rats, led to a reduction in liver TAG levels when compared to the obese group without treatment. Although this reduction is not statistically significant, the value of TAG level in Obese-CE lowered near to Control group. Elsewhere, another study demonstrated that coriander seed extract treatment in HFD-induced obese rats lowered triglyceride and cholesterol levels in blood plasma and improved the hepatic function and cardiac biomarkers as well. This effect was thought to be due to the presence of phlobatannin and flavonoids in coriander seed extract (Hassan *et al*., 2022).

The TAG level result has concurred with the relative mRNA expression of DGAT2 in liver tissues. Diacylglycerol acyltransferase 2 (DGAT2) is the enzyme that catalyzes the final step of TAG synthesis and incorporates a long-chain fatty acyl-CoA into diacylglycerol. The DGAT2 mRNA expression in the liver is parallel to the liver TAG level. The highest expression of DGAT2 was found in the obese group and the expression of DGAT2 in HFD-CE and obese-CE groups showed a significant decrease compared to the obese group. A previous study by Gluchowski *et al*. (2019) reported that DGAT2 was associated with the storage of fatty acids from de novo lipogenesis that contributed to NAFLD generation (Gluchowski *et al*., 2019). Another study by Yenilmez *et al*. (2022) showed that using small interfering RNA (siRNA) targeting DGAT2 in non-alcoholic steatohepatitis (NASH) mouse model decreased triglyceride accumulation (>85%) without increased accumulation of diglycerides, resulting in significant improvement of the fatty liver phenotype.

Liver TAG accumulation is sequestered in lipid droplets. Perilipins (PLIN) are a family of proteins located on the surface of lipid droplets, which have important roles in the formation and maintenance of lipid droplets. PLIN2 is widely expressed and has been used as a marker for hepatic lipid droplets because it is often found on the surface of lipid droplets (Sztalryd and Brasaemle, 2017). This study demonstrated that PLIN2 mRNA expression was increased in the obese group, although not significant when compared to the control group. Histology analysis using HE staining showed a significant increase of lipid droplets in rat liver obese compared to the control. This result indicated that the expression of PLIN2 might be correlated to lipid droplet formation in liver tissues.

In the HFD-CE and obese-CE group, both PLIN2 mRNA expression and lipid droplets were significantly decreased compared to the obese group. This result demonstrated that CE treatment causes a reduction of lipid droplets in the liver tissues. A previous study reported that PLIN2 has a role in promoting the formation of lipid droplets resulting in lipid accumulation in the liver and PLIN2 expression level is correlated to TAG content of lipid droplets (Itabe *et al*., 2017). Tsai *et al*. (2017) revealed that PLIN2-knockout mice have a reduced TAG content of about 60% in the liver, and are protected against fatty liver disease. The data of lipid droplets was also supported by the DGAT2 mRNA expression and TAG level in the liver. There was an increasing number of lipid droplets in obese rats, parallel with the expression of DGAT2 and TAG levels. Meanwhile, the decreasing of lipid droplets was found in HFD and obese rats with coriander extract treatment, parallel with the expression of DGAT2 and TAG levels.

In this study, coriander was used since it was well known for its many biological activities and widely used as an anti-inflammatory, anti-hyperglycemia, anti-hyperlipidemia, and antioxidant. In this study, coriander was used since it was well known for its many biological activities and widely used as an anti-inflammatory, anti-hyperglycemia, anti-hyperlipidemia, and antioxidant. The presence of phenolic compounds, particularly flavonoids, is believed to contribute to these beneficial effects (Scandar *et al*., 2023). A previous study revealed that coriander extract administration to obese rats and HFD rats causes decreasing in triglyceride and total cholesterol in blood plasma compared to obese rats (Hardiany *et al.*, 2022; Hassan *et al.* 2022). This study in general also showed the administration of CE led to decreasing in TAG synthesis and lipid droplet formation in liver tissues. Many researchers have been exploring the use of phytochemicals such as quercetin, epigallocatechin-3-gallate, resveratrol, caffeic acid, and gallic acid to reduce triglyceride accumulation. A previous study reported that coriander oil could prevent the increase of blood glucose, triglyceride and total cholesterol levels in rats with dexamethasone-induced insulin resistance (Mahmoud *et al.*, 2022). Furthermore,

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coriander extracts have been proven to be able to reduce lipid accumulation and prevent adipogenesis due to their significant amounts of flavonoid and phenolic components with antioxidant activity (Nyakudya *et al*., 2014).

The result of PPAR-γ level in the liver showed no significant difference among the five groups. This was because PPAR-γ is highly expressed in adipose tissue and macrophages, and lower expressed in liver and muscle tissues. PPAR-γ plays important roles in adipogenesis, lipid metabolism, insulin sensitivity, and immune regulation (Wang *et al*., 2020). However, several recent studies have shown that PPAR-γ expression is associated with metabolic syndrome. Although PPAR-γ activation is steatogenic, treating obese NAFLD mice with PPAR-γ ligands decreases liver TAG. PPAR-γ also has anti-inflammatory properties, which can regulate inflammatory immune responses (Heming *et al.*, 2018). PPAR-γ activation reduces the inflammatory response through interferes with NF-κB signaling, suppresses TNF-α production and IL-1β and polarizes to anti-inflammatory M2 macrophages (Yu *et al*., 2023).

So far, there has not been much study to reveal the effect of natural products on the formation of lipid droplets in the liver. Some previous studies have demonstrated various plant-derived compounds for their potential anti-lipid droplet accumulation effects mostly in adipocytes (Wong *et al.*, 2014; Haselgrübler *et al.*, 2019). Berberine is a natural compound that has been reported to reduce lipid droplets in vivo and it has been associated with PPAR-γ down-regulation, which plays a role in regulating adipogenesis and lipid storage in adipocytes (Hu and Davies, 2010). While the other study using epigallocatechin-3-gallate, a polyphenol found in green tea, was proven to regulate essential enzymes involved in the de novo lipogenesis pathway in the liver through stimulating the activation of AMPK via liver kinase B1, but they did not evaluate the liver lipid droplets formation (Santamarina *et al*., 2015). There is a dearth of data in evaluating natural compounds for liver lipid droplet formation. Therefore, the results of this study uncover the role of a natural compound (coriander seed extract) in the formation of lipid droplets in the liver of obese subjects.

5. Conclusion

Coriander extract treatment in obese or high-fat diet-induced rats showed a decrease in triacylglycerol synthesis and lipid droplets in liver tissues. Therefore, there is a big potential to explore the effect of coriander seed extract on other lipid metabolism pathways and could be an alternative treatment to prevent complications from obesity.

Conflict of interest

The authors declare no conflict of interest.

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