

CHAPTER I

INTRODUCTION

1.1. Background

High fat diet is associated with body weight gain which can lead to high blood lipid level especially low density lipoprotein (LDL) and Triglycerides and other related metabolic diseases.¹ Changes in the level of fat product from high fat diet lead to increased LDL and recruitment macrophages in blood vessels, lead to enhanced macrophage uptake by a novel receptor, termed the "acetyl LDL" receptor (to distinguish it from the LDL receptor).²

Interleukin-6 (IL-6) is a multifunctional cytokine with endocrine and metabolic actions, produced by many types of cells, adipocytes produce and secrete significant amounts of IL-6 in the systemic circulation. IL-6 and CRP are prognostic factors in unstable angina and are associated with cardiovascular and all-cause mortality.³ IL-6 enhances cell adhesion molecule (CAM) expression by endothelial and smooth muscle cells, and enhances the production of acute phase reactants such as C-reactive protein (CRP) by the hepatocytes.⁴ Cardiovascular disease (CVD) likely, a chronic low-level inflammatory process characterized by increased circulating levels of proinflammatory cytokines (IL-6 and cytokine-responsive acute phase proteins including C-reactive protein (CRP)).⁵

Increase the expression of the proinflammatory cytokines interleukin IL-6 on ECs. Further role of Ox-LDL in atherosclerosis could be to initiate and affect inflammatory mediators such as C-reactive protein (CRP), interleukin (IL)-6, and

tumor necrosis factor (TNF). A positive correlation between CRP and Ox-LDL in humans has been suggested.⁶

In human mesangial cells, Ox-LDL has been shown to stimulate IL-6 expressio. Newer risk factors such as elevated C-reactive protein (CRP) levels can also promote endothelial dysfunction by quenching the production of NO and diminishing its bioactivity.⁷ CRP is a sensitive marker of inflammation and infection. The production of CRP is regulated by cytokines, including IL-1, IL-6, and TNF- α . These endothelial modifications promote inflammation within the vessel wall, setting the stage for the initiation and progression of an atherosclerotic lesion.⁸

Virgin Coconut Oil (VCO) is a product of coconut (*coco snucifera*). It is produced by extraction of fresh coconut meat. VCO is derived from fresh coconuts neither bleaches, solvents, nor heating in the process so it is different from hydrogenated coconut oil.⁹ The preparation of virgin coconut oil preserves natural components of the coconut such as phytosterols, polyphenols, vitamin E and provitamin A.¹⁰

VCO consist of 92% saturated fatty acid, 6% monounsaturated fatty acid, 2% polyunsaturated fatty acid. Saturated fatty acid in VCO consist of 90% medium chain triglyserides (MCT) and 10% long chain triglyserides (LCT). MCT contain such as lauric acid , reduce lipid profile (TC, LDL, VLDL) and increases (HDL) in serum and tissues.¹¹ VCO contains of biological active substance such as antioxidant (tocopherols, tocotrienols, polyphenols, and flavonoid)which significant advantage in preventing the oxidation of LDL leading to regulate of

inflammatory response.¹² Study the usefulness of VCO in reducing the IL-6 and CRP as inflammatory markers in rat undergo high fat diet is still needed.

1.2. Research Questions

The major research question in this study:

Does VCO can reduce IL-6 and CRP in wistar rats with high fat diet?

1.3. Research Objective:

1.3.1. General Objective

To prove that VCO can reduce IL6 and CRP in wistar rats with high fat diet.

1.3.2. Specific Objective

- a. To prove that the level of IL6 and CRP would be lower in wistar rats with high fat diet that received VCO compared to those without VCO
- b. To investigate the effective dose of VCO in lowering the level of IL-6 in wistar rats with high fat diet
- c. To investigate the effective dose of VCO in lowering the level of CRP in wistar rats with high fat diet

1.4. Research Benefits:

1. Clinical Application field: the research will give an additional evidence of the effects of VCO to decrease concentrations of IL-6 and CRP due to of high fat diet, in which could be applied in clinical settings.

2. Science: the research will add the explanation about the changes of inflammations indicators towards the effects of VCO in high fat diet.

3. Research: the research will add another explanatory variables of VCO effects on high fat diet which in turn further study to explore the basic mechanism need to be explored

1.5. Research Originality

The role of IL-6 and CRP in the development of atherosclerosis and the effects of VCO on antihypercholesterolaemia and improvement of hepatic lipid metabolism have been reported in the literature. However, the effects of VCO on IL-6 and CRP profile have not been described yet, therefore the effects of VCO on those inflammatory indicators in wistar rats with high fat diet have to be studied.

Table1: Previous report related to study on protective effect of VCO

No	Title publication and authors	Method	Results
1	Abdominal Adiposity Is Associated With Elevated C-Reactive Protein Independent of BMI in Healthy Non Obese People. EMANUELA LAPICE MD, SIMONA MAIONE BS, LIDIA PATTI PHD, et al.2009 ⁽¹³⁾	We studied 350 people with abdominal adiposity (waist-to-hip ratio [WHR] 0.9 in male and 0.85 in female subjects) and 199 control subjects (WHR 0.9 in male and 0.85 in female subjects) matched for BMI and age. We measured hs-CRP and major cardiovascular risk factors.	Participants with abdominal adiposity had BMI similar to that in control subjects, but significantly higher waist circumference. Compared with the control subjects, participants with abdominal adiposity had an adverse cardiovascular risk factor profile, significantly higher hs-CRP and a twofold prevalence of elevated CRP values (3 mg/dl).
2	C-ReactiveProtein, Interleukin-6, and Soluble Adhesion Molecules as Predictors of Progressive Peripheral Atherosclerosis in the General Population : Edinburgh Artery Study.Tzoulaki I, Murray G.D, Lee A.J,RumleyA,Lowe G and Fowkes G. R. 2005. ⁽¹⁴⁾	The Edinburgh Artery Study is a population cohort study of 1592 men and women aged 55 to 74 years. CRP, IL-6, ICAM-1, VCAM-1, and E-selectin were measured at baseline. Valid ABI measurements were obtained on 1582, 1081, and 813 participants at baseline and 5-year and 12-year follow-up examinations, respectively.	The results showed that At baseline, a significant trend was found between higher plasma levels of CRP and increasing severity of PAD, after adjustment for baseline cardiovascular risk factors.IL-6 at baseline was associated with progressive atherosclerosis at 5 years (ABI change from baseline), and CRP, IL-6, and ICAM-1 were associated with changes at 12 years, independently of baseline ABI, cardiovascular risk factors, and baseline cardiovascular disease

No	Title publication and authors	Method	Results
3	Antihypercholesterolemia property and fatty acid composition of madi-produced virgin coconut oils. Zakaria Z, Ahmad M.N, Somchit, A.K, Arifah H M.Khairi1, M. R. Sulaiman, L. K.Teh, M. Z. Salleh and K. Long .2010. ⁽¹⁵⁾	9 groups of New Zealand White male rabbits were used in this study. Group 1, 2 animals were treated with 0.9% normal saline, but fed either with a normal or cholesterol-added diet (negative control), respectively. Group 3 - 5 and 6 - 8 were given orally with the different volume (0.5, 1.0 and 2.5 ml/kg/day) of VCOA or VCOB followed by the cholesterol-added diet. Group 9 were treated with 5 mg/kg Atorvastatin and fed a cholesterol-added diet. All groups were treated for 8 weeks	The rabbits fed with different volume of VCOs showed significant reduction in plasma cholesterol and LDL cholesterol levels compared to the control group in weeks 4 and 8. The triglycerides level increased significantly on week 4 before reduced on week 8, to a level that is still significant when compared to week 0. The HDL level also increased significantly on weeks 4 and 8 after treatment. Fatty acid analysis revealed the presence of all important fatty acids. Both VCOs showed insignificant effect on all parameters measured when compared together.
4	Virgin Coconut Oil Improves Hepatic Lipid Metabolism in Rats compared with Copra Oil, Olive Oil and Sunflower Oil. Arunima S and Rajamohan T.2012. ⁽¹⁶⁾	Design: experimental Subjects: male sprague-dawley rats were fed different oils (4 groups) at 8% level for 45 days along with synthetic diet	VCO feeding significantly lowered levels of total cholesterol, LDL+VLDL-c, Apo B and TC in serum and tissues compared to rats fed CO, OO and SFO, while HDL-cholesterol and Apo A1 were significantly higher in serum of rats fed VCO than other groups. In addition, VCO significantly increased the activities of lipoprotein lipase, lecithin cholesterol acyl transferase and enhanced formation of bile acids.