

# STEeping OF GINGER (*ZINGIBER OFFICINALE ROSCOE*) POTENTIALLY DECREASE THE RISK OF ATHEROSCLEROSIS BY ATTENUATE OF TUMOR NECROSIS FACTOR (TNF)- $\alpha$ EXPRESSION

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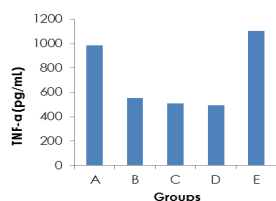
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## Graphical abstract



## Abstract

Cardiovascular disease still one of the highest death factor in Indonesia. Ginger as an anti-atherosclerosis could be one of the alternatives that is being developed to decrease the cardiovascular disease. The general aims of this research were determining the mechanism of ginger as anti-atherosclerosis to decrease the risk of cardiovascular disease. Research design used was "The Randomized Posttest only Control Group Design". In this research, the experimental unit was *Rattus norvegicus*, male; in the age of 3 months and total number were thirty. Independent variable of this research was steeping of ginger, the dose various of steeping ginger (control, 1g, 3g, 3g + bay leaf, and 5g), and dependent variable was Tumor Necrotic Factor (TNF) $\alpha$  of tissue lipid. TNF  $\alpha$  expression was measured by using ELISA method. The data was analyzed by using ANOVA. Based on the analysis, it showed that steeping of ginger was decreased the expression of TNF- $\alpha$  in fat tissue (1g = 551 pg/mL, 3g = 511 pg/mL, 3g + bay leaf = 493 pg /mL) compare to control (986.8 pg/mL) but on the 5 g dose there is contradictory effect that is there is increasing TNF  $\alpha$  (1103.5 pg/mL). Conclusion, steeping of ginger potentially decrease the risk of atherosclerosis by attenuate of TNF  $\alpha$  expression.

Keywords: Steeping of ginger, atherosclerosis, TNF- $\alpha$  expression

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## 1.0 INTRODUCTION

Based RISKESDAS 2013, cardiovascular disease is still the mayor cause of death in Indonesia and also in the world. People in almost all parts of the world changed in life style because of the technological advance such as high-fat diet with a little fruit and vegetables and low physical activity (sedentary life style) that can induce increased incidence of cardiovascular disease such as atherosclerosis [1].

Atherosclerosis is an inflammatory disease of the wall of large and medium-sized artery that it participated by elevated levels of low density lipoprotein (LDL) cholesterol in the blood [2]. An increased concentration of plasma low density

lipoprotein (LDL) cholesterol constitutes a mayor risk factor for atherosclerosis. Clinical, epidemiological and genetic study convincingly demonstrated that LDL promotes atherosclerosis [3]. LDL is required to transport cholesterol from the liver to tissue [4], but if the plasma level of LDL exceeds a threshold they enter the artery faster than they can remove and thus accumulate. When they accumulate they become modified including being oxidized [5] that may contribute to the initiation and progression of the atherosclerotic process [3].

Modified LDL induce endothelial cell to express protein monocyte chemo tactic protein-1 (MCP-1) that attracts monocyte from the blood in to artery wall and promote the differentiation of monocyte in

to macrophage [5]. LDL bind to the LDL receptor on hepatocytes in and other type in normal condition but modified LDL is not recognized by the LDL receptor and is taken up by scavenger receptor on macrophage. The uptake of modified LDL by macrophage does not lead to its degradation but it accumulated in macrophage in the form of cholesterol ester and convert accumulates in the macrophages and convert them to foam cell which amass in the sub endothelial space contributing to the formation of atherosclerotic plaques [4].

Macrophages express a range of cytokines including TNF and IL (interleukin)-1 and both of which activate endothelial cells to express the adhesion molecules VCAM-1, ICAM-1. The adhesion proteins bind plasma monocyte to the endothelium where they are than attracted in to artery wall by MCP-1. The entry of LDLs in the artery wall begins cycle that both commence atherosclerosis [5]. Singh *et al.* [6] further said that more than 50 % death in the developed countries cause of atherosclerosis.

Ginger is known to reduce levels of LDL cholesterol, triglycerides and free fatty acids even though the study was not the case increasing HDL cholesterol [7]. Furthermore, Paul [8] states that ginger extract has hypolipidemic effect in rats fed a diet vanaspati. Vanaspati is hydrogenated vegetable fat (HVF) plays a key role in the development of various human diseases including cardiovascular disease. Several previous studies have also reported that the administration of LPG (lyophilized ginger powder) can reduce obesity and cholesterol [9], through the cold or hot water extraction. Navaei (2008) [10] said that ginger has a significant lipid lowering effect. Ginger is consumed by steeping, it also has the potential to lower blood glucose levels [11], and improves the lipid profile [12], and however, the mechanism of action of ginger in improving the lipid profile was slightly informed.

Atherosclerosis can occur through a fairly complex mechanism of action of one of them through the expression inflammation factor, therefore, study the mechanism of action of ginger as an anti-atherosclerosis still needs to be done. This study aims to determine the role of ginger in reducing the expression of TNF alpha in adipose tissue.

## 2.0 MATERIALS AND METHODS

Research design used was "The Randomized Posttest only Control Group Design". In this research, the experimental unit was *Rattus norvegicus*, 30 male of 3 months old and with body weight  $\pm 200$ g were kept in the animal house Laboratory of Chemistry, University of Muhammadiyah Malang. All animal procedure were approve by the animal ethic committee University of Brawijaya. Ginger (*Zingiber officinale Roscoe*) was purchased from supermarket (Superindo, Malang), and TNF- $\alpha$  kit was purchased from Elabscience. The rats were divided into five

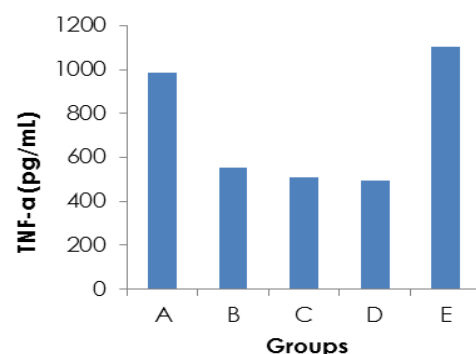
groups, one group for control (A) and four groups with various dose steeping of ginger (*Zingiber officinale Roscoe*) treatment (B-E). The various dose of treatment were 1g/kg BW (B), 3g/kg BW (C), 3g/kg BW with 10% bay-leaf (D) and 5g/kg BW (E). The rats were treated once a day for 2 months. After that, rats were dissected and rats' lipid tissues were taken. Lipid tissues were taken from abdominal lipid. Expression of TNF- $\alpha$  from lipid tissue measured by ELISA methods then the data of TNF  $\alpha$  were analyzed statistically using ANOVA and LSD test.

## 3.0 RESULTS AND DISCUSSION

Table 1 shows the TNF- $\alpha$  expression after treatment with ginger infused and Figure 1 demonstrates the relationship between TNF- $\alpha$  expression of rat's lip id tissue with treatment of steeping ginger. Based on ANOVA it showed that there is influenced steeping of ginger on decreasing TNF- $\alpha$  and based on LSD it showed steeping of ginger significantly not different in decreasing TNF- $\alpha$  of lipid tissue in dose 1g, 3g, 3g + bay leaf, nevertheless on the 5g dose there is contradictory effect that is there is increasing TNF- $\alpha$  if it is compared with control group. The decreasing of TNF- $\alpha$  with steeping of ginger cause it contains a gingerol and shogaol that functioned as antioxidant, in condition of raw and steeping [13-14]. This antioxidant can decrease the condition of lipid per oxidation. The peroxidation caused by food oxidation to change into energy and from the peroxidation that caused by other factor, such as phagocytosis. Bak [15], says that shogaol enhance antioxidant system through the induction of ARE (antioxidant response elements) and HO-1 (hemoxygenase-1) regulated by p38 MAPK and PI3k/Akt pathway in vitro and in vivo.

**Table 1** TNF- $\alpha$  expression after treatment with ginger infused

Groups	TNF- (pg/mL)
A	986.8
B	551.0
C	511.0
D	493.5
E	1103.5



**Figure 1** Relationship between TNF- $\alpha$  expression of rat's lip id tissue with treatment of steeping ginger

## 4.0 CONCLUSION

Steeping of ginger potentially decreases risk atherosclerosis through attenuate TNF a expression in dose dependent. As can be seen from the analysis, it showed that steeping of ginger was decreased the expression of TNF-a in fat tissue (1g = 551 pg/mL, 3g = 511 pg/mL, 3g + bay leaf = 493 pg /mL) compare to control (986.8 pg/mL) but on the 5 g dose there is contradictory effect that is there is increasing TNF a (1103.5 pg/mL). Conclusion, steeping of ginger potentially decrease the risk of atherosclerosis by attenuate of TNF a expression.

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