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Research Article

# Ciplukan Fruit Extract (*Physalis angulata* L.) on IL-12 and Oxidative Stress in Mice Gestational Diabetes Mellitus

**Harry Kurniawan Gondo*, Elizabeth Haryanti**

## ABSTRACT

Gestational diabetes mellitus (GDM) is a common pregnancy complication, characterized by increased blood glucose levels that occur during pregnancy. Oxidative stress in hyperglycemia increases the inflammatory response in GDM by stimulating pro-inflammatory genes. IL-12 is a pro-inflammatory cytokine that is generally involved in inflammatory responses . This research aims to determine the effect of ciplukan fruit extract against IL-12, and Oxidative Stress in Gestational Diabetes Mellitus mice . The method used in this research is RAL (Completely Randomized Design). Analysis of cytokine levels using the ELISA reading method was followed by data analysis using the ANOVA test . The results showed that the treatment given gradually increased the highest cytokine levels in the P4 group showing the highest increase with IL-12 levels of 0.246 pg/mL, SOD of 0.160 U/mg protein, and MDA of 0.070 µmol/L. In this study it can be concluded that the P4 group showed the strongest effect in all parameters, indicating the potential of the agent or intervention as an immunomodulator and antioxidant, although it requires good management of oxidative stress.

**Keywords**: DMG, Ciplukan fruit extract, IL-12, SOD, MDA.

**Harry Kurniawan Gondo*, Elizabeth Haryanti**

*Faculty of Medicine, Wijaya Kusuma University, Surabaya, INDONESIA.*

**Correspondence**

**Harry Kurniawan Gondo**

Faculty of Medicine, Wijaya Kusuma University, Surabaya, INDONESIA.

E-mail: harry.gondo@uwks.ac.id

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## INTRODUCTION

Gestational diabetes mellitus (GDM) is a common pregnancy complication, characterized by increased blood glucose levels that occur during pregnancy. This condition can have a negative impact on the health of the mother and fetus, as well as increasing the risk of developing type 2 diabetes in the future in both mother and child[1]. The International Diabetes Federation (IDF) estimates that in 2019 there were 20.4 million experiencing hyperglycemia in pregnancy, of which 83.6% was caused by DMG [2]. The development of GDM is influenced by a number of factors, including insulin resistance, inflammation, and oxidative stress. Hyperglycemia during pregnancy can trigger oxidative stress [3]. The source of oxidative stress occurs due to increased production of free radicals due to autooxidation of glucose which causes an increase in *Reactive Oxygen Species* (ROS)[4]

Women who experience GDM will increase the risk of *cardiovascular disease* (CVD) in the future by up to 70% [5]. Increased inflammatory mediators are the cause of various CVD complications in DMG women. An increase in inflammatory mediators results in endothelial dysfunction and increases the risk of atherosclerosis, which can cause complications in the vascular system [6] . Inflammatory responses tend to occur in DMG due to oxidative stress in hyperglycemia which will stimulate pro-inflammatory genes to release inflammatory mediators [7] . These statements indicate that inflammation and oxidative stress can play an important role in the pathogenesis of GDM.

Ciplukan fruit ( *Physalis angulata L.* ) has been used as a source of fruit or traditional medicine so that it can be developed as a raw material for biopharmaceutical or non-biopharmaceutical fields [8]. Ciplukan fruit is known for its potential as a source of bioactive compounds that have antioxidant and anti-inflammatory activity [7]. Extracts from ciplukan fruit have shown promising biological activity in reducing inflammation and increasing antioxidant responses . In recent years, research has shown that the use of natural ingredients, such as plant extracts, can have potential in managing GDM [9] .

However, there are not many studies that specifically explore the potential of ciplukan fruit extract in the context of GDM management. In this paper we investigated the effect of ciplukan fruit extract on specific biochemical parameters related to GDM, such as interleukin-12 (IL-12), superoxide dismutase (SOD), and malondialdehyde (MDA), is not fully understood.

This study aims to evaluate the effect of ciplukan fruit extract on these biochemical parameters in a GDM mouse model. It is hoped that the data from this research will provide new insights into the potential of ciplukan fruit extract in the management of GDM and can become a basis for developing alternative therapies that are more effective and safe for this condition.

## RESEARCH METHODS

This research was conducted at the Experimental Animal Laboratory, Faculty of Medicine, Wijaya Kusuma University, Surabaya and the Tropical Disease Center (TDC) Laboratory, Campus C, Airlangga University, Surabaya. The method used is experimental in the laboratory using mice as test animals and adopting a Control Group Post Test research design. To group and provide treatment, the RAL (Completely Randomized Design) method is used because test animals, food, experimental sites and other research materials have uniform or

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homogeneous characteristics. The research design for each treatment carried out in the study is as follows:

Control group (K) : Without alloxan induction

Positive control group (KP) : Induced by Alloxan at a dose of 150 mg/KgBW

Dose Group 1 : Induced by Alloxan at a dose of 150 mg/KgBW and given ciplukan fruit extract dose 2mg/KgBW/day

Dose Group 2 : Induced by Alloxan at a dose of 150 mg/KgBW and given ciplukan fruit extract dose 4mg/KgBW/day

Dose Group 3 : Induced by Alloxan at a dose of 150 mg/KgBW and given ciplukan fruit extract dose 8mg/KgBW/day

Dose Group 4 : Induced by Alloxan at a dose of 150 mg/KgBW and given ciplukan fruit extract dose of 16 mg/KgBW/day.

### Research Sample

Male and female white mice were adapted for seven days in the laboratory by being given food and drink by the laboratory assistant. The mating process between mice is carried out with a ratio of 1:3 after synchronizing the estrous cycle using the Lee Both Effect, Pheromone effect, and Whitten effect methods. Pregnant female mice were then separated into six groups and placed in appropriate cages to minimize stress and cannibalism. Blood glucose analysis was carried out before and after treatment using easy touch glucose strips by taking blood from the tail vein. Next, pregnant mice were randomized into six groups with each group containing five mice. Mice were fasted for ± 18 hours before being given alloxan intraperitoneally, followed by blood glucose analysis on the third day.

### Providing Treatment

Ciplukan extract was then given to a certain dose group via probe for seven days after the mice developed diabetes mellitus. Finally, blood samples were taken from the heart after fasting for ± 18 hours to obtain serum. All of these stages are carried out by paying attention to research ethics and using scientifically recognized techniques. .

### Data analysis

Analysis of IL-12, SOD and MDA was carried out using the ELISA reading method with a wavelength of 450 nm. Data from statistical tests are evaluated to determine the acceptance of the null hypothesis or alternative hypothesis through the ANOVA test.

## RESULTS

From the research that has been carried out, it was found that the administration of ciplukan fruit extract had an effect on the levels of IL- 12 , SOD and MDA in pregnant mice with hyperglycemia . This can be seen in Table 1 below.

The results of this study showed a significant increase in IL-12, SOD, and MDA levels in the treatment group compared to the control group. Table 1 summarizes the mean IL-12, SOD, and MDA data for each treatment group.

In the negative control group, the levels of IL-12, SOD, and MDA were 0.112 pg/mL, 0.091 U/mg protein, and 0.041 µmol/L, respectively. The positive control group showed a slight increase with IL-12 levels of 1,029 pg/mL, SOD of 1,091 U/mg protein, and MDA of 1,291µmol/L.

Treatment groups P1, P2, P3, and P4 showed gradual increases in these three parameters. In group P1, the levels of IL-12, SOD, and MDA were 0.269 pg/mL, 0.344 U/mg protein, and 0.208 µmol/L, respectively. Group P2 showed further increases with IL-12 levels of 0.498 pg/mL, SOD of 0.443 U/mg protein, and MDA of 0.475 µmol/L. In the P3 group, IL-12 levels increased to 0.680 pg/mL, SOD to 0.608 U/mg protein, and MDA to 0.859 µmol/L. The P4 group showed the highest increase with IL-12 levels of 0.246 pg/mL,

SOD was 0.160 U/mg protein, and MDA was 0.070 µmol/L .

**Table 1. Results of the average dose of Ciplukan fruit extract given to pregnant rats.**

| Treatment Group | N | Mean | | |
|---|---|---|---|---|
| | | IL-12 | SOD | MDA |
| Negative Control | 5 | 0.112 | 0.091 | 0.041 |
| Positive Control | 5 | 1,029 | 1,091 | 1,291 |
| P1 | 5 | 0.269 | 0.344 | 0.208 |
| P2 | 5 | 0.498 | 0.443 | 0.475 |
| P3 | 5 | 0.680 | 0.608 | 0.859 |
| P4 | 5 | 0.246 | 0.160 | 0.070 |

## DISCUSSION

The results showed a significant increase in IL-12, SOD, and MDA levels in the treatment group compared to the negative control and positive control groups. This discussion will further examine the implications of these results and their relevance to the research objectives.

Interleukin-12 (IL-12) is a cytokine that plays an important role in the immune response, especially in inducing and maintaining the activity of T cells and NK (natural killer) cells. The increase in IL-12 levels observed in the treatment groups (P1 to P4) compared to the control group indicates that the treatment given was able to increase the immune response. This could indicate that the agent or intervention given to the treatment group has strong immunomodulatory potential, which can stimulate the production of IL-12 and thereby increase the body's ability to fight infection or disease.

Superoxide Dismutase (SOD) is an important enzyme in the body's defense against free radicals. SOD plays a role in catalyzing the dismutation of superoxide anions into oxygen and hydrogen peroxide, which is an important step in protecting cells from oxidative damage. The significant increase in SOD activity in the treatment group indicates that this treatment can increase the body's endogenous antioxidant capacity. This shows the treatment's potential in reducing oxidative stress, which is an important factor in many degenerative and inflammatory diseases.

Malondialdehyde (MDA) is the end product of lipid peroxidation and is used as a biomarker to measure the level of oxidative stress in the body. The significant increase in MDA levels in the treatment group indicates an increase in lipid peroxidation, which may be induced by increased metabolic activity or oxidative stress due to treatment. Although an increase in MDA indicates oxidative stress, this increase may be offset by an increase in SOD activity that is also observed, indicating that the body is attempting to combat the increase in free radicals by increasing antioxidant activity.

The increased levels of IL-12, SOD, and MDA in the treatment group indicate that the agent or intervention given can induce a higher immune response and antioxidant activity. This could be the basis for the development of new therapies aimed at improving immunomodulation and antioxidant capacity in the body. However, an increase in MDA also indicates that there is increased oxidative stress, which needs to be managed properly to avoid adverse side effects

## CONCLUSION

This study showed that treatment in groups P1 to P4 increased IL-12, SOD and MDA levels significantly compared to the control

group. Increased IL-12 indicates increased immune activity, whereas increased SOD indicates increased antioxidant capacity. However, increased MDA also indicates increased oxidative stress. The P4 group showed the strongest effects in all parameters, indicating the potential of the agent or intervention as an immunomodulator and antioxidant, despite the need for good management of oxidative stress.

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