

## **POTENCY OF SWALLOW NEST EXTRACT (*Collocalia fuciphago*) AS PANCREAPROTECTOR THROUGH OXIDATIVE MECHANISM IN RATS (*Rattus norvegicus*) INDUCED BY STREPTOZOTOCIN**

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**Abstract:** Diabetes mellitus is a clinical syndrome with characteristics of hyperglycemia. Hyperglycemia can lead to the formation of excessive free radical compounds that trigger oxidative stress, especially on pancreatic  $\beta$  cells. Swallow nest contains amino acids which are insulin-forming compounds and glutathione that can act as a major reducing agent and antioxidant defense. The purpose of this study is to analyze the effect of swallow's nest water extract as a pancreaprotector through oxidative mechanism in rats (*Rattus norvegicus*) induced by streptozotocin. The rats induced by streptozotocin at a dose of 40 mg/kg BW and then randomly divided into 4 groups. Control groups were given aquades and 3 treatment groups, respectively were administered swallow's nest water extract at doses of 1, 10, 100 mg/kg BW for 21 days. Fasting blood glucose levels were measured on 7, 14 and 21 day. MDA measured after the animal is determined at day 28th. Level of fasting blood glucose and MDA were analyzed by statistic using Kruskal Wallis test followed by multiple comparisons *Mann Whitney* test. There was a significant decrease in fasting blood glucose level with  $p = 0.04$  in all treatment groups compared the control group. The administration of swallow nest extract significantly decreased MDA pancreas with  $p$  value = 0.000 and dose 100 mg/kgBW extract of swallow's nest significantly decrease pancreatic MDA level. The administration of swallow's nest water extract shows decrease of fasting blood sugar and has a protective effect on the rats' pancreas through oxidative mechanism.

**Keywords:** Swallow's nest extract, MDA

## INTRODUCTION

In 2014, 8.5% of adults aged 18 years and older had Diabetes Mellitus (DM). In 2015, diabetes is the direct cause of 1.6 million deaths and in 2012 high blood glucose is the cause of 2.2 million more deaths.<sup>1</sup> Based on the definition of American Diabetes Association (ADA) 2014, diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both<sup>2</sup>. Insulin is a hormone that regulates blood sugar, which is produced by pancreatic  $\beta$  cells.

Hyperglycemia a result of Diabetes Mellitus (DM) could lead to an increase in free radicals that lead to oxidative stress, it will end with the formation of Advanced Glycation Ends Products (AGEs) and dyslipidemia which contributed in the complications of diabetes.<sup>3</sup> Elevated levels of blood glucose can lead to the formation of excessive free radical compounds that trigger oxidative stress. The presence of free radicals in the body can cause cell damage, especially pancreatic  $\beta$  cells.

Oxidative stress in diabetes mellitus caused by the imbalance of redox reaction due to changes in carbohydrate and lipid metabolism.<sup>4</sup>

Pancreatic  $\beta$  cells are susceptible to oxidative stress because to the high endogenous production of reactive oxygen species (ROS) and low expression of antioxidant enzymes.<sup>5</sup> One of the studies on the effects of antioxidants on pancreatic  $\beta$  cell proliferation, study on boiled water extraction of sun-dried bitter melon have free radical scavenging activity and showed that the higher antioxidant activity of the fraction, an appropriate higher proliferation activity was observed on the treated  $\beta$  cells.<sup>6</sup>

White swallow nest contains both essential and nonessential amino acids. Amino acids are the chemical compounds that make up the hormone insulin, the

hormone insulin is a hormone that is able to open GLUT 2 and GLUT 4 for glucose into the cells to be metabolized into energy and stored into energy reserves so that plasma blood glucose levels can be down to an adequate level.<sup>5</sup> Swallow nest contains amino acids which are insulin-forming compounds, and glutathione (GSH) that can act as a major reducing agent and antioxidant defense.<sup>7</sup>

Based on research by Robertson and Harmon that antioxidants can protect beta cells lines and rodent models of type 2 diabetes against oxidative stress, thereby preserving the expression of insulin gene and  $\beta$  cell function.<sup>8</sup>

Based on the introduction, antioxidant compounds on swallow nest extract can protect pancreatic  $\beta$  cells from free radicals due to hyperglycemia and consequently the aim of this study is to analyze the effect of swallow's nest water extract as a pancreaprotector through oxidative mechanism in rats (*Rattus norvegicus*) induced by streptozotocin.

## RESEARCH METHODS

Twenty adult male Wistar rats *Rattus norvegicus* weighting 150-250g (3-4 months old) were used for inducing diabetes and randomly divided into 4 groups. The animals were injected by streptozotocin (STZ) at the dose of 40 mg/kg of the body weight intravenously. Streptozotocin induces diabetes within 7 days by destroying the beta cells.

A total of 150 g of swallow bird's nest samples were dissolved in 4.5 L aquades, then heated to 600°C for 30 minutes then at homogenizer 800 rpm for 30 minutes. Next sonicated for 30 minutes and then filtered by using 2 layers of cheesecloth. The filtrate was dried by the freeze dry method and stored at minus 20°C.

On the seventh day after induced by streptozotocin all groups were administrated

of substance test for 21 day. Control groups were given aquades (K1) and 3 treatment groups, respectively were administered swallow nest extract at doses of 1 mg/kg BW (K2), 10 mg/kg BW (K3), 100 mg/kg BW (K4).

Fasting blood glucose levels were measured on the first, seventh, fourteenth day and the twenty-first day. MDA measured after the animal is determined at day 28<sup>th</sup>.

Fast blood glucose levels and malondialdehyde (MDA) level in pancreatic were analyzed by statistic using Kruskal Wall is test followed by multiple comparisons *Mann Whitney* test to know which groups were different, where the difference was considered statistically significant when  $p < 0.05$ .

## RESULTS AND DISCUSSION

Fasting blood glucose levels in all groups showed an increase after induced by streptozotocin. There was a significant decrease in fasting blood glucose level with  $p = 0.04$  in all treatment groups compared with the control group.

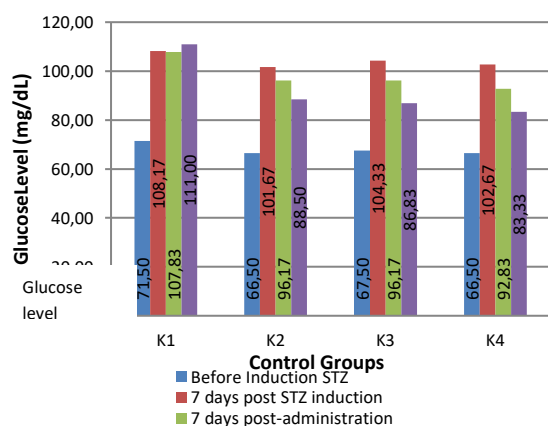


Figure 1. Fasting Blood Sugar Levels in all groups (K1: Control groups; K2, K3, K4: respectively swallow nest extract at doses of 1 mg/kg BW; 10 mg/kg BW; 100 mg/kg BW)

The administration of swallow nest extract significantly decreased MDA pancreas with  $p$  value = 0.000 and dose 100 mg/kg BB extract of swallow nest significantly decrease pancreatic MDA level

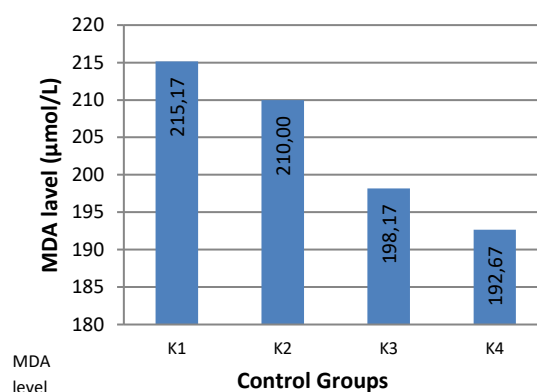


Figure. 2. MDA Levels in all groups (K1: Control groups; K2, K3, K4: respectively swallow nest extract at doses of 1 mg/kg BW; 10 mg/kg BW; 100 mg/kg BW)

Based on the results of this study showed the induction of streptozotocin single dose 40 mg / kgBB can increase blood sugar levels in rat *Rattus novergicus*. Streptozotocin is a synthetic antineoplastic agent that is classically an anti-tumor antibiotic<sup>9</sup> this agent is synthesized by soil microorganisms *Streptomyces achromogenes* and is used to induce both insulin-dependent and non-insulin-dependent diabetes mellitus<sup>10</sup>.

The elevated levels of blood glucose or hyperglycemia could lead to an increase in free radicals that lead to oxidative stress.

Research by Hun et al. showed the content of swallow's nest is carbohydrates (46.47%) and proteins (35.8%) were the major constituents, with little fats (1.5%) and no fibre. Amino acid analysis by AccQ.Tag method revealed all eighteen types of amino acids including the eight essential ones<sup>11</sup>. Swallow nest contains three

amino acids that form thioxy and naturally in the body. Swallow nest contains glutathione. Glutathione ( $\gamma$ -glutamyl-cysteinyl-glycine) formed from the incorporation of three amino acids, namely cysteine, glutamate and glycine. GSH is considered an important factor in cell function and defense against oxidative stress<sup>12</sup>.

Hyperglycemia a result of Diabetes Mellitus (DM) could lead to an increase in free radicals that lead to oxidative stress. Malondialdehyde (MDA) is an end product of lipid peroxidation. Lipid peroxidation was caused by reactive oxygen species, which were induced to hyperglycemia.

Hydrogen peroxide ( $H_2O_2$ ) is converted to highly reactive ROS in the form of hydroxyl radical with the help of transition metal such as iron ( $Fe^{+}$ ) and copper (Cu). Hydroxyl radicals induce DNA cleavage and lipid peroxidation in the membrane structure of phospholipids causing cell death and disposal of metabolic products in the form of MDA<sup>13</sup>.

According to research by Hun etc, it is not exactly known how the walet nest extracts work as anti-oxidants, however some of the proteins and amino acids detected in walet nest extracts have known anti-oxidant activities. For example, Cys, Met, His, Try and Lys are the amino acids that have been proven for their anti-oxidant activities, mechanism of anti-oxidant activity may be due to the involvement of hydroxyl and carboxyl groups of the amino acid chains<sup>11</sup>. Antioxidant compounds from walet nest extracts may trap organic free radicals from lipid oxidation and help reduce lipid peroxidation and may cause MDA decreases.

The results of MDA levels measurements showed that MDA levels in rat's pancreatic tissue induced by streptozotocin increased. MDA levels in the control group (K1) showed the highest

level compared to the treatment group. This means that the induced Streptozotocin in rats causes the capacity of free radicals in the body to increase as a result of the release of nitrogen oxide (NO) radicals from STZ. In the treatment group administered of swallow's nest water extract for 21 days showed significantly MDA levels decreases. group therapy with a dose of 100 mg/kg BW (K4) showed the lowest decrease in MDA levels. This means that the greater the dose of the swallow's nest water extract, the higher the inhibitory activity of the oxidation process. Inhibition of the oxidation process is caused by the antioxidant glutathione that contained in the swallow's nest water extract.

## CONCLUSIONS

The administration of swallow's nest water extract shows decrease of fasting blood sugar and has a protective effect on the rats' pancreas through oxidative mechanism.

Further research needs to be done regarding the glutathione compounds contained in the swiftlet nest extract as pancreaprotector

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