Swallow nest extract can be able to prevent nephropathy diabetic of the white rats streptozotocin-induced

by Triawanti Triawanti

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T Triawanti[1*], F D Alexandra[2], A Frethernity[2] and S Mahmud[3]

[1]Department of Biochemistry of Medical Faculty of Lambung Mangkurat University, Banjarmasin, Indonesia
[2]Department of Pharmacology of Medical Faculty of Palangka Raya University, Palangka Raya, Indonesia
[3]Medical Faculty of Palangka Raya University, Palangka Raya, Indonesia

*Corresponding author's email: tria_fkunlam@yahoo.co.id

Abstract. Hyperglycemia that occurs in diabetic mellitus leads to glycation reactions in protein molecules and oxidative stress resulting in damage to cells and organs. Swallow nest believed society can lower blood glucose. The objective of the study was to analyze the potency of water swallow nest extract to prevent nephrophaty diabetic. The study used Post test-Only with Control Group Design, which consisted of 1 control group (K = aquadest) and 3 treatment groups (nest swallow nest dose 1, 10 and 100 mg / kg BW) each group consisted of 6 *Rattus Norvegicius*. Before treatment, means of glucose level rats have been 68 mg/DL, then rats were induced Streptozotocin in a dose of 40 mg / kg BW intraperitoneally. Day 7th after induction, rats had elevated glucose ± 102 - 108 mg / dL. Then the rats were given water extract nest swallow white for 28 days orally. All data were analyzed by Kruskall-Wallis test followed by Mann-Whitney test with 95% confidence level. The results of blood glucose levels in each group (K, P1, P2 and P3) were 111.0 vs 88.5 vs 86 vs 83 mg / dL (p = 0.004), pancreas H_2O_2 levels were 10.16 vs 9.20 vs 8.81 vs 7.27 (p=0,000), serum H_2O_2 levels were 17.35 vs 16.39 vs 15.01 vs 11.96 (p=0.044), renal methylglioxal levels were 242.55 vs 134.34 vs 67.12 vs 50.48% (p = 0,000) and renal AOPP levels were 1.17 vs 1.09 vs 1.05 vs 1.00 (p=0.000) respectively. The Mann-Whitney test showed a dose of 100 mg / kgBW has the greatest potential. In conclusion the swallow nest water extract has potential as an antidiabetic and prevent of renal's damage.
Keywords: Swallow Nest (*Collocalia fuciphaga*) Water Extract, hyperglycemia, oxidative stress, nephropathy diabetic

1. Introduction

Diabetic Nepropathy is kidney damage that occurs due to the accumulation of protein in the glomerular basal mesangial membrane in the condition of diabetes mellitus. Kidney damage can occur through a mechanism of oxidative stress and an inflammatory response. Chronic hyperglycemia will trigger the formation of reactive oxygen species (ROS). The combination of the glycation and oxidation reactions of glucose forms compounds of AGEs [1]. Previous studies have shown an increase in the levels of AGEs in streptozotocin-induced mice (STZ) [2]. The accumulation of AGEs compounds will aggravate diabetes mellitus because it causes fibrosis formation, atherosclerotic plaques, increased systolic and

diastolic blood pressure [3]. One of the potent AGEs compounds, methylglioxal (MG) is formed from the degradation of glycolytic intermediates, protein glycation and lipid peroxidation [4, 5].

Advanced oxidation protein products (AOPPs) are protein products that contain dityrosin and cross-linking and are formed during oxidative stress. AOPP is a marker of oxidative stress and inflammatory mediators. AOPP in the diabetic group of patients is significantly higher than the control [6]. The chronic accumulation of AOPPs can trigger renal inflammation in diabetes presumably through activation of renal NADP oxidase. Increased AOPP triggers an increase in the expression of monocyte chemoatractan protein 1 (MCP-1) and infiltration of macrophages as markers of inflammation in diabetic kidneys [7].

DM therapy still uses pharmacotherapy drugs. However, it is not uncommon for people to choose traditional treatments that are believed to be able to treat diabetes mellitus, including white swallow nests (Collocalia fuciphagus). The wallet bird nest in Indonesia contains amino acid histidine, leucine, threonine, valine, methionine, isoleucine, phenylalanine, serine, aspartate, arginine, lysine, proline, glutamate acid, glycine, alanine, and tyrosine [8]. Administration of amino acids can increase insulin secretion in type 2 DM patients [9]. Lysine, arginine, alanine, aspartate and glutamate amino acids showed antiglycating effects by means of competitive inhibition. Amino acids can also increase tissue sensitivity to insulin and reduce oxidative stress [10]. Administration of the alanine to obese mice can improve systemic glucose tolerance by activating the AMP kinase system and modulating systemic glucose metabolism [11]. So far, not many studies have evaluated the potential extract of swallow nest water as antidiabetic while preventing kidney damage. This study aims to analyze the potential of swallow nest extract in preventing diabetic nephropathy.

2. Material and method

2.1. Animal study

This study used male white rats *(Rattus norvegicus)* as the models. This work was approved by the Animal Care and Experimentation Committee (Ethical Committee], Faculty of Medicine Palangka Raya University) by letter of number 839/UN24.9/LL/2018. This research is a true experimental design that uses Posttest Control Group Design. The treatment group was divided into 4 groups: (K) rats induced Streptozotocin + aquadest; (P1) rats induced strptozotocin + swallow's nest water extract 1 mg/kgBW; (P2) rats induced streptozotocin + swallow's nest water extract 10 mg/kgBW; (P3) rats induced strptozotocin + swallow's nest water extract 100 mg/kgBW.

2.2. Preparation of swallow's nest water extract

Swallow nest swiftlet cleaned of feathers attached using tweezers. Then swallow nest is cleaned under running water for ± 5 minutes, then dried at room temperature. Once clean, the sample is smoothed using a blender. 300 grams swallow's nest was smoothed using of mortar and dissolved in 4.5L aquades and homogenized for 30 minutes. Then in centrifuge at 10000 rpm for 10 minutes. The dosage of swallow's nest water extract in rats was divided into three doses: 1 mg/kgBW, 10 mg/kgBW, and 100 mg/kgBW.

2.3. Induction of streptozotocin in experimental animals

Rats underwent acclimatization weighed, then fasted for 10 hours. After being fasted for 10 hours, blood samples were taken from the vein of the tail at minute 0 to determine baseline blood glucose levels. Furthermore, white rats were induced streptozotocin (Bioworld®) with a dose of 40 mg/kgBW of intra-peritoneal[12]. After induced rats continue to be given food and drink, wait in 4 days, then measure blood glucose levels. Mice are considered hyperglycemia when blood glucose levels >100 mg/dL. On the seventh day, blood glucose levels were measured to determine whether there was an increase.

2.4. Administration of swallow's nest water extract

The swallow nest water extract is made into a solution and administered daily using gastric tube, 2 hours after meals with a dose of 1mg/kgBW, 10 mg/kgBW, and 100 mg/kgBW. Glucose levels were measured at weeks 4th after administration of the test solution using a glucometer.

2.5. Measurement of hydrogen peroxide (H_2O_2) levels

Measurement of H_2O_2 was using a spectrophotometer. At first, making a standard curve. A total of 20 µmol H_2O_2 (Merck®) was added with 2 ml of dichromate:glacial acetic acid (Merck®) (1:3) mixture. Then the mixture was heated in boiling water for 10 minutes. Then the cooled mixture was measured for absorbance at a wavelength of 570 nm. The same procedure was done for 40, 60, 80, 100, 120, 140, 160 and 180 µmol H_2O_2. A graph was made between the absorbance on the Y axis with levels of H_2O_2 on the X axis to obtain a linear equation.

Preparation of test solution was made with a total of 1 ml of serum homogenate was added 5 ml of PBS (Merck®) pH 7.4. A mixture of 1 ml was taken and added to 2 ml of dichromate:acetate (Merck®) (1:3) mixture and then wrapped in aluminum foil for 30 minutes. The mixed solution was heated using a water bath for 10 minutes at 100˚C. The solution was cooled to room temperature. The solution was then transferred into the cuvette and measured its absorbance using UV-VIS at a wavelength of 570 nm [13].

2.6. Measurement of methylglioxal levels

On the 29th day the rats were sacrificed and the kidneys were taken to be homogenized. A total of 25 µL homogenate was added 350 µL DNPH (Merck®) (0.1% DNPH in 2 N HCl) and then added 2.125 mL of aquadest. After that incubated for 15 minutes at 37°C, then add 1.5 mL 10% NaOH (Merck®). Read the absorbance at λ = 576 nm (A1). Furthermore, as much as 0.25 mL of renal homogenate was added DNPH of 1 mL. Then the solutions were incubated for 45 min at room temperature and shielded from light, and shaken with vortex every 15 minutes. The next step adds 1 mL of TCA (Merck®) 20% to then incubated in ice for 5 minutes. Centrifuged for 5 minutes at 1400 rpm, and discarded the supernatant. After washing by adding 1 mL of ethanol-ethyl acetate into each tube, centrifugation for 5 minutes at a speed of 1400 rpm, then discard the supernatant. Washing is repeated 3 times. The end stage of measuring this carbonyl compound is to add 1 mL of urea 9 M, and incubate the solution at 37°C for 10 min while shaken. After that the solution was centrifuged at 1400 rpm for 5 minutes. Furthermore, the resulting color measured uptake at a wavelength of 390 nm. (A2) [14].

$$\text{Level of methylglioxal} = \frac{A1}{A2} \text{ x } 100\% \quad (1)$$

2.7. Measurement of AOPP levels

The test solution was prepared by mixing 200 µL homogenate, 600 L PBS, and 100 L KI 1.16 M (Merck®). Then the blank solution was prepared by mixing 800 L of PBS, 100 L KI 1.16 M. Test and blank solution were placed for 2 min and then add 200 µL of acetic acid. Absorbance was measured at = 340 nm. The concentration of AOPPs were expressed through A = ε b C with ε = 26 $mM^{-1}cm^{-1}$ and b = 1 cm [15,16].

2.8. Statistical analysis

Data were analyzed by normality and homogenity test. Therefore, the data is not normal then the non parametric test is Kruskall Wallis followed by Mann Whitney test with 95% confidence level.

3. Results

In this study, the protein content of swallow's nests was tested using spectrophotometric examination methods with a wavelength of 546 nm and with repetitions three times, the average yield obtained was 38.33%.

3.1. Blood Glucose Level

STZ-induced rats at a dose of 40 mg / kgBW intraperitoneally, after the seventh day obtained an increase in glucose levels of 36.3 mg / dL (Table 1). Then followed by giving swallow nest water extract at a dose of 1 mg / kgBW, 10 mg / kg BW and 100 mg / kgBW for 28 days (Figure 1).

Table 1. Blood glucose level of rats before and after Streptozotocin-induced.

Streptozotocin-induced	Glucose level	p value
Before	68 mg/dl	0.000
after	104.2 mg/dl	

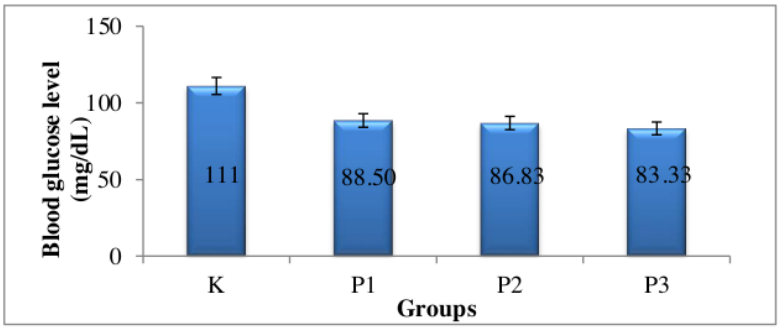

Figure 1. Mean of blood glucose level after Swallow nest water extract treatment ($p<0.05$) K = Control (aquadest); P1 = 1 mg/kg BW; P2 = 10 mg/kgBW; P3 = 100 mg/kgBW.

Kruskal Wallis test obtained $p < 0.05$, then continued by post hoc test by using Mann Whitney test. The results of the Mann Whitney test showed differences between treatment groups and negative control groups. This proves that the water extract of bird nest can lower blood glucose levels in STZ-induced mice. Between dose of 1 mg/kgBW vs. 10 mg/kgBW vs. 100 mg/kgBW did not significant difference, meaning dose of 1 mg/kgBW had the same ability with dose of 100 mg/kgBW in lowering blood glucose level.

3.2. Pancreas Hydrogen peroxide (H_2O_2) levels

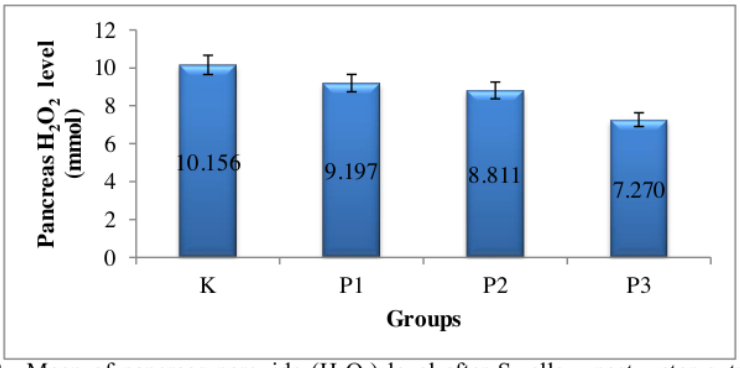

Figure 2. Mean of pancreas peroxide (H_2O_2) level after Swallow nest water extract treatment K = Control (aquadest); P1=1 mg/kgBW; P2=10 mg/kgBW; P3=100 mg/kgBW ($p=0.000$).

The results of the Kruskal Wallis standard test obtained a value of $p = 0{,}000$. Then followed by post hoc test using the Mann Whitney test. The results of the Mann Whitney test found differences between all treatment groups and negative control groups, P1 and P2 ($p = 0.002$), P1 and P3 ($p = 0.002$) and P2 and

P3 ($p = 0.002$). This proves that the administration of swallow's nest water extract can reduce levels of H_2O_2 in STZ-induced rat pancreas. The higher the dose of swallow nest extract, the lower the H_2O_2 content is formed.

3.3. *Serum H_2O_2 levels*

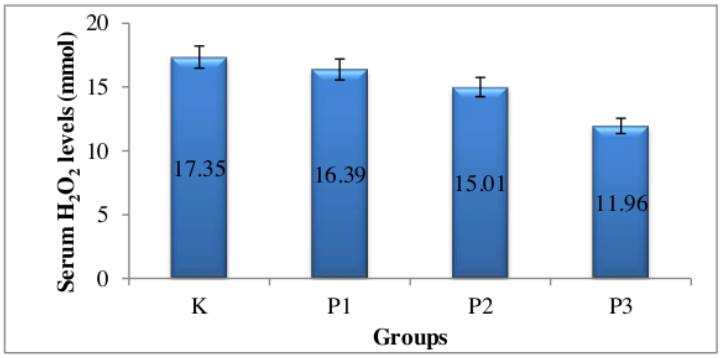

Figure 3. Mean of serum peroxide (H_2O_2) level after Swallow nest water extract treatment K = Control (aquadest); P1=1 mg/kgBW; P2=10 mg/kgBW; P3=100 mg/kgBW (p=0.044).

The results of the statistical test with nonparametric analysis, namely the Kruskal Wallis test showed that $p = 0.044$ ($p < 0.05$), which means that there are minimal differences in the 2 treatment groups. Then followed by post hoc test using the Mann Whitney test. The results of the Mann Whitney test found that there were differences between all treatment groups and negative control groups, but there was no difference between P1, P2, and P3. This proves that the administration of swallow's nest water extract can reduce serum H_2O_2 levels of hyperglycemic mice at a dose of 1 mg / kgBW.

3.4. *Renal methylglioxal (MG) levels*

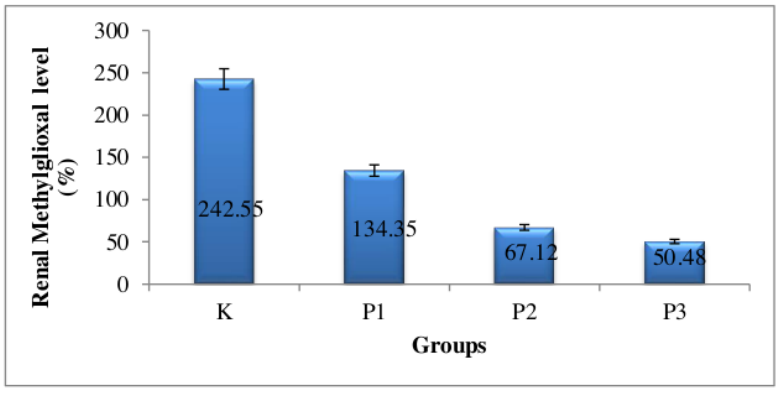

Figure 4. Mean of Methylglioxal (MG) level after Swallow nest water extract treatment K = Control (aquadest); P1=1 mg/kgBW; P2=10 mg/kgBW; P3=100 mg/kgBW (p=0.002).

Data was analyzed used Kruskal Wallis test followed by Mann Whitney test with 95% confidence level. The result of statistical test showed that there was significant difference between the negative control

group and the group given the extract of swallow nest (p = 0.002), and between group of dose 1 mg/kgBW vs. 10 mg/kgBW vs. 100 mg/kgBW obtained significant difference (p = 0.002). This suggests that the swallow's nest water extract can reduce the formation of MG compounds where the higher the dose given the less the resulting MG will be.

3.5. Renal Advanced oxidation protein products (AOPPs) level

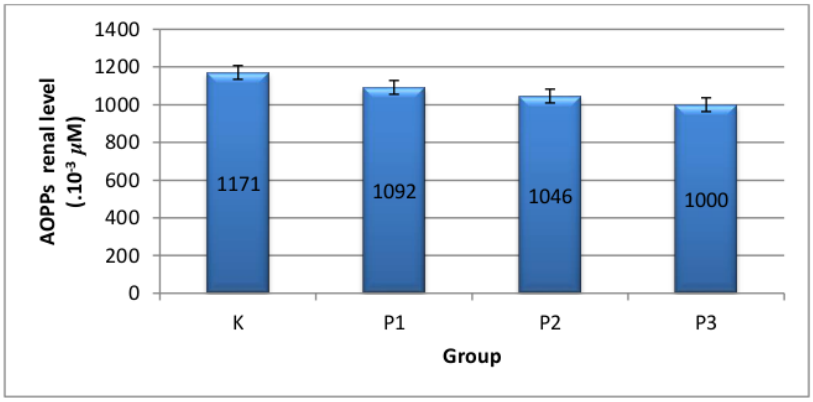

Figure 5. Mean of renal AOPPs level after Swallow nest water extract treatment K = Control (aquadest); P1=1 mg/kg BW; P2=10 mg/kgBW; P3=100 mg/kgBW (p=0.000).

The results of the Kruskal Wallis statistical test p value = 0.000, followed by the Mann Whitney post hoc test. The results of the Mann Whitney test found differences between all treatment groups and negative control groups, P1 and P3 (p = 0.009), and between groups P2 and P3 (p = 0.041). This proves that the administration of swallow's nest water extract can reduce AOPPs levels in hyperglycemic mice. The higher the dose of swallow nest extract, the lower the level of AOPPs formed.

4. Discussion

In this study, intraperitoneal low doses of Streptozotocin 40 mg / KgBB were used to induce rats of Type 2 diabetes mellitus, because high doses were reported to cause many deaths in the first week because of extensive damage to the pancreatic beta cells which caused an increase in blood glucose levels that were not under control. In small doses, pancreatic beta cell partial damage occurs. The increase in fasting blood glucose levels in STZ administration is caused by pancreatic beta cell damage and death. Initial damage to pancreatic beta cells occurs within 2-4 days after STZ administration, which is characterized by pancreatic swelling and beta cell degeneration in Langerhans island [12].

Based on table 1 the results of the average glucose level of the rat before it was induced by streptozotocin 68 mg/dL. After streptozotocin was induced, the rat's blood glucose levels increased to 104.2 mg/dL. Based on the results obtained, normal fasting blood glucose levels are in the range between 56 - 80 mg/dL. After being induced by STZ, blood glucose levels experienced a significant increase, which was an average of 104.2 mg/dL, so that it could be said that rats had experienced hyperglycemia.

The formation of the hormone insulin requires essential amino acids obtained from outside intake. In this study the administration of swallow's nest water extract which contains many essential amino acids can increase the synthesis of the hormone insulin. With the increase in the production of the hormone insulin, blood glucose levels can be lowered, as evidenced from this study where the blood glucose levels of rats given swallow nest extract with various doses were lower than that in the aquadest group (Figure 1). Previous study which provided a carbohydrate + free amino acid diet in patients with

Type 2 diabetes showed an increase in insulin secretion. Leucine amino acids, arginine and phenylalanine and their derivatives stimulate pancreatic Beta cell function and insulin secretion [9].

Lower pancreatic peroxide levels and serum in the group given swallow nest extract proved that swallow nest extract at a dose of 1 mg/kgBB was able to reduce free radicals formed in the pancreas due to STZ induction (Figures 2 and 3). STZ cytotoxicity causes the release of free radicals which trigger intracellular oxidative stress. Streptozotocin selectively tends to enter and accumulate in pancreatic beta cells, which are mediated by glucose 2 transporter bonds (GLUT2) in the plasma membrane. Other organs expressing GLUT2 such as the liver and kidneys also suffer damage from STZ induction [12].

The decrease in serum and pancreatic peroxide levels is thought to be due to the influence of the amino acid alanine contained in swallow nest. Among the amino acids that play a role in increasing insulin secretion, alanine has a long action in regulation of the function and integrity of pancreatic beta cells. Alanine stimulates the beta cell anti-apoptotic mechanism which involves decreasing levels of nitrogen species (RNS) and ROS. This is related to changes in gene expression involved in cellular signaling, metabolism, gene regulation, protein synthesis, apoptosis and cellular stress response. The greatest protective effect of Alanine does not depend on the decrease in NO production but is related to upregulation of catalase. This speeds up the conversion of H_2O_2 and its implications, decreasing levels of O_2- and peroxynitrite [10].

High level of blood glucose is chronic hyperglycemic state form advanced glycation products (AGEs) because glucose which binds to proteins (glycated protein) through the Maillard reaction can be oxidized and produce reactive Oxygen Species (ROS). The combination of glycation and glucose oxidation results in the formation of AGEs [1]. Methylglyoxal is one of the AGEs compounds. Glioksal, methylglioxal (MG) and 3-deoxyglucosone (3-DG) are powerful glycation compounds formed from the degradation of the compounds of glycolytic intermediates, protein glycation and lipid peroxidation. They react quickly with proteins to form AGEs, especially in arginine residues. The most important quantitative AGEs are arginine-derived hydroimidazolones formed by glyoxal, methylglioxal and 3-DG [4]. Physiologically, MG could detoxified by the enzyme glyoxalase 1 (Glo1) , using reduced glutathione as a co-factor. In the diabetic mellitus MG has also been shown to cause pathologic structural alterations and impair kidney function. Conversely, MG scavengers (such as N-acetylcysteine, aminoguanidine or metformin) or Nrf2/Glo1 activators (such as trans-resveratrol / hesperetin) are shown to be useful in preventing MG-induced cardiovascular and renal complications in diabetes [17].

In the study of Triawanti et al [2] it was reported that hyperglycemic rats given caramunting fruit juice at a dose of 1 mg / gBB had a low level of methylglioxal compared to those given aquadest significantly. When compared with the group given metformin, the levels were not significantly different. This is presumably because of the antioxidant content in caramunting fruit juices, namely flavonoids. Antioxidants function to reduce free radicals (ROS) that are formed due to glycation reactions.

In this study, swallow's nests have been shown to reduce levels of methylglyoxal kidney, where at a dose of 1 mg / kgBB it has shown significantly lower levels compared to those given only aquadest. Meanwhile at higher doses of 10 and 100 mg / kgBW the decrease in methylglioxal levels was greater (Figure 4). Swallow nests also contain the amino acid glycine. Previous studies have shown that diabetic rats given glycine showed less enlargement of the glomerular basal membrane than controls. This is because the secondary effect of glycine is its high solubility which prevents the formation and precipitation of AGEs products [10].

Advanced oxidation protein products (AOPPs) are a family of oxidized protein compounds that appear as new inflammatory mediators. AOPPs are protein products that contain dityrosin and cross-linking, formed during oxidative stress. Plasma AOPPs are mainly carried by albumin. The accumulation of AOPPs was first found in dialysis patients and is clearly shown in diabetic patients. Shi et al [7] reported that administration of AOPP-albumin infusion significantly increased macrophage infiltration in rat kidneys. Increased macrophage influx was also shown in the aorta of hypercholesterolemic mice stimulated by AOPPs. Apriani et al [15] study reported that in diabetic model rats, bone AOPP levels were positively correlated with increased blood glucose levels.

In this study it was seen that mice with hyperglycemia showed a high increase in AOPP levels. However, after administration of swallow nest extract at a dose of 1 mg/kgBW, 10 mg/kgBW and 100 mg/kgBW there was a significant decrease. The dose that shows the best decrease is 100 mg/kgBW. If it is associated with a decrease in glucose levels, the effective dose of swallow nest extract can reduce glucose levels as well as AOPPs levels starting at a dose of 1 mg/kgBW. Meanwhile at higher doses of 10 and 100 mg/kgBW the decrease in AOPPs levels looks bigger.

Swallow nests contain amino acids glycine, glutamic acid, and cysteine which are the substrate of the gluthathion enzyme which is an enzymatic antioxidant that plays a role in converting hydrogen peroxide compounds to H_2O and O_2. Previous studies have reported that the administration of seluang fish containing cysteine can reduce oxidative stress in the brains of malnourished mice. In this study the H_2O_2 levels of the groups given Seluang fish proved to be lower compared to those given standard feed. It is suspected that the cysteine content found in Seluang fish can increase gluthathion production [18]. Glutathione is a three-amino acid antioxidant tripeptide, cysteine, glycine, and glutamate, which catalyzes the reaction of H_2O_2 to H_2O and O_2. Glutathione is an important antioxidant contained in vital organs and bone marrow of life [19].

In this study it was proven that H_2O_2 levels in the pancreas and blood were significantly lower after administration of swallow nest extract. This indicates that the amino acids contained in swallow nests can increase insulin secretion, and reduce oxidative stress that occurs in the pancreas, so as to reduce glucose levels and prevent kidney damage due to glycation and inflammatory process.

5. Conclusion

Swallow's nest water extract had potency as an antidiabetic and prevent to renal's damage through the mechanism of (1) increased production of insulin so that glucose can be lowered; (2) the reduction of free radicals by enzymes gluthathion peroxidase thus lowering production methylglioxal and advanced oxidation protein products as a marker oxidative stress and inflamation.

References

[1] Novotny K T, Jung A, Hohn D, Weber and T Grune 2015 Advanced glycation end products and oxidative stress in type 2 diabetes mellitus *Biomolecules* **5** 194-222

[2] Triawanti, Suhartono E, Ramadhan Y, Zakina OF, Nurikhwan PW, Sanjaya A and Alam G A A 2017 Effect of karamunting fruit juice (Melastoma malabathricum L) to advanceds glycation end products (AGEs) and lipid profile as advanced complications of diabetes mellitus *Journal of engineering and Applied Sciences* **12** (2) 186-194

[3] Sadowska-Bartoz I and Bartosz G 2015 Prevention of protein glycation by natural compounds *Molecules* **20** 3309-3334

[4] Karachalias N, Babaei-Jadidi R, Rabbani N and Thornalley P J 2010 Increased protein damage in renal glomeruli, retina, nerve, plasma and urine and its prevention by thiamine and benfotiamine therapy in a rat model of diabetes *Diabetologia* **53** (7) 1506–1516

[5] Turk Z 2010 Glycoptoxine, carbonyl stress and relevance to diabetes and its complications *Physiol. Res.* **59** 147-156

[6] Jakus V, Sandorova E, Kalninova and Krahulec B 2014 Monitoring of glycation, oxidative stress and inflammation in relation to the occurence of vascular complications in patients with type 2 diabetes mellitus *Physiol. Res.* **63** 297-309

[7] Shi X Y, Hou F F, Niu H X, Wang G B, Xie D, Guo Z J, Zhou Z M, Yang F, Tian J W and Zhang X 2008 Advanced oxidation protein products promote inflammation in diabetic kidney through activation of renal nicotinamide adenine dinucleotide phosphate oxidase *Endocrinology* **149** (4) 1829-1839

[8] Elfita L 2014 Analisis profil protein dan asam amino sarang burung walet (*Collocalia fuchiphaga*) asal Painan *Jurnal Sains dan Farmasi Klinis* **1** (1) 27-37

[9] Van Loon L J C, Kruijshoop M, Menheere P P C A, Wagenmakers A J M, Saris W H M and Krezer H A 2003 Amino acid ingestion strongly enhances insulin secretion in patients with long-term type 2 diabetes *Diabetes Care* **26** (3) 625-630
[10] Anuradha C V 2009 Aminoacid support in the prevention of diabetes and diabetic complications *Current protein and Peptide Science* **10** 8-17
[11] Adachi Y, Sousa-Coelho A L D, Harata I, Aoun C, Weimer S, Shi X, Herrera K N G, Takahashi H, Doherty C, Noguchi Y, Goodyear L J, Haigis M C, Gerszten R E and Patti M E 2018 L-alanine activates hepatic AMP-activated protein kinase and modulates systemic glucose metabolism *Molecular Metabolism* **17** 61-70
[12] Nugroho A E 2006 Hewan percobaan diabetes mellitus: patologi dan mekanisme aksi diabetogenik *Biodiversitas* **7** (4) 378-382
[13] Suhartono E and Setiawan B 2010 Model Indeks Peroksidatif dan Indeks Protein Teroksidasi Saliva Penderita Tuberkulosis Paru Berdasarkan Lama Pengobatan *JKM* **2** (9) 118-123
[14] Biswas U K, Banerjee S, Das A and Kumar A 2011 Elevation of serum methyglyoxal may be used as a screening marker in oral premalignant lesions *Biomedical Research Journal* **22** (3) 273-278
[15] Apriani N, Suhartono E and Akbar I Z 2011 Korelasi kadar glukosa darah dengan kadar advanced oxidation protein products (AOPP) tulang pada tikus putih model hiperglikemia *Jurnal Kedokteran Maranatha* **11** (1) 15-18
[16] Setiawan B, Adenan and Suhartono E 2012 Model indeks peroksidatif dan kadar advanced oxidation protein products (AOPPs) saliva penderita tuberkulosis paru berdasarkan lama pengobatan *J. Respir. Indo.* **32** (2) 72-77
[17] Sankaralingam S, Ibrahim A, Rahman M, Eid A H and Munusamy S 2018 Role of methylgyoxal in diabetic cardiovascular and kidney diseases: insight from basic science for application into clinical practice *Current Pharmaceutical design* **24** (26)
[18] Triawanti, Sanyoto D D and Nur'amin H W 2017 Reduction of oxidative stress by seluang fish (Rasbora Spp.) in brain of malnourished rats (Rattus norvegicus) *International Journal of Food Enginering* **3** (2) 107-111
[19] Piste P 2013 Cysteine-master antioxidant *Int. J. Pharm. Chem. Biol. Sci.* **3** (1) 143–149

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