Antidiabetic Activity Studies of White Tea (*Camellia sinensis* (L.) O. Kuntze) Ethanolic Extracts in Streptozotocin-nicotinamide Induced Diabetic Rats

Lia Ardiana, Rani Sauriasari*, Berna Elya

**ABSTRACT**

**Background:** The high polyphenol content of white tea exhibits antiseptic and antioxidant properties that can prevent free radicals, inhibit oxidative stress and inflammation associated with various diseases such as obesity, diabetes and other degenerative diseases. Oral administration of white tea ethanolic extract (WTE) is expected to use as an alternative in the treatment of diabetes mellitus. **Objective:** This study aims to evaluate the effect of WTE on reducing fasting blood glucose levels in diabetic rats. **Methods:** Antidiabetic activity study of white tea extract performed on diabetic Sprague-Dawley male rats induced streptozotocin-nicotinamide for 14 days of oral administration. The antidiabetic effect compared to control, diabetic control, and standard control groups. **Results:** The administration of WTE for 14 days showed decreased fasting blood glucose level in diabetic rats. The dose of 100 mg/kg BW of WTE has the highest effect on reducing fasting glucose level significantly compared to negative control group (p<0.05). The content of flavonoids, especially catechin compounds are suspected to play a role in lowering fasting blood glucose levels. **Conclusion:** The administration of WTE for 14 days has potentially antidiabetic activity in diabetic rats induced streptozotocin-nicotinamide.

**Key words:** Antidiabetic, *Camellia sinensis*, Catechin, Hypoglycemic, Streptozotocin, White tea.

**INTRODUCTION**

Diabetes mellitus (DM) is a major public health problem, and its incidence has increased rates continuously. Insulin ineffectiveness in DM patients causes metabolic disorders characterized by high levels of blood glucose or hyperglycemia and accompanied by changes in lipid metabolism, carbohydrates, and proteins that may lead to an increased risk of complications from vascular disease. The global study report states that DM is one of the non-communicable diseases based on the number of cases and its prevalence has continued to increase over the last few decades. Research and development to get new drugs as an alternative medicine for DM have been mostly done mainly from herbal materials. One of popular herb in public is a tea leaf, *Camellia sinensis* (L.) O. Kuntze (family Theaceae). White tea is one type of tea taken is a very young shoot or tea leaves or buds that are known to have high polyphenol content and exhibits antiseptic and antioxidant properties. The process of white tea is quite simple that is through of steaming and drying to prevent the occurrence of the enzymatic oxidation process. The antioxidant properties of white tea can prevent free radicals, inhibit oxidative stress and inflammation associated with various diseases such as obesity, dyslipidemia, diabetes, cardiovascular, neurodegenerative and cancer. The recent research showed the *in vitro* inhibitory activity of WTE against the α-amylase enzyme (with 99.11 ± 0.01% inhibition percentage); α-glucosidase (IC₅₀, 10.54 μg / mL); and dipeptidyl peptidase IV (DPP-IV) enzyme (with 30.57 ± 0.08% inhibition rate). This research considered that WTE has the highest inhibitory activity against DPP-IV enzyme. Therefore, to prove the *in vivo* antidiabetic activity of WTE, the study on the effect of reducing fasting blood glucose levels in diabetic animals will be carried out.

**MATERIALS AND METHODS**

**Plant Material and Extraction**

The white tea leaves (*Camellia sinensis* (L.) O. Kuntze) obtained from the Tea Plantation and Quinine Research Center in Gamboeng, West Java, Indone-

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nesia, was determined by Center for Plant Conservation Botanic Garden, Indonesian Institute of Science, Indonesia. The extraction process conducted by using reflux method with ethanol 70% as a solvent at 60 °C for 3 h and three times re-extraction. The filtrate from extraction process then evaporated using rotation evaporator.

**Chemicals**

Streptozotocin purchased from Sigma-Aldrich (Germany), and all other chemicals materials purchased from Merck (Germany) or Brataco Chemika (Indonesia).

**Animals**

Twelve-week-old male Sprague-Dawley rats weighing 300-350 g obtained from National Drug and Food Laboratory Center, at National Agency Drug and Food Control (NADFC), Indonesia. The animals used in this study have received approval from the Medical Research Ethics Commission of the Faculty of Medicine, University of Indonesia. All animals housed in an air-conditioned room and supplied with standard pellet food and drinking water ad libitum. All rats were divided into six groups of four animals each and acclimatized for seven days before the antidiabetic studies conducted.

**Induction of Diabetes**

Diabetic induction prepared by intraperitoneal injection of 55 mg/kg of STZ (dissolved in 0.05 M citrate buffer solution, pH 4.5) 20 min after intraperitoneal administration of 100 mg/kg nicotinamide (dissolved in normal saline solution) in overnight fasting rats. After 1 h after STZ-nicotinamide induction, the animals were given 5% glucose solution orally for 12 h to prevent hypoglycemia and fasting blood glucose was measured 48 h after the induction. The rats with fasting blood glucose levels greater than 150 mg/dL considered as diabetic animals.

**Experimental design**

The animals divided into six groups of four rats of each, consisting of three control groups and three treatment groups. Group I as standard control, healthy rats administered with daily oral of 0.5% carboxymethylcellulose (CMC). Group II as the negative control, diabetic rats administered with daily oral of 0.5% CMC. Group III as the positive control, diabetic rats administered with daily oral of 90 mg/kg sitagliptin. Group IV as lowest dose, diabetic rats administered with daily oral of 50 mg/kg white tea ethanolic extract (WTE). Group V as middle dose, diabetic rats administered with daily oral of 100 mg/kg WTE. Group VI as highest dose, diabetic rats administered with daily oral of 200 mg/kg WTE. The materials test administered at two days after induction of diabetic by injection of STZ for 14 days. Initial fasting blood glucose levels determined and after the induction fasting blood glucose were determined on the first day (D1) before the administration of the extracts and the 14th day (D14) after. Fasting blood glucose levels were determined by collecting the blood from the tail of the rats and measured using glucometer (Accu-Check’ Active). Body weight of all animals was measured once before the treatment and twice after the treatment, on the 7th day (D7) and the 14th-day end of studies (D14).

**Statistical Analysis**

Statistical analysis determined as mean value ± standard error (SE). The data with normal distribution analyzed with one-way ANOVA followed by multiple comparisons using Tukey test. However, abnormal distribution analyzed with Kruskal-Wallis test. Probability level of less than 5% (p < 0.05) was considered significant.

**RESULTS**

**Hypoglycaemic effect**

Table 1 shows the fasting blood glucose levels in control and treatment groups. The fasting blood glucose levels significantly increase greater than 200 mg/dl compared to the normal group, 48 h after induction of STZ. Administration of WTE for 14 days in diabetic rats showed a decrease in fasting blood glucose levels in diabetic rats. White tea extract at the middle dose 100 mg/kg BW shows highest reducing fasting blood glucose level (101± 8.33 mg/dl) than at lower dose 50 mg/kg BW (195.67 ± 16.22 mg/dl) and maximum dose 200 mg/kg BW (149± 52.21 mg/dl). The fasting blood glucose levels of all treatment groups at the end of studies showed a significant difference between the negative control group, (P <0.05).

**Body weight effect**

The record of body weight during the studies represented in Table 2. The increase in body weight in the treatment group was shown by the group of 100 mg/kg BW WTE although the increase was not significant when compared with the initial burden. The development of body weight in the group of 50 mg/kg BW WTE tended to be stable even though on the 7th day also decreased, whereas body weight loss also occurred in the group of 200 mg/kg BW WTE although not significant compared before treatment.

**DISCUSSION**

The present study was conducted to evaluate the effect of WTE on reducing fasting blood glucose levels in diabetic rats. The result of this studies shows that consumption of WTE for 14 days reduced fasting blood glucose levels in streptozotocin-induced diabetic rats. However, this data

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**Table 1: Effect of white tea extract on fasting blood glucose of diabetic rats.**

<table>
<thead>
<tr>
<th>Group Dose (mg/kg BW)</th>
<th>Fasting Blood Glucose (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
</tr>
<tr>
<td>Normal (CMC 0.5%)</td>
<td>83.67±2.60</td>
</tr>
<tr>
<td>Negative control (CMC 0.5%)</td>
<td>79.00±2.64</td>
</tr>
<tr>
<td>Positive control (Sitagliptin 90)</td>
<td>74.67±3.18</td>
</tr>
<tr>
<td>WTE 50</td>
<td>90.33±8.37</td>
</tr>
<tr>
<td>WTE 100</td>
<td>87.67±10.20</td>
</tr>
<tr>
<td>WTE 200</td>
<td>72.00±0.57</td>
</tr>
</tbody>
</table>

The data represent the mean ± SE (n=4); *Significantly different as compared to the normal group, p<0.05; **Significantly different as compared to negative control, p<0.05; BW-body weight, WTE-white tea ethanolic extract.
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did not show any correlation between dose and response. The highest decrease in fasting blood levels reaches at the dose of 100 mg/kg BW which statistically significantly different compared to negative control group, (p<0.05).

Several studies in green tea extract have reported that this chemical-induced hyperglycemia can ameliorate by feeding green tea or its polyphenols, flavonoids, and catechins. Therefore, the hypoglycemic activity of WTE in this studies possibly related to the content of bioactive compounds such as polyphenols in tea leaves that play a role in providing health benefits to humans. Tea flavonoids are antioxidants that can protect the damage of pancreatic cells from free radicals. The content of alkaloids and tannins (epigallocatechin) also play a role in lowering blood glucose levels possible through inhibition of glucose absorption in the intestine. This condition support by other studies suggesting that epigallocatechin-3-gallate (EGCG) has a role in reducing blood glucose levels by inhibiting the absorption of intestinal glucose by glucose transporter and decreasing the expression of genes that control gluconeogenesis.

Increased insulin-stimulated by glucose uptake, inhibition of intestinal glucose transporters and decreased gene expression that control gluconeogenesis is a mechanism that contributes to the antihyperglycemic effect of tea leaf extract. The other in vivo studies on green tea reported that insulin-like effects of polyphenols play a role in lowering blood glucose, but they also increase insulin sensitivity and reduce oxidative stress in experimental animals. Based on the above there is a direct relationship between antioxidant activity and hypoglycemic produced by white tea leaves. However, the studies with a treatment time longer than 14 days is required to ensure the antidiabetic effect of white tea extracts and confirm this mechanism.

Based on the data of body weight changes, Table 2, the STZ induction diabetic shows a tendency of body weight decrease in all groups of diabetic rats, and it is seeing up a 7th day after the treatment. Body weight loss in diabetic animal associated with dehydration and catabolism of fats and proteins due to proteolysis on muscular tissues occurred in insulin deficiency conditions. At the end of the study, the body weight of the diabetic rat's group tended to increase but did not occur in diabetic rats of the negative control group that managed to continue diabetes mellitus; IC$_{50}$: Inhibition concentration; DPP-IV: Dipeptidylpeptidase IV; STZ: Streptozotocin; CMC: Carboxy methyl cellulose; SE: Standard error, EGCG: epigallocatechin-3-gallate.

### REFERENCES


### CONCLUSION

In conclusion, the study showed that white tea leaf ethanolic extract has a potential effect on reducing fasting blood glucose levels in diabetic rats induced by streptozotocin-nicotinamide compared with the negative control group. The highest decrease fasting glucose level showed at doses of 100 mg/kg BW white tea extract. However, the studies with a treatment time longer than 14 days is required to ensure the antidiabetic effect of white tea extracts and confirm this mechanism.

**ACKNOWLEDGEMENT**

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**CONFLICT OF INTEREST**

The authors have no conflict of interest to declare.

**ABBREVIATIONS**

WTE: White tea ethanolic extract, BW: Body Weight; DM: Diabetes mellitus; IC$_{50}$: Inhibition concentration; DPP-IV: Dipeptidylpeptidase IV; STZ: Streptozotocin, CMC: Carboxy methyl cellulose, SE: Standard error, EGCG: epigallocatechin-3-gallate.

**SUMMARY**

- Administration of WTE at dose 100 mg/kg BW for 14 days in diabetic rats showed a decrease in fasting blood glucose levels in diabetic rats.
- The fasting blood glucose levels of all treatment groups at the end of studies showed a significant difference between the negative control group, (P <0.05).
- The body weight of the diabetic rat's group shows a tendency of body weight decrease, although it is no significant difference in body weight changes at the end compared with before treatment.

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**ABOUT AUTHORS**

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