

# Saurauia vulcani Korth. leaves Down-regulation of Receptor for Advanced Glycation End-products (sRAGE) in Hyperglycemic Rats

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**Keywords:** Down Regulation, sRAGE, Saurauia Vulcani Korth Leaves Extract.

**Abstract:** To evaluated level of receptor of advanced glycation end-products (sRAGE) in hyperglycemic rats which treatment with leaves extract. **Methods:** *Saurauia vulcani* Korth. leaves powder was extracted by maceration method with ethanol 96%. Blood glucose reduction was inspected on rats that injected with streptozotocin (STZ) 40 mg/Kg BW with dosage 25; 50; 100 mg/Kg BW. sRAGE level on serum was determined with ELISA method. **Results:** Ethanol extract of pirdot leaves (EEPL) in hyperglycemic rats indicated a dramatical level decrease in sRAGE level ( $p < 0.001$ ) at dosage 50 mg/Kg BW. **Conclusion:** The research reported *Saurauia vulcani* Korth. leaves ethanol extract has down regulation level of sRAGE.

## 1 INTRODUCTION

Diabetic mellitus (DM) is a heterogeneous syndrome which is characterized by an increased of blood sugar level which causes relative or absolute insulin activity (Moridi, et al., 2015). Hyperglycemic condition leads to microvascular and macrovascular complications and early death. AGEs (Advanced glycation end products) producing from binding of glucose with lipids, proteins, and nucleic acids through nonenzymatic reaction which involved as the main pathogenic factors in initiation and progression of diabetic complications (Sing, et al., 2001). Receptor of AGE (RAGE) is part of the immunoglobulin superfamily of cell surface molecules (Bierhaus, et al., 2005; Bierhaus, et al., 2009).

*Saurauia vulcani* Korth. Is one of the plant which used as antidiabetic traditionally in Tapanuli Utara, North Sumatera, Indonesia. Ethanolic extract of *Saurauia vulcani* Korth. Leaves can reduce blood glucose level in mice which induced by glucose 50%, aloxan at dose 200 mg/Kg BW and STZ at dose 50 mg/Kg BW (Sormin, et al., 2014; Sitorus, et al., 2015; Sitorus, et al., 2018). The purpose of our research was to determine down regulation effect sRAGE of *Saurauia vulcani* Korth. Leaves ethanol extract.

## 2 EXPERIMENTAL

### 2.1 Plant and Chemicals Material

The materials used in this study were *Saurauia vulcani* Korth. leaves. which taken from Tapanuli Utara, North Sumatera, Indonesia. The chemicals used are pro-analysis grade: STZ (streptozotocin) (Nacalai), sodium CMC (Merck), sRAGE elisa kit (FineTest), technical grade of ethanol and distilled water.

### 2.2 Preparative of Extract

The air-dried and powdered leaves of *Saurauia vulcani* Korth. leaves. (1 kg) were extracted by cool maceration with ethanol 96% based on previous study (Sitorus, et al., 2018; Forbes, et al., 2013; Zhong, et al., 1979).

### 2.3 Antidiabetic Assay

#### 2.3.1 Animal Preparation

The animals used in this study are manly rats weighing 180-200 grams. Before the probationary, rats were nurtured for 2 weeks in a well cage to adapt

to the surroundings live, i.e., the acceptance of glow, 12 h sooty and 12 h glow.

### 2.3.2 Preparative of Extract Suspension and STZ Solution

Suspension of extract was preparated by using 0.5% CMC-Na with definite concentration. Solution of STZ was set by dissipate STZ in aquabidest (Sitorus, et al., 2018; Silalahi, et al., 2016).

### 2.3.3 Preparative of STZ Induced Diabetic Rat

The rat were induced with STZ solution 40 mg/Kg intra-peritoneal (ip). Based on previous study by (Sitorus, et al., 2018).

### 2.3.4 Analysis of sRAGE with ELISA

To investigate the effect of EEPL to sRAGE level in serum was examined with ELISA. 0.1 mL of serum was added to plate and the procedure was followed based on sRAGE ELISA kit instruction (FineTest).

## 2.4 Statistical Analysis

Data were interpreted as ANOVA and descriptive which were analyzed using by SPSS 21 edition

## 3 RESULTS

### 3.1 sRAGE Expression

The sRAGE (soluble receptor of advanced glycation end-product) level (Table 1) in serum were showed significant difference among all the studied groups. The best group (EEPL 50 mg/Kg BW) was expressed the smallest of sRAGE if compare with other groups. There are significantly differences between groups ( $p < 0.05$ ).

Table 1: sRAGE serum level with various treatment.

Treatment	sRAGE level (pg/mL)
Sodium CMC 0.5%	169.07 ± 4.36
EEPL 25 mg/Kg BW	40.60 ± 0.57
EEPL 50 mg/Kg BW	15.46 ± 1.60
EEPL 100 mg/Kg BW	20.53 ± 1.14
Metformin 45 mg/Kg BW	18.72 0.68

## 4 DISCUSSION

STZ has been exhibited to bring a damage to pancreatic islet of Langerhans which specific attack to  $\beta$ -cells, cause the degranulation and uncapability to produce insulin (Harfina, et al., 2012).

Phytochemical screening of the EEPL were shown flavonoids, steroids/ triterpenoids, tannins, glycosides and saponins (Sitorus, et al., 2018). Flavonoids, their glycosides and saponins have been put up to be accountable for blood glucose decreasing capacity through increased insulin secretion, as indicate in our experiment by STZ-induced diabetic rats, which is competent of stimulating pancreatic secretion (Sitorus, et al., 2014; Sihotang, et al., 2016).

High level of sRAGE caused by constant and prolonged hyperglycemia. sRAGE is apart of RAGE (receptor of advanced glycation end-product) which expressed in cell membranes (Raucci, et al., 2008). AGEs produced by adducts resulting from non enzymatic condensation of sugar such as glucose and amino group of proteins. Complex AGEs and RAGE causes endothelial dysfunction which increase level of oxidative stress. The activation of RAGE by AGEs is the major pathogenic cause of vascular complication in diabetes condition (Fleming, 2011).

Flavonoids was found in EEPL and their role are to decrease sRAGE level. Flavonoids in general were presented anti-glycation properties (Wu, et al., 2012). Quercetin is a flavonols member which found to be an inhibitor of glycation. Extract of cloves, ground Jamaican all spice and cinnamon amongst to be the most effective inhibitors of glycation.

## 5 CONCLUSION

The result of this study showed that EEPL posses sRAGE in diabetic condition.

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