EFFECT OF BAY LEAF ETHANOL EXTRACT ON BLOOD GLUCOSE LEVEL IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Previous studies showed that bay leaf or *Syzygium polyanthum* (Wight) Walp ethanol extract (SPEE) had antioxidant activity. It is safe for use in human. This study aimed to investigate SPEE effect on fasting blood glucose level (FBGL) among patients with type 2 diabetes mellitus.
Subjects and Method: This was a pilot study using a randomized controlled trial (RCT) design. A total sample of 8 patients with type 2 diabetes mellitus were selected for this study. The intervention group were given 350 mg SPEE in capsule, once daily for 14 days. The control group were given placebo (Pl). The dependent variable was fasting blood glucose level (FBGL). The data were collected at day 0 and after 14 days administration. The effect of EESP was determined by comparing mean FBGL in the EESP-group and Pl-group after intervention. This effect is also shown by Effect Size (ES). The effect is large if ES > 0.3. The mean difference after intervention was tested by Mann Whitney test. The means of FBGL of the two groups should be comparable as a result of randomization.
Results: After the intervention, the FBGL (mg/dL) was lower in the EESP-group (Mean= 169.75; SD= 43.72) than the Pl-group (Mean= 225.25; SD= 73.48), and it was not statistically significant (p= 0.14). This statistical non-significant effect was anticipated in the pilot study, due to the very small sample size (n=8). Effect Size= -0.91, indicating large effect of EESP in lowering the fasting blood glucose level (large if Effect Size > 0.30).
Conclusion: *Syzygium polyanthum* (Wight) Walp ethanol extract (EESP) is effective to lower fasting blood glucose level in patients with type 2 diabetes mellitus.

Keywords: *Syzygium polyanthum*, bay leaf, blood glucose level, diabetes mellitus

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BACKGROUND

Diabetes mellitus (DM) is one of metabolic diseases that characterized by the high level of blood glucose level (BGL) (American Diabetes Association, 2018). This condition affects the human body at multiple organ levels (Bharti et al., 2018).The treatment has become more challenging as conventional oral antidiabetic agents are heterogeneous in their mode of action and causes unwanted effects such as hypoglycaemia, abdominal discomfort, lactic acidosis, etc. (Ghadge and Kuvalekar, 2017). Long term treatment was also as an important issue that related to the patient adherence (Awodele and Osuolale, 2015; Polonsky and Henry, 2016).

Many plants are traditionally believed to heal diabetes (Bharti et al., 2018), one of which is Salam leaf (bay leaf). Salam leaf is a plant that easily found in Indonesia. Its leaves commonly used as cuisine. This plant has Latin name as *Syzygium polyanthum*

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(Wight.) (*S. polyanthum*), which synonyms as *Eugenia balsamea* Ridley, *Eugenia nitida* Duthie and *Eugenia polyantha* Wight (Widyawati et al., 2015a). Other local names are ubar serai, meselengan (Sumatera); samak, kelat samak, dan manting (Jawa) and serah (Malaysia) (Harismah, 2017; Har and Intan, 2012). The efficacy of this plant was known related to its active compounds ie eugenol, *methyl chavicol*, flavonoids, alkaloids, tannin, steroids, triterpenoid, and squalene (Hidayati et al., 2017; Widyawati et al., 2015b; Silalahi, 2017).

Utilization of medicinal plants in the community needs to be supported by its safety data. Pre-clinical study showed that *S. polyanthum* leaf infusion for 28 days was not affecting ureum and creatinine level of Swiss webster mice. At dose 4.5g dried leaves safe to be consumed by human (Kurniawati and Sianturi, 2016). Antihyperglikemic activity of ethanolic extract *S. polyanthum* leaf (30% and 70%) in glucose loading male rabbits showed significant effect (Wahyono, 2008).

Widyawati et al. (2015a) demonstrated that *S. polyanthum* methanol extract 1 g/kg had antihyperglycemic effect in streptozotocin-induced diabetic rats. Studies of its mechanism of actions show the inhibitory activity of the enzyme dipeptidyl Peptidase-IV, alpha glycosidase and alpha amylase and inhibiting glucose absorption in jejunum (Widyawati et al., 2015b; Permatasari and Yuniarni, 2015).

Our previous study showed that 28 days administration of 350 mg of *S. polyanthum* ethanol extract safe to be used in healthy human volunteer. Therefore, the present study was conducted to evaluate its activity in type 2 diabetic patients.

SUBJECT AND METHODS

1. Study Design

This was a pilot study using a randomized controlled trial (RCT) design. The study was caried out at Medical Faculty, Pharmacy Faculty-Universitas Sumatera Utara and Puskesmas Glugur Darat, Medan, Indonesia from April-September 2019.

2. Population and Sample

A total of 8 patients with type 2 diabetes mellitus were selected for this study using inclusion and exclusion criteria. Inclusion criteria i.e.: diabetic type 2 patients; fasting BGL >126 mg/dl; do not smoke, not taking drugs that may affect BGL in acceptable range and signed the informed consent. The patients that showed any adverse effect or subjective symptoms that cannot be tolerated were excluded from the study. The patients were randomly divided to get either SPEE or Placebo (Pl).

3. Study Method

S. polyanthum fresh leaves were obtained from Kedai Durian, Medan, Indonesia. The plant was identified by Herbarium Medanense (MEDA), Universitas Sumatera Utara. The fresh leaves were washed with running water followed by drying under shade (30-40°C). The dried leaves then were grinded to form powder. To obtain extract (SPEE), the powder were extract using ethanol 96%. The extract then were formulated in capsule at dose 350 mg.

The treatment was administered once daily for 14 days accompanied by oral antihyperglycemic agent, metformin 500 mg twice daily. Blood glucose levels were measured at day 0 (before intervention) and after 14 days of taking capsules. During the administration of the treatment, any complaints experienced was recorded every day. Data were analysed using Mann-Whitney and Wilcoxon sign rank test.

RESULTS

During administration all volunteer completed the study. In EESP-treated group, there were no complaints during observation, while in Pl-treated group, at day 1 as follows

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confuse (1 subject (A8), sleepy (1 subject (A11), numb (1 subject (A20). Afterwards A8 mentioned itchy, polyuria, polyphagia.

As shown in Table 1 and Figure 1-2, after the intervention, the FBGL (mg/dL) was lower in the EESP-group (169.75± 43.72) than the Pl-group (225.25 ± 73.48). FBGL of EESP-treated group decreased (8.85%; BGL difference 16.5 mg/dL) from 186.25 ± 58.57 to 169.75 ± 43.72, contrarily PL-treated group increased (11.23%; BGL difference 22.75 mg/dL) from 202.5 ± 50.17 to 225.25 ± 73.48.

Statistically, there was no significant different between PL- and EESP-treated group at the end of the study (p= 0.14). This statistical non-significant effect was anticipated in the pilot study, due to the very small sample size (n=8). We calculated the effect Size= -0.91 that indicated large effect of EESP in decreasing the FBGL (large if Effect Size > 0.30).

Table 1. Effect of EESP on Fasting Blood Glucose Level

Group	FBGL (mg/dL)		p^b
	Day 0	Day 15	
PL	202.5 ± 50.17	225.25 ± 73.48	0.27
EESP	186.25 ± 58.57	169.75 ± 43.72	0.46
p^a	0.76	0.14	

(a: Kruskall-Wallis; b: Wilcoxon sign rank test)

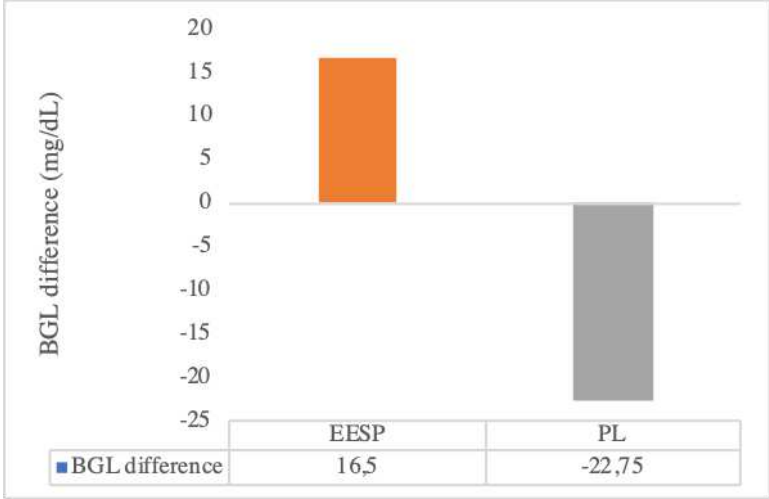

Figure 1. Blood glucose level difference

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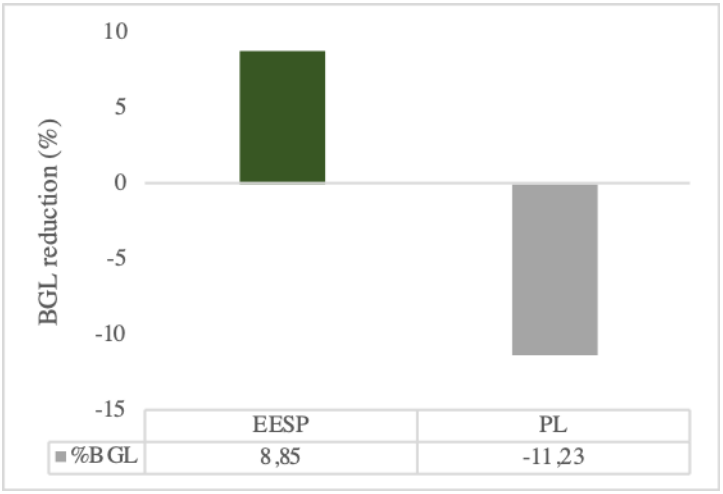

Figure 2. Percentage of blood glucose level difference

DISCUSSION

Fasting blood glucose level is one of parameters to diagnose type 2 diabetes mellitus (American Diabetes Association, 2018) which the value should below 126 mg/dL (Wilson and Sexton, 2003). In the present study showed that the diabetic volunteers had high BGL to confirm their diabetic uncontrolled condition. After EESP 14 days administration, the FBGL decreased to 8.85 % or achieved to 16.5 mg/dL reduction.

Suharmiati and Roosihermiatie (2012) reported that metformin in combination to the 700 mg extract of *Andrographis paniculata* and *Syzygium polyanthum* mixture (1:1) for 28 days could significantly decrease FBGL in comparison to control group given metformin with placebo. The FBGL difference was around 37.3 mg/dL.

The higher effect in lowering FBGL of their study probably due to the long term administration. The present study suggested that EESP alone was comparable to Suharmiati and Roosihermiatie study due to the dose and duration of treatment. However, identifying effective drug combinations that significantly improve over single agents still a challenging problem (van Griensven et al., 2010). More drug used more cost spent.

The decreasing of FBGL in the present study insignificant statistically due to the number of sample as it is for the pilot study. The necessary sample size to achieve stable estimates for correlations depends on some parameters, one of which is the effect size (Schönbrodt and Perugini, 2013). The effect size calculation showed that the EESP has potency as antihyperglycemic agent. This study concluded that *Syzygium polyanthum* (Wight.) Walp ethanol extract (SPEE) is effective to lower fasting blood glucose level in patients with type 2 diabetes mellitus.

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