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by Netty Ino Ischak

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Preliminary Study of Clinical Antidiabetic Activity of Salam Leaves (*Eugenia Polyantha*) and Sambiloto Leaves (*Andrographis Paniculata*) In Type 2 Diabetic Patients

N I Ischak and D N Botutihe

Chemistry Department Faculty of Mathematic and Natural Science, State University of Gorontalo Indonesia

Corresponding Author: nettyischak@gmail.com

Abstract. Diabetes mellitus is one of disease with high prevalence in the world. Salam (*Eugenia polyantha*) and Sambiloto (*Andrographis paniculata*) are plant that widely used traditionally for medicine including to treat diabetes mellitus. Many studies have revealed that these herbs have bioactive compounds that contribute to antidiabetic properties. The objective of the present study is to analyze the clinical antidiabetic properties of *Eugenia polyantha* and *Andrographis paniculata* leaves in type 2 diabetic patients. Clinical test with before and after design was used as method. Sample was designed by consecutive sampling with inclusion and exclusion consideration. Total subject of this study are 40 peoples and were divided into two group. One group consumed *Eugenia polyantha* leaf and the other one consumed *Andrographis paniculata* leaf. 300 mg of these medicinal plants was given as capsule. The prescription was 1-2 capsule per day for one week. During this study we observed several parameters include: patients characteristic, blood glucose level, uric acid, total cholesterol, blood pressure and other subjective complaints. The result showed that among 20 respondents of each group, there are 70% and 80% respondents decreased fasting blood glucose level (<140 mg/dL) compared to before treatment with these herbs. It can be concluded that *Andrographis paniculata* and *Eugenia polyantha* leaf may have positive role in type 2 diabetic patients.

1. Introduction

Diabetes Mellitus (DM) is degenerative disease in which characterized by high blood glucose level. Diabetes is classified into two main types that are diabetes type 1 and type 2. Type 1 of DM caused by destruction of the beta cells then the body cannot produce insulin (insulin deficiency). Type 2 of DM caused by interference insulin secretion.

The World Health Organization (WHO) reported that its sufferer has reached 239,3 million over the world. According to an International Diabetes Federation report (2014), 387 million people have been diagnosed with diabetes and that is expected to increase to 592 million by 2035[1]. Indonesia is one of the countries that have highest prevalence of DM in the world. Many factors that contribute to this high prevalence including people lifestyle transformation, unbalance diet nutrition and lack of regular exercise.

Medicinal plants have been used for a long time to treat various diseases [1]. Its utilization by peoples based on empirical experiences, advert or through traditional health service provider. Medicinal plants were used as single or combination of plants in the form of dry extract.



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Andrographis paniculata and *Eugenia polyantha* known that shown in figure 1 and 2 respectively, are plant that widely used traditionally for medicine. *A. paniculata* known as *sambiloto* in Indonesia have been used to treat diabetes, hypertension, fever, liver diseases, diarrhoea, anti-inflammation, cold, etc. [2],[3]. *E. polyantha* or bay tree or *salam* in Indonesia, used traditionally to treat hypertension, diabetes mellitus, skin infection, hyperuricemia, diarrhoea, rheumatism, hypercholesterolemia, gastritis and besides that it widely used in Indonesia and Malayan food as additive [4],[5]. Based on scientific studies with animal model it was revealed that *A. paniculata* and *E. polyantha* have antidiabetic properties [6],[7],[8],[9].



Figure 1. Salam (*E. polyantha*).

Bay tree or salam can be planted in the garden, although they generally grow in the forest at lowlands until 1,400 meters above sea level. The length of bay leaf is 2.5-8 centimetre with flat margin. The base of leaf is sharp and the tip is blunt [10].



Figure 2. Sambiloto (*A. paniculata*)

A. paniculata grows well at height 180-861 m above sea level. The shape of leaf is ovoid with sharp tip and base. It has 5-13 cm long leaf and the width is 1.5-3.5 cm [11]. Preclinical study reported that *A. paniculata* extract can reduce blood glucose level of animal model [6]. This study reported that 27 mg/200 g body weight (bw) or 1.5 g/ 70 kg human body weight as effective dosage for antidiabetic properties. There is no significant difference of the dosage with positive control i.e. tolbutamide 9 mg/ 200 g bw. 25,2 mg/200 g, 126 mg/ 20 g, 252 mg/ 200 g and 504 mg/ 200 g bw were reported as oral safe dosages that given once a day for 4 months. These dosages do not lead hematologic abnormalities on wistar [6].

The antidiabetic properties of *E. polyantha* have been reported by Lutfiana et al. [7]. About 312,5-1250 mg/kg bw of this ethanol extract can lower blood glucose level to 64,4-77 mg/dL [7]. Another

study has been investigated that 2,62 mg/kg bw and 5,24 mg/kg bw of *E. polyantha* extract can reduce glucose level in alloxan-induced diabetic male rats [8].

However, there are limited clinical study that report the antidiabetic properties of *A. paniculata* and *E. polyantha* on type 2 diabetic patients. Furthermore, several factors support to *A. paniculata* and *E. polyantha* as potent medicinal plants for treating type 2 diabetic patients such as preclinical studies, empirical experiences, high cost of conventional medical treatment that currently available and high prevalence of type 2 DM. There are various medicinal plants have antidiabetic properties but their effect and usefulness still questionable. Therefore, it is necessary study the antidiabetic activity (i.e. blood glucose reducing effect) of *A. paniculata* and *E. polyantha* in type 2 diabetic patients.

2. Material and Method

2.1. Subjects Criteria

Sampling method in this study use inclusion and exclusion criteria, i.e. subjects of study are the patients who have been taking medical treatment, have fasting blood glucose level >140 mg/dL and <400 mg/dL, have suffer DM for over 1 year, HbA1c concentration 7-12%, have no other acute or chronic diseases: have not allergy to medicine, hyperglycaemic coma, liver failure (SGPT), renal impairment disorder, ages 28-65 year old, have not pregnant and agreed to become subjects for this study. If the subjects have been taking medical treatment, they have to stop their medicine temporary to undergoing this herbal treatment.

2.2 *Eugenia polyantha* and *Andrographis paniculata* Dry Powder Capsule

Herbs samples were collected in fresh condition. The samples are cleaned and then air-drying until the weight is constant. In order to get fine dry particle, the sample have carried out several process such as milling and sieving. Then packed in capsule which each capsule is about 300 mg of herb. There is no extraction procedure. The administration of this capsule followed the standard dosage for human i.e. about 1.5 g/ 70 kg bw [6].

2.3 Research Design

Research design is a preliminary trial of clinical test with pre and post uncontrolled design. About 40 patients with type 2 DM are divided into 2 group each group consist of 20 peoples. First group treat with *E. polyantha* and another group with *A. paniculata*. The dosage is about 1-2 capsule per day and observation was carry out for 7 days. Each capsule contains 300 mg of herbs and the dosage based on safety dose of preclinical study i.e. about 22 mg/kg bw for mice or similar to 1.5 g/70 kg bw for human [6]. Parameters of the treatment of this study are fasting blood glucose level (KGDP), blood uric acid concentration, total cholesterol and blood pressure.

3. Result and Discussion

According to our investigation, 40 subjects have fasting blood glucose level about 150 mg/dL to 400 mg/dL i.e. 10 subjects are men and 30 are women. The characteristics of 40 subjects in this study was given in table 1.

Table 1. Physical characteristic feature of Subjects

Characteristic	Number			
		min	max	Modus
Age (year)	52,31 ± 6,56	28	65	54
Men	10			
Women	30			
Duration of DM (year)	7,3 ± 2,78	2	17	6
Body mass index (kg/m ²)	26,4 ± 2,45	22	33.5	24

There are studies that revealed relationship between body mass index (BMI), sex, gender, with type 2 diabetes mellitus. Based on our investigation type 2 diabetic patients have BMI about 26.4 ± 2.45 kg/m². In general BMI of subjects has 4 categories, BMI about <18,5 were classified as **underweight**, 18,5 - <23 kg/m² as **normal weight**, 23.0 - <25 kg/m² as at risk or overweight and those with a BMI greater than or equal to 25 kg/m² were classified as obese [12]. Study that conducted by Agrawal et al (2017) showed that 73,5% and 26,5% diabetic patients classified as overweight and obese, respectively. BMI is biological factor that considered to affect the risk and outcome of DM. BMI is measure of body fat according to height and weight. Fatty acid that constitute body fat content is synthesized by glucose. Then, it may be expected that blood glucose levels and BMI have correlation [13].

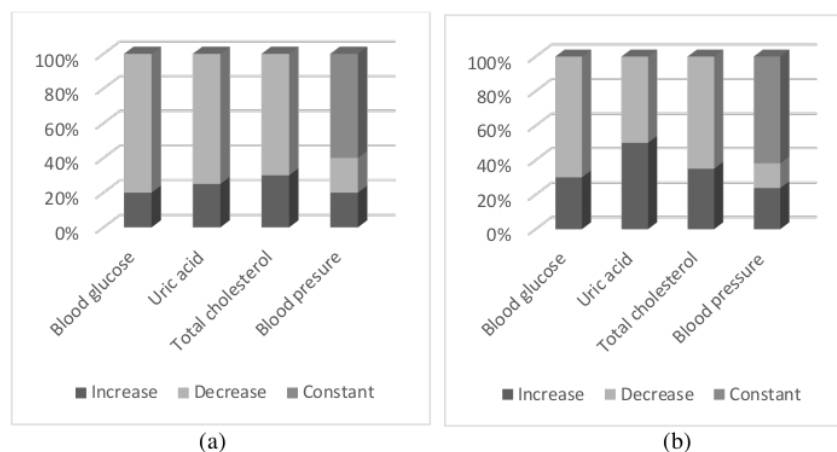


Figure 3. Presentation of patients on medical parameters after administered by *A. paniculata* (a) and *E. polyantha* (b) capsules

In this study woman with DM was more than man (table 1). Risk and outcome of type 2 DM in both sexes were influenced differently by many factors such as genetic, epigenetic mechanisms, nutritional, and sedentary lifestyle. Endocrine imbalances related to unfavourable cardiometabolic characteristics can be observed in women with androgen excess or men with hypogonadism. Biological and psychosocial factor also contribute to outcome of this disease. In general, women seem to have greater impact of psychosocial than men [14].

The result of *A. paniculata* and *E. polyantha* leaves administration on blood serum characteristics was given in figure 3. Among 20 respondents of each group, about 70% and 80% of respondents have decreased fasting blood glucose level (<140 mg/dL), 50% and 75% decreased of uric acid (<7), 65% and 70% decreased of total cholesterol (<200 mg/dL). Moreover, there are subjective experienced after consume this herb capsules that summarized in figure 4. In general respondents feel good or have not complaints after consume *A. paniculata* and *E. polyantha* capsules.

Based on statistical analysis with paired test, there are difference result between before and after subjects consume the herb capsules. The t-value and correlation value of *A. paniculata* administration was about 3,88 and 0,858 respectively. The t- and correlation value of *E. polyantha* administration was about 0,789 and 0,874 respectively. Similar study report by Rahayu et al (2016) revealed that *jamu clinic* which is *A. paniculata* and *E. polyantha* as one of its composition, can decrease blood glucose level of DM patients [15]. In that study these 2 herbs have mixed together along other herbs such as brotowali (*Tinospora crispa* (L) Miers ex Hoff. I), turmeric (*Curcuma longa* Linn), ginger (*Curcums xanthoriza* Roxb) and meniran (*Phyllanthus niruri* L).

There are many studies have revealed medicinal properties of *A. paniculata* and *E. polyantha*. Based on review by Jayakumar et al (2013) and Chao et al (2010) *A. paniculata* have antiinflammation,

anticancer, immunomodulation, antiinfection, antihepatotoxicity, antiatherosclerosis, antidiabetic and antioxidation properties [2],[3]. While *E. polyantha* have antioxidant, free radical scavenging, antimicrobial, antidiabetic properties [4],[9], [15].

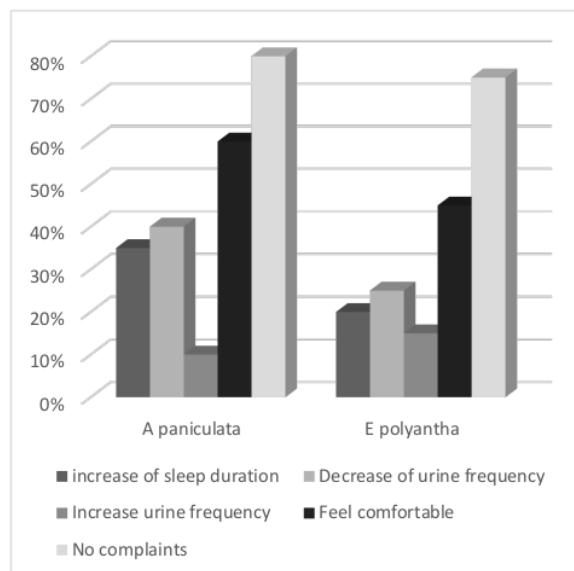


Figure 4. Subjects experienced after consume *Andrographis paniculata* and *Eugenia polyantha*

Phytochemical constituents that may contribute to biological activity of plants such as flavonoid, alkaloid, terpenoid, steroid, and tannin were found in *A. paniculate* [2],[3] and *E. polyantha* [9],[16]. Moreover, andrographolide as one of bioactive compound of *A. paniculata* was reported have hypoglycaemic effects in streptozotocin-diabetic rats and in a model of type 1 DM rats. Based on review that have been undertaken by Hossain et al [3] (2014) the mechanisms of antihyperglycemic activity of *A. paniculata* extract and andrographolide are by (a) reducing blood glucose level through inhibition of α -glycosidase and α -amylase (b) stimulating glucose uptake and oxidation by peripheral tissues due to increasing insulin sensitivity (c) regulating lipid metabolism abnormality (d) as free radicals scavenger from circulation which disrupt integrity of plasma membrane thus lowering number of efficient plasma membrane receptors or transporter proteins require to glucose uptake from the bloodstream [17]. *E. polyantha* contain triterpenoid i.e squalene as one of major constituents [5],[16]. In general, triterpenoid have antihyperglycemic activity by act as a glycosidase and a amylase inhibitor which delay the absorbance of carbohydrates in the intestine, leading to a decrease in the postprandial insulin level [18],[19].

4. Conclusion

Although the total of respondents of this present study is small, but the result may describe the positive role of *A. paniculata* and *E. polyantha* in type 2 diabetic patients. Further clinical study must be conduct to reach concrete conclusion of the effect of *A. paniculata* and *E. polyantha* leaf in type 2 diabetic patients.

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