ANTI-DIABETIC ACTIVITY OF SAMBILOTO EXTRACT (*Andrographis paniculata* Ness) TO DECREASE BLOOD GLUCOSE LEVEL OF ALOXAN-INDUCED DIABETIC RAT

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This research aimed to measure dosage of sambiloto (*Andrographis paniculata* Ness) extract to decrease blood glucose level of diabetic rats (*Rattus norvegicus*). Completely randomized design was applied for experiment in triplicate sampling and 7 treatments: D0, D1, D2 of normal, diabetic, and 0.9 mg glibenclamide control, respectively; D3, D4, D5 of 100, 200, 400 mg sambiloto extract respectively; and D6 of 200 mg sambiloto + 0.9 mg glibenclamide; all dosage in 200 g body weight basis of 2 months old male white Wistar rats weigh ± 200 g for 21 days. Anova and Kruskal-Wallis were used as statistic analysis; results then furtherly analyzed using Moods Median Test at α 5%. Results showed that sambiloto extract at dosage of 100 mg, 200 mg, 400 mg/200 g body weight as well as combination of 200 mg sambiloto + 0.9 glibenclamide able to reduce rat blood glucose level. Interestingly, 400 mg sambiloto/200 g body weight was comparable to the result obtain using 0.9 mg glibenclamide/200 g body weight of 56%. While rats treated with combination of 200 mg sambiloto + 0.9 mg glibenclamide/200 g body weight had 58% lower blood glucose compare to initial blood glucose level, however hypoglycemic risk need to be considered.

Keywords: anti-diabetic, sambiloto extract, blood glucose level

1. Introduction

Constant high level of blood glucose has been known as diabetes melitus indicator. Insufficient amount of insulin produced by pancreas was among reasons for diabetes, thus reduce consumed carbohydrate oxidation [13]. Oral synthetic anti–diabet drugs such as glibenclamide and tolbutamid commonly had undesired side effect, thus researchers also developed relatively safer medical system using natural herbs for diabetes [1].

Herbal and prescribed synthetic drugs are commonly applied by diabetes patients without notification to health practicioners. Some believe that such combination is safe, reduce side effect or toxicity risk, and able to gain synergistic effect as well, despite possibility of pharmacokinetic interaction when during body metabolism which able to hamper glibenclamide metabolism, prolong glibenclamide effect, and increase anti-diabetes. Anti-diabetic effect of drugs could be dangerous due to accute hypoglychemia occurrence [3].

Green chirayta or andrographis plant, locally known as Sambiloto, has been known as medicine plants widely used as traditional herbal (*jamu*) in Indonesia [10, 16 , 11] with all parts of the plants are particularly bitter. Sambiloto is known for several names in different regions such as Papaitan (Malay); Ki Oray, Ki Peurat (Sunda); Bidara; Sambiloto (Java); Pepaitan (Maluku) and Ampadu (Sumatra) (5, 12, 14]. It contains several bioactive components such as andrographolid, neoandrographolid, saponin, alkaloids, glycosides, flavonoids, all procuced as second metabolite [17 , 14]. Sambiloto can be utilized as anti-pyretic, anti-hepatoxic, anti-malaria, anti trombogenic, anti-HIV, anti inflammatory agent, anti-fever, anti-biotic, anti-diarrhea, anti-swelling, and anti-diabetes [7, 5, 15]. As mentioned by Winarto [14], sambiloto extract able to impair trophocyt and trophoblast cell, play role in tumor cell cytoplasm condensation, pyknosis and dissintegrate cancer cell nucleus.

Based on previous researches, andrographolid was able to reduce glucose blood level by enhance plasma betaendorphin level, neurotransmitter with analgesic and anti-pyretic effect, beneficial to reduce patient physical stress. Glucose-blood controlling effect of andrografolid was also carried through reduction of glucose-synthesis activity from non-carbohydrate compounds such as pyrivate and lactate.

Sambiloto utilization as part of diabetes mellitus medicine should be balanced and followed by carbohydrate and sugar diet, given the extract

ability to prevent glucose absorbtion in intestinal gut when consumed just before eat. It was also noted that sambiloto extract consumption at dosage of 1000 mg and 2000 mg/200 g body weight was able to reduce blood glucose for 28.7% [15]. Moreover, after processed into simplicia and powder, sambiloto was still able to reduce blood glucose level [9, 15].

Beside commonly planted sambiloto, previous research noted that there was also sambiloto that cultivated among teak and mahogany stands in agroforestry-based cultivation. A research was needed to explain anti-diabetes activity of this particular sambiloto extract at lower dosage. The objective of this research was to study sambiloto extract to reduce blood glucose level of aloxane-induced diabetic rat.

2. Research Methods

Research was conducted from February to September 2014 in laboratory facilities of Medical Faculty of UNS Surakarta. Completely Randomized Design was used as experiment model with tri replicate data sampling. After 1 week adaptation period at 28^{0}C controlled temperature, 63 two months old male white Wistar rats weigh ± 200 g were divided into 7 treatment groups (n=9) and induced using aloxane tetrahydrate at dosage of 125 mg/kg body weight, prior to 21 days intervension. Treatments were Do, D1, D2 of normal, diabetic, and 0.9 mg glibenclamide control, respectively; D3, D4, D5 of 100, 200, 400 mg sambiloto extract respectively; and D6 of 200 mg sambiloto + 0.9 mg glibenclamide; all dosage in 200 g body weight basis. Glucose level was measured at day-1, 4, 8, 14, and 21 using blood taken from rat's tail. Extract was orally administered from day–8 to 21. Anova and Kruskal-Wallis were used as statistic analysis; results then furtherly analyzed using Moods Median Test at α 5% [2, 4].

3. Results and Discussions

Kruskal-Wallis analysis on rat blood glucose at day–8 (before sambiloto treatment) showed that sambiloto concentration had significant effect at p value of 0.046 (0.01 < p < 0.05), as well as results at day–14 and day–21 (after sambiloto treatment), both at p value of 0.005 (p < 0.01). Analysis was followed by Mood Median Test at α 5%, (Table 1).

Table 1. Rat blood glucose level at day-8 (before sambiloto administration), day-14 and day-21.

Treatments	Blood glucose level (mg/dl)		
	Day-8	Day-14	Day-21
Do	97.00^a	97.33^a	97.00^a
D1	267.33^d	282.67^d	299.67^d
D2	277.33^d	165.00^b	120.00^b
D3	278.00^d	191.33^c	129.00^c
D4	270.00^d	181.00^c	125.33^b
D5	273.00^d	173.00^b	122.00^b
D6	268.00^d	135.00^b	112.00^a

Same superscript means in same column means not significant different using Mood Median Analysis at alpha 5 %.

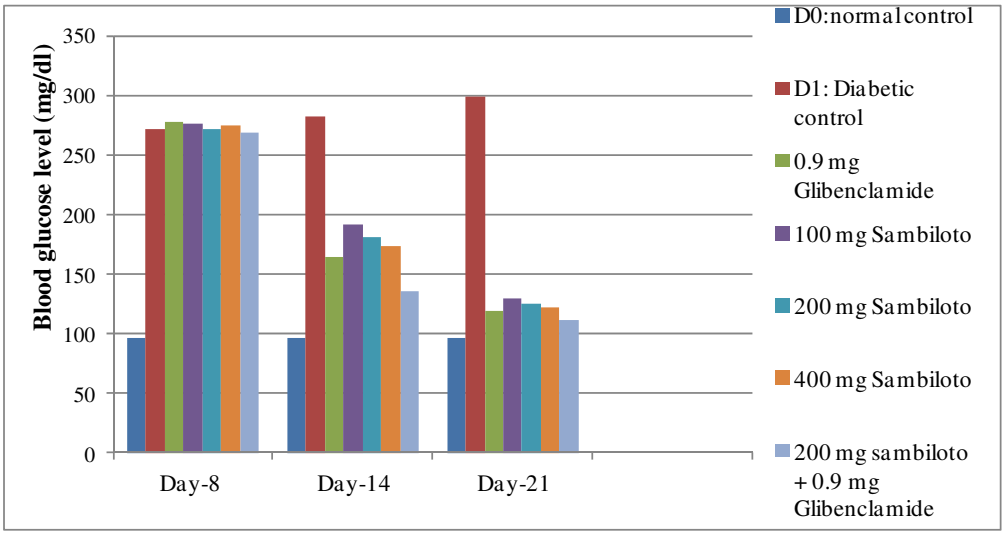

Figure 1. Fasting blood glucose level of normal control, diabetic control, and sambiloto–treated group

It was also noted that during 8 initial days before sambiloto treatment, all diabetic rat blood glucose were above 250 mg/dl. Diabetic control blood glucose level remained high during intervension. While even though blood glucose of sambiloto–treated groups remain higher than normal control, but the results showed significant decreased level after sambiloto treatment (Figure 1). Result varied with dosage used, with the lowest blood glucose level obtained by combination of 200 mg sambiloto and 0.9 mg glibenclamide at day–21. Interestingly, 400 mg sambiloto had comparable result to those obtained by 0.9 mg glibenclamide/200 g body weight.

Discussion

Fasting blood glucose level of rat before aloxane induction was varied but homogen in normal range (± 95 mg/dl), which was stable for normal control group (D0) to the final period of intervension, thus feasible to be used as initial blood glucose level. After aloxane induction, blood glucose of diabetic gropus (D1- D6) at initial stage before sambiloto administration (day-8) was significantly higher those of normal control (D0) (Figure 1).

Moods Median Test at alpha 5% was used as statistic analysis on blood glucose level at day–14 and day – 21. The results indicated that D0 group was significantly different with D1, D2, D3, D4, D5, and D6. Those obtained by aloxane-induced diabetic rat control group (D1) were also significantly different with normal control group and sambiloto-treated groups, as well as glibenclamide group used as comparison, and a group treated using sambiloto combined with glibenclamide.

Moods Median Test at alpha 5% analysis also showed that glibenclamide-treated group (D2) used as comparison at day–14 was not significantly different than treatment D5 and D6. While at day–21, blood glucose of D2 group (120 mg/dl) was also not significantly different with D5 group (122 mg/dl). The results indicated that the ability of sambiloto extract at dosage of 400 mg/200 g body weight and comparison drug glibenclamide to decrease rat blood glucose was comparable.

Blood glucose of D3 group at day – 14 and 21 analyzed using Moods Median Test alpha 5% was significantly different to D2, D5, D6 but not to D4. The results indicated that sambiloto ekstrak at 100 mg and 200 mg/200 gr body weig had similary low ability compare to those ofD5, D6 as well as D2. D4 group result at day–14 and 21 analyzed using Moods Median Test at alpha 5% was not significantly different with D2, D5 and D6 as well as D3. It indicated that sambiloto extract able to decrease diabetic rat blood glucose. Sambiloto extract at dosage of 100mg and 200mg/200 g body weight (D3 and D4, respectively) had comparable ability to decrease blood glucose up to 53%, while at dosage of 400 mg/200 g body weight had similar ability to 0.9 mg glibenclamide/200 g body weight of 56 %. Sambiloto extract at dosage of 200 mg/200 g body weight combined with 0.9 mg glibenclamide able to decrease diabetic rat blood glucose up to 58 compare to initial blood glucose level, however hypoglycemic risk need to be considered.

4. Conclusions

Sambiloto extract at dosage of 100 mg/200 g body weight; 200 mg/200 g body weight; 400 mg/200 g body weight and combination of 200 mg sambiloto and 0.9 glibenclamide were all able to decrease aloxane-induced diabetic rats. While the extract at dosage 400 mg/200 g body weight had comparable results to those obtained by

0.9 mg/200 g body weight glibenclamide of 56% decrease. Sambiloto extract at 200 mg/200 g body weight combined with 0.9 mg glibenclamide/200 g body weight was able to decrease 58% rat blood glucose, however hypoglycemic risk need to be considered.

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