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Effect of *Andrographis paniculata* on Blood Sugar Levels Through Regulation of Alpha-Glucosidase Enzyme Expression: An In Vivo Study

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A B S T R A C T

Diabetes mellitus (DM) is a disease characterized by an increase in blood glucose levels caused by insulin deficiency, either absolute or relative. The α-glucosidase enzyme functions to accelerate the absorption of glucose by the small intestine by catalyzing the hydrolytic cleavage of oligosaccharides into monosaccharides. This study aims to explore the potential of AP extract in regulating blood sugar levels through inhibition of α-glucosidase activity in the intestine. This study is an in vivo experimental study. A total of 30 \ rats were divided into a control group and treated with *Andrographis paniculata*. Examination of blood sugar levels was carried out by spectrophotometry and examination of alpha-glucosidase enzymes by ELISA. Data analysis was performed using SPSS software with univariate and bivariate analysis. *Andrographis paniculata* extract was able to reduce blood sugar levels and was able to decrease the activity of the alpha-glucosidase enzyme as the dose increased. *Andrographis paniculata* extract is able to reduce blood sugar levels by inhibiting the activity of the alpha-glucosidase enzyme in the intestine.

1. Introduction

Diabetes mellitus (DM) is a disease characterized by an increase in blood glucose levels caused by a lack of insulin, either absolute or relative. Currently, diabetes mellitus is a serious threat to humans and is the 7th leading cause of death in the world, and Indonesia is ranked 4th after the United States, India, and China for the largest number of people with diabetes mellitus in the world.[1] The incidence of DM from year to year will increase. The prevalence of diabetes mellitus in Indonesia in 2013 was 6.9%, while in 2018, it was 8.5%.[2] There is one therapeutic approach that can be used to treat diabetes mellitus, namely, by inhibiting enzymes related to glucose absorption in the body, such as the α-glucosidase enzyme. The enzyme α-glucosidase functions to accelerate the absorption of glucose by the small intestine by catalyzing the hydrolytic cleavage of oligosaccharides into monosaccharides, which causes an increase in blood glucose levels in the body after eating. To slow or delay the absorption of glucose in

the intestine that can prevent a postprandial rise in blood glucose levels, α-glucosidase enzyme inhibitors are needed.[3]

Andrographis paniculata (AP) is one of the most common plants in Indonesia. This plant is known as sambiloto and has the characteristic that bitter leaves taste bitter. AP has been widely used ethnopharmacological in overcoming various health problems, among others, to treat fever, diarrhea, high blood pressure, and diabetes mellitus. AP is used by the community in overcoming DM by boiling and drinking boiled water. Several studies demonstrated the potential of AP extracts in the regulation of blood sugar levels in vivo.[4-8] This study is the first study aimed at exploring the potential of AP extract in regulating blood sugar levels through inhibition of α-glucosidase activity in the intestine.

2. Methods

This study is an experimental study with a post-test-only approach with a control group design. A total of 30 rats (*Rattus norvegicus*) Wistar strain was acclimatized for 7 days, then grouped randomly into 5 groups (K1, K2, P1, P2, and P3). Group K1 is a negative control, where the rats were induced by DM and only given intragastric aquadest. Group K2 is a positive control, where the rats were induced by DM and given acarbose 1 mg/kg BW. Groups P1-P3 were the treatment group with 50 mg/kg BW, 100 mg/kg BW, and 200 mg/kg BW intragastrically administered AP extracts for 7 days. This study was approved by the medical and health research ethics committee CMHC-Science & Research Center, Palembang, Indonesia (No. 112/CMHC/KEPK-X/2021).

A total of 1 kg of wet AP leaves were cleaned and dried using an oven at a temperature of 60^{o}C. After the AP leaves were dry, then the AP leaf was refined to obtain AP Simplicia powder. The AP Simplicia powder was then extracted by the maceration method using 96% 1:10 ethanol solvent for 3x24 hours. Next, the pulp and macerate separation process is carried out. The macerate is evaporated so that it becomes a thick extract using a rotary evaporator. The DM induction process was carried out by intraperitoneal induction of Alloxan at a dose of 110 mg/kg BW. If the results of the examination of blood sugar levels by spectrophotometry have shown more than 200 mg/dL, the rat has been considered to have DM.

After being treated for 7 days, the rats were evacuated from their intestines by first being anesthetized with the anesthetic agent Biopenthyl® 0.1 ml/10 g BW. Intestinal organs are washed, cleaned, and put into a container for further homogenization. Then the process of examining the activity of the alpha-glucosidase enzyme was carried out using the enzyme-linked immunosorbent assay (ELISA) examination method.

Data analysis was carried out with the help of SPSS 25 software. Next, univariate analysis was carried out to present the distribution of data, followed by bivariate analysis with a T-test and followed by post hoc test (Bonferroni). The p-value is set at 5% or 0.05, where the p-value <0.05 indicates a statistical difference in the mean levels between groups.

3. Results and Discussion

Table 1 shows the potential of AP extract in lowering blood sugar levels. The P1, P2, and P3 groups showed that they were able to lower blood sugar levels better than the K1 group that did not receive treatment. Treatment groups P1 and P2 reduced blood sugar levels not as optimally as K2, which received acarbose treatment. The P3 group was able to lower blood sugar levels more optimally than the K2 group, which received acarbose treatment. The higher the dose of the AP extract, the more optimal the ability of the AP extract to lower blood sugar levels.

Table 1. Comparison of mean blood sugar levels between groups

Group	Mean blood sugar levels (Mean±SD) mg/dL
K1	453.5±21.2
K2	243.4±11.3
P1	398.7±23.4*
P2	298,7±15.6*
P3	189.6±11.1*

*Post Hoc Test (Bonferroni) VS K2, p<0.05

Table 2 shows the potency of AP extract in reducing alpha-glucosidase enzyme activity. Groups P1, P2, and P3 showed that they were able to reduce the activity of the alpha-glucosidase enzyme better than the untreated group K1. Treatment groups P1 and P2 decreased the activity of the alpha-glucosidase enzyme not as optimally as K2, which received acarbose treatment. The P3 group was able to reduce the activity of the alpha-glucosidase enzyme more optimally than K2, which received acarbose treatment. The higher the dose of AP extract showed the ability of AP extract to reduce the activity of the alpha-glucosidase enzyme more optimally.

Table 2. Comparison of mean levels of alpha-glucosidase between groups

Groups	Mean levels of alpha-glucosidase (Mean±SD) pg/mL
K1	212.5±11.4
K2	77.4±5.3
P1	198.2±12.1*
P2	135,4±11,2*
P3	89,6±6.1*

*Post Hoc Test (Bonferroni) VS K2, p<0.05

The AP extract contained various secondary metabolites, especially flavonoids. Several studies show that AP extract is rich in flavonoids.[9,10] Other studies have shown that flavonoid compounds (quercetin, kaempferitrin, rutin, and kaempferol) have the ability to inhibit the activity of digestive enzymes in the duodenum, both maltase, sucrase, and lactase.[11,12] The ability to inhibit digestive enzymes in the duodenum causes the ability of flavonoids to prevent the breakdown of disaccharides into monosaccharides. Other studies have also shown that flavonoid compounds (quercetin and rutin) have the potential to inhibit alpha-glucosidase enzyme activity in vitro.[13] Enzyme alpha-glucosidase is an enzyme located in the brush border of the intestine that plays a role in the absorption of glucose in the intestine.[14] The ability of AP extract to reduce the activity of the alpha-glucosidase enzyme causes a decrease in the activity of glucose absorption in the intestine so that it will reduce blood sugar levels.[15]

4. Conclusion

Extract of *Andrographis paniculata* is effective in reducing blood sugar levels by inhibiting the activity of the alpha-glucosidase enzyme in the intestine in rats.

5. References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27(2):1047-53.
2. Shenfield, G. Metformin: Myths, misunderstandings, and lessons from history. Aust Prescr. 2013: 36(2):38-9.
3. Okhuarobo A, Falodun JE, Erharuyi O, Imieje V, Falodun A, et al. Harnessing the medicinal

properties of *Andrographis paniculata* for diseases and beyond: A review of its phytochemistry and pharmacology. Asian Pac J Trop Dis. 2014; 4:213-22.

4. Jarukamjorn K, Nemoto N. Pharmacological aspects of *Andrographis paniculata* on health and its major diterpenoid constituent Andrographolide. J Health Sci. 2008; 54: 340-81.
5. Niranjan A, Tewari SK, Lehri, A. Biological activities of Kalmegh (*Andrographis paniculata Nees*) and its active principles-A review. Indian J Nat Prod Resour. 2010; 1:125-35.
6. Akbar, S. *Andrographis paniculata*: A review of pharmacological activities and clinical effects. Altern Med Rev. 2001; 16:66–77.
7. Subramanian R, Asmawi MZ, Sadikun A. A bitter plant with a sweet future? A comprehensive review of an oriental medicinal plant: *Andrographis paniculata*. Phytochem Rev. 2012; 11:39-75.
8. Hossain MS, Urbi Z, Sule A, Rahman KMH. *Andrographis paniculata (Burm. f.)* Wall. ex Nees: A review of ethnobotany, phytochemistry, and pharmacology. Sci World J. 2014; 23(2): 234-8.
9. Jada SR, Matthews C, Saad MS, Hamzah AS, Lajis NH, et al. Benzylidene derivatives of andrographolide inhibit growth of breast and colon cancer cells in vitro by inducing G1 arrest and apoptosis. Br J Pharmacol. 2008; 155:641-54.
10. Lim JC, Chan TK, Ng DSW, Sagineedu SR, Stanslas J, et al. Andrographolide and its analogues: Versatile bioactive molecules for combating inflammation and cancer. Clin Exp Pharmacol Physiol. 2012; 39:300-10.
11. Dai GF, Xu HW, Wang JF, Liu FW, Liu HM. Studies on the novel á-glucosidase inhibitory activity and structure-activity relationships for andrographolide analogue. Bioorg Med Chem Lett. 2006; 16:2710-3.
12. Fiehn O. Metabolomics-the link between genotypes and phenotypes. Plant Mol Biol. 2002; 48:155-71.
13. Kinross JM, Holmes E, Darzi AW, Nicholson JK. Metabolic phenotyping for monitoring surgical patients. Lancet. 2011; 377:1817-9.
14. Zhang A, Sun H, Wang X. Saliva metabolomics opens door to biomarker discovery, disease diagnosis, and treatment Appl Biochem Biotechnol. 2012; 168:1718-27.
15. Zhang A, Sun H, Yan G, Wang P, Wang X. Metabolomics for Biomarker Discovery: Moving to the Clinic. BioMed Res Int. 2015; 15(2):213-9.