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THE EFFECT OF TURMERIC EXTRACT (*Curcuma longa*) ON THE IMPROVEMENT OF MUSCLE MASS IN SWISS DIABETES MELITUS MICE SKELETAL MUSCLE INDUCED BY STREPTOZOTOCIN

Alfin Ihza Trimahendra[1*], Yora Nindita[2], Vega Karlowee[3], Muhamad Thohar Arifin[4], Mochamad Ali Sobirin[2]

[1]Undergraduate Student of Faculty of Medicine, Diponegoro University
[2] Lecturer, Department of Pharmacology, Faculty of Medicine, Diponegoro University
[3] Lecturer, Department of Pathology Anatony, Faculty of Medicine, Diponegoro University
[4] Lecturer, Department of Anatony, Faculty of Medicine, Diponegoro University
[*)]Corresponding author : alfinihzatrimahendra@gmail.com

ABSTRACT

Backgrounds. Diabetes mellitus is a degenerative disease that has various complications. One of neglected diabetes mellitus complication is skeletal muscle atrophy. Turmeric and java turmeric extracts were need to be clarified due to those effect as antihyperglycemic agent which might affected muscle atrophy as one of diabetes mellitus complication. **Aim.** To compared the efficacy of turmeric and java turmeric extract on reducing the progression of skeletal muscle atrophy in streptozotocin-induced diabetes mellitus. **Methods.** We conducted experimental animal studies with a post test only control group design using 25-30 grams male Swiss mice aged 12 weeks. Diabetes mellitus was induced by streptozotocin (STZ) administration. All 28 samples were randomly divided into 4 groups : control + PBS, control + STZ, STZ + turmeric, and STZ + java turmeric groups. Before treatment, blood glucose and body weight were examined on 3rd day. Blood glucose, body weight, hindlimb muscle weight, and muscle diameter results were examined after treatment (on 21st day). Data was analyzed with statistical software after all procedures were done. **Results.** STZ + turmeric group showed insignificant decreased in blood sugar levels (p=0.107). Control + STZ group showed significantly reduced hindlimb muscle weight compared to other groups. Hindlimb muscle weight was significantly ameliorated by STZ + turmeric extract (p=0.048). There were no significant improvement on skeletal muscle diameter among groups. **Conclusion.** The administration of turmeric extract improved hindlimb muscle weight but may not mediated by glucose lowering effect in streptozotocin induced diabetic mice.

Keywords : Diabetes Mellitus, Java Turmeric Extract (*Curcuma xanthorrhiza*) Skeletal Muscle Atrophy, Streptozotocin, Turmeric Extract (*Curcuma longa*)

INTRODUCTION

Diabetes mellitus is a metabolic disease characterized by chronic hyperglycemia due to defects in insulin. Diabetes is a disease that causes many complications.[1] These complications can affect several organs include skeletal muscle through its negative effects on skeletal muscle progenitor cells. Effects that can appear on skeletal muscle include atrophy. Muscle development is strongly influenced by type 1 diabetes mellitus which manifests with a decreased in muscle mass, decreased in muscle fiber size, poor metabolic control, and a tendency to switch to glycolytic phenotypes. Similar to what happens in type 1 diabetes mellitus, type 2 diabetes mellitus also shows some damage including an increase in the number of glycolytic fibers, muscle atrophy, and decreased capillary density.[2,3]

Turmeric and java turmeric are two herbs that have proven ingredients that can improve the condition of diabetic patients through various mechanisms that they have.[4,5] Curcumin found in turmeric and java turmeric has a very large influence

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on inflammation and beta cell dysfunction. Although it is not yet known specifically how the effect of curcumin on inflammation occurs in the muscles of diabetic patients, its anti-inflammatory mechanism is able to improve insulin resistance in skeletal muscle which will also have an impact on the damage that can occur in muscle fibers. [4,6,7]

The purpose of this study is to compared the efficacy of turmeric with java turmeric extract to decrease the progression of skeletal muscle atrophy in the condition of diabetes mellitus using experimental animals that had been injected with streptozotocin. This research is expected to be useful in the further use of herbal plants in for treating various complications of diabetes mellitus, one of which is skeletal muscle atrophy.

METHODS

This research is an experimental laboratory research with a post test only control group design using male Swiss mice aged 3 months weighing 25-30 grams. DM is induced by streptozotocin (STZ) administration. All 28 samples were randomly divided into 4 groups : control + PBS, control + STZ, STZ + turmeric, and STZ + java turmeric groups. Skeletal muscle atrophy in mice was examined by HE staining on the 21st day after STZ administration. Data normality was tested with Saphiro-Wilk. Normal data distribution was analyzed by One Way ANOVA followed by LSD test for post-hoc analysis and for abnormal data distribution examined by Kruskal-Wallis H. Ethical clearance was obtained from the Medical and Health Research Ethics Commission (KEPK) of the Faculty of Medicine, Diponegoro University.

RESULTS

There was no effect seen on body weight and blood glucose in the STZ + turmeric (p=0.247,p=0.521) and STZ + java turmeric groups (p=0.106,p=0.565). There was a decrease in muscle weight in the STZ group but it could be alleviated in the STZ + turmeric group (p=0.048) and almost alleviated by the STZ + java turmeric group (p=0.072). No visible improvement in skeletal muscle diameter by the STZ + turmeric and STZ + java turmeric groups.

Table 1. Pre-Termination Data (n=20)

Data	Group			
	control + PBS n = 5	**control + STZ n = 5**	**STZ + Turmeric n = 5**	**STZ + java turmeric n = 5**
Blood glucose, mg/dl	163.6 ± 53.5	150.4 ± 17.0	180.6 ± 17.8	207.0 ± 21.1
Body weight, gram	26.6 ± 1.14	27.4 ± 1.94	27.6 ± 1.51	27.2 ± 1.09

PBS, phosphate buffer sulfate, STZ, streptozotocin. Data expressed in mean ± SD, Data tested with One Way ANOVA.
*p<0.05 compared to the control group + PBS.
#p<0.05 compared to the control group + STZ.

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Table 2. Post-Termination Data (n=20)

Data	Group			
	control + PBS n = 5	**control + STZ n = 5**	**STZ + turmeric n = 5**	**STZ + java turmeric n = 5**
Blood glucose, mg/dl	100.3 ± 56.9	193.6 ± 14.3*	167.7 ± 45.8	216.7 ± 12.3*
Body weight, g	30.4 ± 1.67	32.0 ± 2.34	30.2 ± 0.83	30 ± 2.0
Muscle weight, g	0.076 ± 0.005	0.046 ± 0.005*	0.066 ± 0.009#	0.064 ± 0.006
Muscle diameter, µm	52.8 ± 4.3	45.6 ± 2.8	55.4 ± 3.2	54.0 ± 2.5

PBS, phosphate buffer sulfate, STZ, streptozotocin. Data expressed in mean ± SD, Data tested with One Way ANOVA.
*p<0.05 compared to the control group + PBS.
#p<0.05 compared to the control group + STZ.

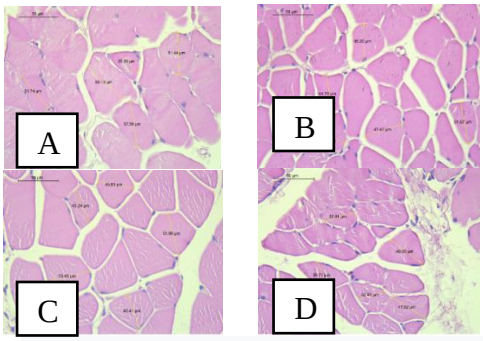

Figure I. Histopathological examination
PBS, Phosphate Buffer Sulfate, STZ, streptozotocin. Myocyte cross-sectional picture of mice skeletal muscle stained with Haematoxylin and Eosin (400x magnification). Control + PBS (A), Control + STZ (B), STZ + Turmeric (C), STZ + Java Turmeric (D).

DISCUSSION

The results obtained in the STZ + turmeric group were 167.7 mg/dl for blood sugar, 30.2 gram for body weight, 0.066 gram for skeletal muscle weight, and 55.36 µm for skeletal muscle diameter. The results obtained from blood sugar and body weight examination are not in accordance with some previous studies which have stated that the administration of turmeric extract has positive impact on mice in the condition of diabetes mellitus with various mechanisms that can reduce blood sugar levels and prevent the decrease of body weight in mice due to STZ administration.[8,9] In this study, blood sugar levels seen at termination did not show a significant difference when compared with the control + STZ and STZ + java turmeric group (p>0.05). Body weight examination also showed no significant differences between all groups (p>0.05). However, the muscle weight seen in this group showed significant results, which was a noticeable difference when compared to control + STZ group (p<0.05). Although the muscle weight experienced a significant improvement, the diameter of the muscle

seen on the histopathological examination did not show a significant difference when compared with control + STZ group (p>0.05). The results of the skeletal muscle diameter seen in this study are not in

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accordance with the research conducted by Ratna Darjanti et al.

Which showed that the administration of turmeric extract had a good effect on skeletal muscle diameter of mice that had been induced with diabetes mellitus even though the results of muscle weight examination showed results which is quite significant.[7,10]

The results obtained in the STZ + java turmeric group were 216.7 mg/dl for blood sugar, 30 gram for body weight, 0.064 gram for skeletal muscle weight, and 53.96 µm for skeletal muscle diameter. The results obtained from blood sugar and body weight examination are not in accordance with several studies that have been done previously which stated that java turmeric extract has a good effect on blood sugar levels in mice that have been induced with diabetes mellitus and were able to improved the weight of mice that are declining due to streptozotocin administration.[5,11,12] In this study, blood sugar levels seen at termination did not show significant differences when compared with control + STZ and STZ + turmeric group ($p>0.05$). Body weight examination also showed no significant differences between all groups ($p>0.05$). Skeletal muscle diameter showed no significant difference when compared to the control + STZ group ($p>0.05$) but the results were almost significant on muscle weight exam ($p=0.072$). These results are not accordance with several researches which states that the substances contained in java turmeric extract have a good effect on the skeletal muscle condition by reducing the atrophy induced by diabetes mellitus.[5,7,12]

The results of this study still have some shortcomings such as there were no specific measurements for curcumin and xanthorrhizol levels that contained in turmeric dan java turmeric extract work in mice, there were no tools to get perfect muscle cuts thus affecting the histopathological examination and glucose testing before induction of streptozotocin is not done so that it can only be examined the effect of treatment.

CONCLUSION AND SUGGESTION

Conclusion

The research results obtained are not in accordance with several journals that examine similar things. The results of this study showed that turmeric and java turmeric extracts did not significantly affect the blood glucose, body weight, and diameter of skeletal muscle fibers but turmeric extract had a significant effect on the muscle weight of mice while java turmeric extract had only nearly significant effect.

Suggestion

Need further research on various external influences that affect the blood sugar of mice during the treatment process such as stressors, food intake, cages, etc. In addition, further research is concerned with solvents that can increase the bioavailability of the contents in extracts to maximize the desired effect and the need for research on the addition of other variables in order to give a clearer histological picture.

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