International Journal of Sciences

Research Article Volume 3 - January 2014 (1)

Potential Assessment of Leaf Ethanolic Extract Honje (Etlingera Hemisphaerica) in Regulating Glucose and Triglycerides on Mice (Mus Musculus)

Aceng Ruyani[1], Agus Sundaryono[1], Zico Fakhrur Rozi[2], Dian Samitra[2], Efri Gresinta[3]

[1]Magister Program in Science Education, Bengkulu University, Jalan Raya Kandang Limun, Bengkulu 38371, Indonesia
[2]Department of Biology Education, Collage of Teacher Training and Education, PGRI, Lubuk Linggau, Indonesia
[3]Department of Biology, Indraprasta University, Jalan Nangka No 58, Jakarta, Indonesia

ABSTRACT: This study was aimed to assess potential of leaf ethanolic extract *Etlingera hemisphaerica* in regulating glucose and triglyseride on mice (*Mus musculus*). METHODS: Two extract assesments were composed of five group (1 control, 3 dosages of extract, and 1 comparator drug), and each group were replicated by 5 of *M. musculus*. Pathological conditions were performed by giving 10 % sugar in drink for hyperglycemia, and a high fat diet for hypertriglyceride during 10 days. There were three dosages of the extract (0.13, 0.26, and 0.39) mg/g body weight (bw), and two comparator drugs (*glibenclamid* 0.52 mg/g bw as anti diabetic and *simvastatin* 0.052 mg/kg bw as anti hypertriglyceride). Both dosage extract and comparator drug were administrated by gavage on day 11, while the control group received only sesame oil solvent in the same manner. Blood samples were obtained from the tail to determine glucose and triglyceride levels before and after treatment. RESULTS: Treatment with 0.39 mg/gbw extracts decreased glucose from baseline (117.8 mg/dL) to the end (75.20 mg/dL) on day 13 as much as 36.16 % while glibenclamid decreased 38.00%. Triglyceride test revealed that 0.39 mg/gbw extract decreased from baseline (127.4 mg/dL) to the end (100.4 mg/dL) on day 13 as much as 21.19% which was equivalent to 21.20% caused by simvastatin. CONCLUSION: Leave ethanolic extract of *E. hemisphaerica* (0.39 mg/g bw) potentially decrease blood glucose (36.2 %) and triglyceride (21.19%) in *M. musculus*.

Keywords: E.hemispaerica, ethanolic extract, M. musculus, glucose, triglyceride

INTRODUCTION

Honje (*Etlitinga hemisphaerica*) is a chronic life spice plant flowers, fruits, and seeds are used by people of Bengkulu as a vegetable or food seasonings. This plant can also be used as a cure for skin related diseases, including measles. Results of chemical analysis flowers *E. hemisphaerica* suggests that part of the plant contain alkaloids, flavonoids, folifenol, steroids, saponins, and volatile oil (Naufalin *et al*., 2005). Recently research has addressed that the antioxidant content of plant leaves *Etlingera* higher when compared to the flowers and rhizomes (Chan *et al*., 2011). Therefore, having active compounds such as polyphenols and flavonoids makes *Etlingera* be efficacious. Another *Etlingera* extract, *Etlingera elatior*, causes a decrease in lipid hydroperoxides and protein-carbonyl-contents, as well as a significant increase in total antioxidants and antioxidant enzymes in rats (Jackie *et al*., 2011).

Diabetes mellitus (DM) is known as diabetes or sugar disease is a group of chronic diseases characterized by elevated levels of blood glucose as a result of a disturbance in the body's metabolic system. In the DM condition pancreas unable to produce insulin the body needs. It has been reported that flavonoids found in plants of *Daluman* can help overcome the body's natural antioxidant system of oxidative stress underlying the pathogenesis of type 2 DM (Gina, 2010). This phenomenon is reinforced by the results of studies Wan *et al*. (2013) showed that the extract of *Swertia kouitchensis* that contain lots of antioxidants proven potential as an anti-diabetic and able to alter metabolism in mice made diabetic condition. Based on the information alleged that the active chemical compounds in the form of antioxidants derived from plants, expected potential as an alternative medicine for DM cases.

Coronary heart disease (CHD) was ranked first (80%) as the cause of death (Santoso *et al*., 2007). Results of a survey conducted by the Ministry of Health showed that the prevalence of CHD in Indonesia from year to year increase (Majid, 2007). Investigation of hipolipidemia drugs which derived from natural materials are enterprising done. Natural medicine in addition was assumsed to cheap and

Aceng Ruyani (Correspondence)
ruyani@lycos.com
+

readily available is also expected to have minor side effects compared with the synthetic drugs. Some plants which contain secondary metabolites, such as flavonoids, steroids, trepenoid, and alkaloids potential as raw material of natural medicine. Metwally *et al.* (2009) stated that the administration of silymarin (flavonoid) in mice can reduce significantly levels of fat in the blood, triglycerides, cholesterol, and lipoprotein. Research conducted by Hil *et al.* (2011) showed that flavonoids can reduce blood levels of triglycerides and free fatty acids. Furthermore Liu *et al.* (2013) reported that the antioxidant content in the extract of *Catathelasma ventricosum* able to decrease triglyceride levels in mice.

Based on the above description is deemed necessary to be made *E. hemisphaerica* leaf ethanol extract and then test the potential of the extract in the regulation of blood glucose and triglyceride level in mice (*Mus musculus*).

METHODS

a. Flavonoid detection and extract preparation

Detection of flavonoids in the leaves of *E. Hemisphaerica* was be performed by the Wilstater Test. Fresh leaves of *E. hemisphaerica* 4 g are still fresh finely chopped and then cooked in 30 mL of 70% ethanol, and filtered in hot conditions. The filtrates was concentrated by half, and then add 1 drop of concentrated HCl 6 M and 2 cm along the magnesium ribbon is cut into small pieces. If formed sorrel it could be concluded that samples positive containing flavonoids (Ayoola *et al*., 2008).

Leaf sample *E. hemisphaerica* as research plant material were collected from the sourounding of Curup, Rejang Lebong, Bengkulu. Selected leaves located at the base of the stem, then washed and cut into small pieces. Then placed on the paper and closed with paper and dried for 2 weeks indoors without sunlight. The aim was that the content of flavonoid compounds on *E. hemisphaerica* not damaged. Leaves that have been dried, blended, and then macerated with 96% ethanol for 7 days. Maceration results separated by filtration, and the filtrate was concentrated by evaporation using a rotary evaporator and heated electrically to obtain a thick leaf extract (Sopi and Khan, 2013) of *E. Hemisphaerica*

b. Experimental animals

Swiss Webster mice (*Mus musculus*) were used as experimental animals. The animals ware reared in a room at 23-27 ^{o}C, and 83 % humidity. Food and water were given *ad libitum* (Ruyani *et al*., 2005; Ruyani *et al*., 2011). Total number of male *M. musculus* aged 6-8 weeks with 25-35 g body weight (bw) were used for potential assesment of ethanolic leaf extract *E.hemisphaerica* in regulating blood glucose and triglyceride as much as 50 animals. Distribution of the experimental animals in this study is presented on Table 1.

c. Dosages

Sunarso (2011) reported that the effective dosage of *Mulitinga calbura* extract which contains flavonoids in mice was 0.13 mg/g bw. Based on the report it was selected in this study three single dosage of leaf ethanolic extract of *E. hemispaerica* were 0.13, 0.26, and 0.39 mg/g bw. For comparison the glucose test was used glibenclamid at dosage of 0.52 mg/gbw (Azmi *et al*., 2012; Odo *et al*., 2012), meanwhile for the triglycerida test was used simvastatin at single dosage of 0.52 mg/kg bw (Fu *et al*., 2006; Xu *et al*., 2009; Table 1).

Tabel 1. Experimental design to assess the potential of leaf ethanolic extract *Etlingera hemisphaerica* in regulating glucose and triglyceride on mice (*Mus musculus*). Both control and treated animals obtained *ad libitum* standar drink and food on day 11-13.

Group	**N**	**Day 1-10**	**Day 11**		**Day 13**
A. Glucose test		Drink	Blood samples for.	Administrated by *gavage*	Blood samples for.
Control (CG)	5	Standard	Glucose test	Sesame oil solvent	Glucose test
Treatment 1 (TG1)	5	10% sugar	Glucose test	0,13 mg/g bw extract	Glucose test
Treatment 2 (TG2)	5	10% sugar	Glucose test	0,26 mg/g bw extract	Glucose test
Treatment 3 (TG3)	5	10% sugar	Glucose test	0,39 mg/g bw extract	Glucose test
Treatment 4 (TG4)	5	10% sugar	Glucose test	0,52 mg/g bb glibenclamid	Glucose test
Number of mice	**25**				
B.Triglyceride test		Food	Blood samples for.	Administrated by *gavage*	Blood samples for.
Control (CT)	5	Standard	Triglyceride test	Sesame oil solvent	Triglyceride test
Treatment 1 (TT1)	5	High fat	Triglyceride test	0,13 mg/g bw extract	Triglyceride test
Treatment 2 (TT2)	5	High fat	Triglyceride test	0,26 mg/g bw extract	Triglyceride test
Treatment 3 (TT3)	5	High fat	Triglyceride test	0,39 mg/g bw extract	Triglyceride test
Treatment 4 (TT4)	5	High fat	Triglyceride test	0,052 mg/kg bw *simvastatin*	Triglyceride test
Number of mice	**25**				

d. Glucose test

Twenty-five (25) of *M. musculus* were prepared for glucose test, and then were divided randomly into 5 groups with 5 replicates (Table 1). The control group (CG) obtained only drinking standard water *ad libitum* on days 1-10, and then on day 12 were given sesame oil solvent. Treatment group 1 (TG1), 2 (TG2), and 3 (TG3) for 10 days (day 1 -10) were given a drink with 10% sugar to make the condition of hyperglycemia. On day 12, groups of TG1, TG2, and TG3 were administrated by gavage single dosage of leaf extract *E. hemispaerica* 0.13, 0.26, and 0.39 mg/gbw respectively. Treatment group 4 (TG4) was made hyperglycemic by the drink with 10 % sugar for 10 days, and then single dosage of 0.52 mg/gbw glibenclamid was given by gavage (Ruela *et al*., 2013) on day 11. Blood samples were collected from the tail of both control and treatment group on day 11 and 13 to determine blood glucose levels using the Glucose test (multiCarein**;** http://www.biosys.it/ en/pr_multicarein.html).

d. Triglyceride test

Twenty-five (25) of *M. musculus* were prepared for triglycerides test, and then were divided randomly into 5 groups with 5 replicates (Table 1). The control group (CT) obtained only food standard *ad libitum* on days 1-10, then on day 12 were given sesame oil solvent. Treatment group 1 (TT1), 2 (TT2), and 3 (TT3) for 10 days (day 1-10) were fed a high-fat diet (adding 50 % duck egg yolks into the standard feed) *ad libitum* to make the condition of hyperlipidemia. On day 11, groups of TT1, TT2, and TT3 were admistered by gavage single dosage of leaf extract *E. hemispaerica* respectively 0.13, 0.26, and 0.39 mg/gbw respectively. Treatment group 4 (TT4) was made hyperlipidemic by the high-fat diet for 10 days, then given singel dosage of 0.52 mg/kg bw *simvastatin* by gavage (Sang *et al*., 2012) on day 11. Blood samples were collected from the tail of both control and treatment group on day 11 and 13 to determine blood glucose levels using the Triglyceride test (multiCarein**;** http://www.biosys.it/en/pr_multicarein.html).

RESULTS AND DISCUSSION

a. Leaf extract of *E. hemispaerica*

Flavonoid compounds from the leaves of *E. hemispaerica* was identified using the test HCl and Mg tape, as a comparator was also determined flavonoid compounds in leaves of cherry (*Mulitinga calbura*). In the flavonoids, observations were made based on the color change that occurs during reagent addition. After testing, it is known that flavonoids in the leaves of *E. hemispaerica* flavonoid compounds contained qualitatively marked + +, the fact that mean levels of flavonoid compounds contained in the leaves of *E. hemispaerica* have lower levels of flavonoids when compared with the levels in the leaves of *M. calbura* which is qualitatively marked +++. This is consistent with the results of research conducted by Jackie *et al*. (2011) which states that the flavonoids found in *Etlingera sp.*

Weighing 3,000 g of leaves *E. hemispaerica* was wind dried for 7 days, obtained 800 g of dried leaves, and then blended to be a fine powder. The leaf powder was macerated in 2 liters of ethanol for 7 days, and the resulting filtrate concentrated by rotary evaporator so that the concentrated extract obtained weighing 3 g. After ethanol contained in the concentrated extract was allowed to evaporate, finally got pasta weighing 2 g was ready to be used as tested material of this research. Although rendemen leaf extract of *E. hemispaerica* lower than ethanol extracts of *M. calbura* (Sunarso, 2011), however it was potential in regulating glucose and triglycerides are not yet sure more lower than the ethanolic extract of *M. calbura*.

b. Blood glucose level

Results of analysis of variance showed that the average body weight day 11 (prior to the extract) showed significant results. Weights of *M. musculus* on day 11 were measured after administration of 10 % sugar drink for 10 days. Variance analysis indicated that average body weight of treated group (TG1, TG2, TG3, and TG4) increased significantly compated the control (CG). The facts could can be interpreted that provision of the treatment effect on body weight *M. musculus*. While the results of analysis of variance average body weight on day 13 showed no significant difference between treated gorups comparing the control, and all weights back toward to the normal condition. It is could be intepretated that extract of leaves of *E. hemispaerica* has a potential as anti-obesity effect (Table 2).

Results of analysis of variance showed that sugar levels day 11 in the control group generally markedly lower than the treatment group (Table 3), this fact proves that giving sugar water for 10 days affects the sugar content *M. musculus*. There is a similarity data pattern for body weight and blood sugar levels at day 11 (Table 2 and Table 3) which showed a positive correlation between body weight with blood sugar levels. On day 13, it appears that the blood sugar levels of the control and treatment groups showed no significant results. When comparing glucose levels before (day 11) and after (day 13) treatment seemed that extracts *E. hemispaerica* able to recover from the hyperglycemia condition to normal. It can be interpreted that the leaf extract *E.hemispaerica* give real effect *M.musculus* blood glucose levels. Further note that treatment with 0.39 mg/gbw extract decreased glucosa levels from baseline (117.8

mg/dL) to the end (75.20 mg/dL) as much as 36.16 % while *glibenclamid* decreased 38.00% (Table 3).

Table 2. Average body weight of mice (Mus musculus) before (day 11) and after (day 13) sesame oil solvent (CG), *E.hemispaerica* leaf extract (TG1, TG2, TG3), or glibenclamid (TG4) were administrared by gavage.

Group of experimental animals	**N**	**Day 11. Body weight ± SD g (A)**	**Day 13, Body weight ± SD g (B)**	**Difference B-A g**
Sesame oil solvent (CG)	5	22,00 ± 1,22[a]	25,20 ± 1,30	3,2
0,13 mg/gbw extract (TG1)	5	25,80 ± 0,83[b]	26,00 ± 0,70	0,2
0,26 mg/gbw extract (TG2)	5	24,60 ± 1,14[b]	26,20 ± 1,30	1,6
0,39 mg/gbw extract (TG3)	5	24,60 ± 1,14[b]	25,60 ± 1,14	1,6
0,52 mg/gbb glibenclamid (TG4)	5	25,80 ± 1,30[b]	26,80 ± 1,92	1,0

Note: Rates followed by the same letter are not significantly different data addressing the same column (Least Significant Difference test results, LSR; Steel and Torrie, 1981).

Table 3 indicated that there was a difference in lowering blood sugar levels of *M.musculus* that occurred between days 11-13. In the treatment groups (TG1, TG2, TG3 and TG4) revealed that blood glucose levels were caused by the effect of leaf extract *E.hemispaerica*. The results of Ganugapati (2012) investigation showed that flavonoes (naringenin 7-O-β-D-glucoside) which is a subclass of flavonoids play an active role in influencing blood glucosethe levels. Whereas the treatment group GP4 decrease blood sugar levels are affected by drug glibenclamid (Figure 1). The decrease of blood glocuse levels in the treatment group of TG1, TG2, TG3 and TG4 were 46.6%, 32.8%, 48.6%, and 50.8% respectively. Gina (2010) stated that some materials or substances were determined to decrease effectively blood glucose level when it could decrease the levels more than 10%. In this study, flavonoid intervention have a significant effect in lowering the levels, this were evidenced by the decrease in blood glucose levels in each treatment group over than 10%.

Result of the HCl and Mg ribbon test indicated that leaf extracts of *E.hemispaerica* contain secondary metabolites such as flavonoids. The compounds can affect blood glucose levels in the body by inhibiting the work of *M.musculus* glycosidase enzyme (Hogan, 2010). Glycosidase enzyme plays a role in the formation of glucose in the small intestine by the breakdown of carbohydrates into monosaccharide, excessive activity of the enzyme could lead to type 2 of DM disease. The disease is caused by the amount of insulin produced by the pancreas gland is not able to compensate for the amount of blood glucose levels in the body. When done inhibition of the enzyme glycosidase working in duodenal mucosa causing decomposition reaction of carbohydrates into monosaccharide inhibited (Chiasson *et al*., 2004). Thus glucose is released more slowly into the blood and absorbs be slower, lower, and evenly thus preventing hyperglycemic conditions occur in the body. Flavonoids worked as inhibitors competitively, competing with the substrate to reach the active site of enzymes that can inhibit the action of the enzyme glycosidase. It should be generalized that leave ethanolic extract of E. *hemisphaerica* (0.39 mg/g bw) potentially decrease levels of glucose (36.2 %) in *M. musculus.*

Table 3. Average blood glucose levels of mice (*Mus musculus*) before (day 11) and after (day 13) sesame oil solvent (CG), *E. hemispaerica* leaf extract (TG1, TG2, TG3), or glibenclamid (TG4) were administrated by gavage.

Group of experimental animals	**N**	**Day 11, Blood glucose ± SD mg/dL (A)**	**Day 13, Blood glucose ± SD mg/dL (B)**	**Difference A-B mg/dL (%)**
Sesame oil solvent (CG)	5	92,40 ± 3,64[a]	91,00 ± 2,64	0,6 (0,6)
0,13 mg/gbw extract (TG1)	5	120,00 ± 17,33[b]	76,60 ± 12,36	46,6 (37,8)
0,26 mg/gbw extract (TG2)	5	121,00 ± 24,56[b]	88,20 ± 18,21	32,8 (27,1)
0,39 mg/gbw extract (TG3)	5	117,80 ± 20,22[ab]	75,20 ± 14,09	48,6 (39,2)
0,52 mg/gbb glibenclamid (TG4)	5	133,40 ± 30,58[b]	82,60 ± 3,28	50,8 (38,0)

Note: Rates followed by the same letter are not significantly different data addressing the same column (Least Significant Difference test results, LSR; Steel and Torrie, 1981).

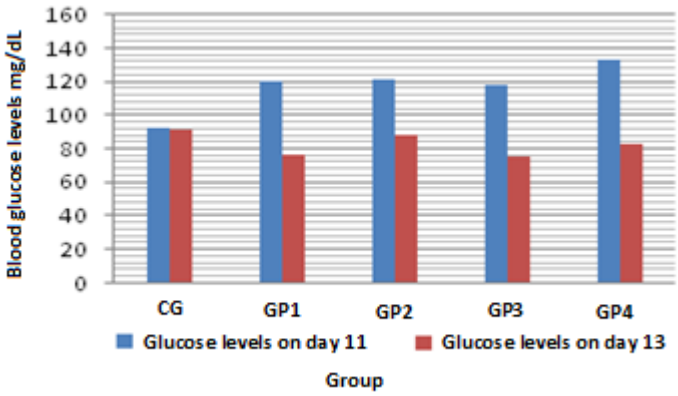

Figure 1. Comparison of blood glucose levels on *M. musculus* before (day 11) and after (day 13) sesame oil solvent (CG), *E.hemispaerica* leaf extract (TG1, TG2, TG3), or glibenclamid (TG4) were administrated by gavage.

c. Blood triglycede level

Results of analysis of variance on day 11 showed that the presence of a significant difference in body weight between the groups of mice. Average body weights of treatment groups (TT1, TT2, TT3, and TT4) were lower than in the control group (CT; Table 4). The phenomenon revealed that high-fat feeding for 10 days real caused weight gain of treated animals. When ingested a high fat diet, the body will produce the calories needed by the muscle cells as energy. If you regularly eat more calories than you burn and have less activity, the excess calories will be stored as fat-cells. On day 11 tested animals received sesame oil solvent (CT), *E. hemispaerica* leaf extract (TT1, TT2, TT3), and simvastatin (TT4). two days later (on day 13) showed no significant difference in body weight between the control and treatment grups. However, if it was compared the situation between day 11 and 13, the fact was appeared that the leaf extract of *E.hemispaerica* and simvastatin caused weight back toward normal conditions. This phenomenon could be interpreted again that leaf extract of *E. hemisphaerica* has the potential as anti obesity effects. Other studies have reported that dietary flavonoids, which include catechin, quercetin, kaempferol, and genistein, inhibit adipogenesis in 3T3-L1 adipocytes (Li *et al*., 2006; Lee *et al*., 2011).

Table 4 Average body weight on *M. musculus* before (day 11) and after (day 13) sesame oil solvent (TK), E.hemispaerica leaf extract (TP1, TP2, TP3), or *simvastatin* (TP4) were adminstered by gavage.

Group of experimental animals	**N**	**Day 11, Body weight ± SD g (A)**	**Day 13. Body weight ± SD g (B)**	**Difference A-B g**
Sesame oil solvent (CT)	5	22,40 ± 2,30[a]	23,80 ± 2,49	1,4
0,13 mg/gbw extract (TT1)	5	27,40 ± 1,8[b]	28,00 ± 2,34	0,6
0,26 mg/gbw extract (TT2)	5	28,40 ± 2,40[c]	29,00 ± 3,31	0,6
0,39 mg/gbw extract (TT3)	5	28,00 ± 1,87[c]	27,60 ± 1,67	0,4
0,052 mg/kgbw simvastatin (TT4)	5	25,00 ± 4,00[c]	25,80 ± 3,56	0,8

Note: Rates followed by the same letter are not significantly different data addressing the same column (Least Significant Difference test results, LSR; Steel and Torrie, 1981).

Results of variance analysis on day 11 showed that blood triglycerides level in treatment groups (TT1, TT2, TT3, and TT4) were significantly higher compared with the control (CT; Table 5). That fact provided that high-fat feeding for 10 days led to increased levels of triglycerides on tested animals. Furthermore it is known there is a positive correlation between body weights with blood triglyceride levels (look for libraries). On day 11 test animals received sesame oil solvent (CT), *E.hemispaerica* leaf extract (TT1, TT2, TT3), and simvastatin (TT4). Two days later (on day 13) showed no differences in levels of actual blood trigluceride between control (CT) and treatment (TT1, TT2, TT3, and TT4). However, if you compare the situation at day 11 and 13, it appears that the leaf extract E.hemispaerica and simvastatin cause blood triglyceride levels return to near normal conditions. Triglycerida test results showed that the leaf extract of *E. hemisphaerica* with three different dosages of giving effect to decrease triglyceride

levels (Table 5). More detailed looks that 0.39 mg/gbw extract decreased from baseline levels (127.4 mg/dL) to the end (100.4 mg/dL) as much as 21.19% roommates is equivalent to 21.20% caused by *simvastatin*.

Table 5 Average blood triglyceride levels on *M. musculus* before (day 11) and after (day 13) sesame oil solvent (TK), *E.hemispaerica* leaf extract (TP1, TP2, TP3), or simvastatin (TP4) were administrated by gavage.

Group of experimental animals	**N**	**Day 11, Blood triglyceride ± SD mg/dL (A)**	**Day 13, Blood triglyceride Day 13 ± SD mg/dL (B)**	**Difference A-B mg/dL (%)**
Sesame oil solvent (CT)	5	106,40 ± 2,51[a]	107,60 ± 1,81	1,2 (1,12)
0,13 mg/gbw extract (TT1)	5	137,80 ± 10,56[b]	107,80 ± 5,89	-30,0 (21,77)
0,26 mg/gbw extract (TT2)	5	130,40 ± 6,02[bc]	102,80 ± 7,08	-27,6 (21,16)
0,39 mg/gbw extract (TT3)	5	127,40 ± 7,89[bc]	100,40 ± 10,18	-27,0 (21,19)
0,052 mg/kgbw simvastatin (TT4)	5	133,00 ± 8,00[c]	104,80 ± 6,26	-28,2 (21,20)

Note: Rates followed by the same letter are not significantly different data addressing the same column (Least Significant Difference test results, LSR; Steel and Torrie, 1981).

The secondary metabolite such as flavonoid was detected by the HCl and Mg ribbon on the leaf extracts of *E.hemispaerica*. It was assumed to decrease blood triglyceride levels due to the influence of flavonoids would affect lipogenesis by the liver. This phenomenon was supported also by Artanti (2008) which stated that the administration of bitter melon juice contains flavonoids that can reduce levels of trigyceride in rats that had been fed a high fat diet. Flavonoid compounds are able to reduce levels in the body is triligserida naringenin, quertin and hespirdin (Hill *et al*, 2012; Mulvihill *et al*, 2009; Gross, 2004). Hardhani (2008) stated that allegedly compounds capable of lowering levels of triglycerides contained in flavonoids are niacin. Niacin suppresses the activity of the enzyme lipoprotein lipase resulting in lower production of very low-density lipoprotein (VLDL) in the liver and can inhibit fat mobilization so that the production of triglycerides, total cholesterol, and low-density lipoprotein (LDL) can be dropped (Khomsan, 2008). It should be generalized that ethanolic extract of *E. hemisphaerica* (0.39 mg/gbw) potentially decrease triglyceride levels (21.19%) in *M. musculus*.

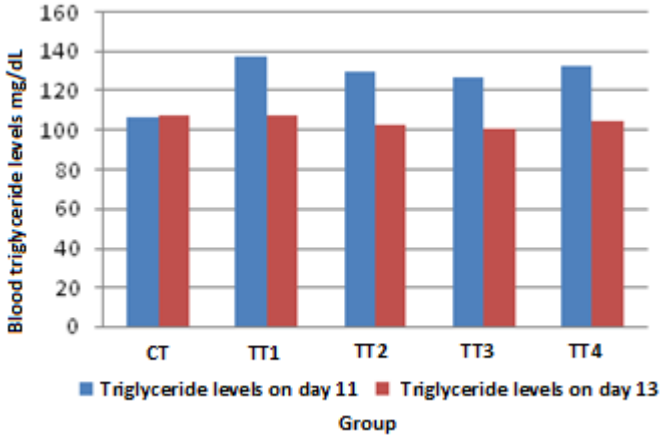

Figure 2. Comparison of blood triglyceride levels on *M.musculus* before (day 11) and after (day 13) sesame oil solvent delivery (CT), *E.hemispaerica* leaf extract (TT1, TT2, TT3), or simvastatin (TT4) were administrated by gavage.

CONCLUSION

Leave ethanolic extract of *E. hemisphaerica* (0.39 mg/g bw) potentially decrease blood glucose (36.2 %) and triglyceride (21.19%) levels in *M. musculus* with hyperglycemia and hypertriglyceride respectivelly.

ACKNOWLEDGEMENT

This research was funded by the Hibah Pascasajana 2012/2013 from the RI goverment (Contract number 189/UN30.10/LT/2013, March 26, 2013). We express our gratitude to Prof. Dr. **Endang Widi Winarni**, MPd. and **Abdul Rahman**, M.Si whom gave

valuable advices and sugestions to conduct the research.

REFERENCES

1) Artanti, D. 2008. Pengaruh Pemberian Jus Buah Pare (*Momordica charantia*) Terhadap Kadar Trigliserida Serum Tikus Wistar Jantan Yang Diberi Diet Tinggi Lemak.
2) Ayoola, GA., Coker, HAB., Adesegun, SA., Adepoju-Bello, AA., Obaweya, K., Ezennia, EC., and Atangbayila, TO. 2008. Phytochemical Screening and Antioxidant Activities of Some Selected Medicinal Plants Used for Malaria Therapy in Southwestern Nigeria. *Trop J Pharm Res*., 7(3): 1019-1024.
3) Azmi, MB., and Qureshi, SA. 2012. Methanolic Root Extract of Rauwolfia serpentina Benth Improves the Glycemic, Antiatherogenic, and Cardioprotective Indices in Alloxan-Induced Diabetic Mice. *Adv Pharmacol Sci*., 376429. doi: 10.1155/2012/376429.
4) Chan, EW., Lim, YY., and Tan , SP. 2011. Standardised herbal extract of chlorogenic acid from leaves of Etlingera elatior (Zingiberaceae). *Pharmacognosy Res*., 3(3):178-84.
5) Chiasson, JL., Josse, RG., Gomis, R., Hanefeld, M., Karasik, A., and Laakso, M. 2004. Acarbose for the prevention of type 2 diabetes, hypertension and cardiovascular disease in subjects with impaired glucose tolerance: facts and interpretations concerning the critical analysis of the STOP-NIDDM Trial data. *Diabetologia* 47: 969–975.
6) Fu, T., and Borensztajn, J. 2006. Simvastatin causes the formation of cholesterol-rich remnants in mice lacking apoE. Biochem Biophys Res Commun., 341(4):1172-6.
7) Ganugapati, J., Baldwa, A. and Lalani, S 2012. Molecular docking studies of banana flower flavonoids as insulin receptor tyrosine kinase activators as a cure for diabetes mellitus. Bioinformation., 8(5):216-20. doi: 10.6026/97320630008216.
8) Gross, M. 2004. Flavonoids and Cardiovascular Disease. *Pharmaceutical Biology*. 42: 21–35.
9) Hardhani, A. S. 2008. Pengaruh Pemberian Ekstrak Daun Salam (*Eugenia polyantha*) Terhadap Kadar Trigliserida Serum Tikus Jantan Galur Wistar Hiperlipidemia [Skripsi]. Semarang: Fakultas Kedokteran Universitas Diponegoro.
10) Hil, EF., De, HV., Beekmann, K., Keijer, J., Hollman, PCH., Ivonne, MC, Rietjens, M., Schothorst, EM 2011. Interference of flavonoids with enzymatic assays for the determination of free fatty acid and triglyceride levels. *Anal Bioanal Chem*. 402:1389–1392.
11) Hogan, Zhang.L, Zhou.K, Sun. S, Canning.C . 2010. Antioxidant rich grape pomace extract suppresses postprandial hyperglycemia in diabetic mice by specifically inhibiting alpha-glucosidase. Nutr Metab (Lond)., 7:71. doi: 10.1186/1743-7075-7-71.
12) Jackie, T., Haleagrahara, N., and Chakravarthi, S. 2011. Antioxidant Effects of *Etlingera elatior* Flower Extract Against Lead Acetate-Induced Perturbations in Free Radical Scavenging Enzymes and Lipid Peroxidation in Rats. *BMJ Reasearch Notes*. 4(67):1-8.
13) Khomsan, A. 2008. *Empat Serangkai Penggempur Kolesterol*. http://www.indomedia.com. Akses 23 Februari 2012.
14) Lee YS, Cha BY, Saito K, Choi SS, Wang XX, Choi BK, Yonezawa T, Teruya T, Nagai K, and Woo JT. 2011. Effects of a Citrus depressa Hayata (shiikuwasa) extract on obesity in high-fat diet-induced obese mice. Phytomedicine. 15:648–654. [PubMed: 21216135]
15) Li RW, Theriault AG, Au K, Douglas TD, Casaschi A, Kurowska EM, and Mukherjee R. 2006. Citrus polymethoxylated flavones improve lipid and glucose homeostasis and modulate adipocytokines in fructose-induced insulin resistant hamsters. Life Sci., 79:365–373. doi: 10.1016/j.lfs.2006.01.023. [PubMed: 16497336]
16) Liu, Y., Sun, J., Rao, S., Su, Y., and Yang, Y. 2013. Antihyperglycemic, antihyperlipidemic and antioxidant activities of polysaccharides from Catathelasma ventricosum in streptozotocin-induced diabetic mice. *Food Chem Toxicol*., 57C:39-45.
17) Majid, A. 2007. Penyakit jantung Koroner: Patofisiologi, pencegahan dan pengobatan terkini. (Pidato pengukuhan jabatan guru besar) http://repository.usu.ac.id/ bitstream/ 123456789/705/1/08E00124.pdf Akses 17 April 2012.
18) Metwally, MAA., El-Gellal, AM, and El-Sawaisi, SM. 2009. Effects of Silymarin on Lipid Metabolism in Rats. *World Applied Sciences Journal*, 6 (12): 1634-1637.
19) Mulvihill, EE., Emma, A., Brian, G S, Dawn, ET, Cynthia, GS., Jane, YE, Janet M. Markle, Robert A. Hegele, and Murray, WH. 2009. Naringenin Prevents Dyslipidemia, Apolipoprotein B Overproduction, and Hyperinsulinemia in LDL Receptor–Null Mice With Diet-Induced Insulin Resistance. *A Journal Of The American Diabetes Assocation*. 58(10).
20) Naufalin, R, Jenie, BSL., Kusnandar, F. Sudarwamto, M. Rukmini, H. 2005. Kajian Sifat Antimikroba Ekstrak Bunga Kecombrang Terhadap Berbagai Mikroba Patogen dan Perusak Pangan. *Jurnal Teknologi dan Industri Pangan*, 16 (2); 119-125.
21) Odo, RI., Asuzu, IU., and Aba, PE. 2012. The antidiabetic activities of the methanolic root bark extract of Afzelia africana in alloxan-induced diabetic mice. *J Complement Integr Med*., 9;9:Article 31. doi: 10.1515/1553-3840.1649.
22) Ruela, HS., Sabino, KC., Leal, IC., Landeira-Fernandez, AM., de Almeida, MR., Rocha, TS., and Kuster, RM. 2013. Hypoglycemic effect of Bumelia sartorum polyphenolic rich extracts. *Nat Prod Commun.*, 8(2):207-10.
23) Ruyani, A., Karyadi, B., Kadir, A. Fitri, D., Tanjung, RY., Puspa, Y. 2011. Alteration of Ossification Rate on Fetal Humerus and Femur Swiss Webster Mice (*Mus muculus*) as the Teratogenic Effects of *Dioscorea hispida* Dennst. *Jurnal Kedokteran dan Farmasi*, *Medika*, 37, 596-603.
24) Ruyani, A., Sudarwati, S., Sutasurya, LA., Sumarsono, SH., Kim, D.J., and Chung, J.H. 2005. A teratoproteomics analysis: Heat shock protein 70 is up-regulated in mouse forelimb bud by methoxyacetic acid treatment. *Birth Defects Research A Clinical and Molecular Teratology*, **73** (7), 517-21.
25) Sang, H., Yuan, N., Yao, S., Li, F., Wang, J., Fang, Y., and Qin, S. 2012. Inhibitory effect of the combination therapy of simvastatin and pinocembrin on atherosclerosis in ApoE-deficient mice. *Lipids Health Dis*., 11:166.
26) Santoso, M., dan Setiawan, T. 2007. *Penyakit Jantung Koroner*. http://www.kalbe.co.id/files /147_05 penyakit jantung koroner.pdf/147_05 penyakit jantung koroner.html. Akses 21 November 2011.
27) Sopi, RB and Khan, MFH. 2013. Bronchodilatory effect of ethanolic extract of the leaves of *Nyctanthes arbortristis*. *Pharmacognosy Res*., 5(3): 169–172. doi: 10.4103/0974-8490.112422. PMCID: PMC3719257.
28) Steel, RGD, and Torrie, JH. 1981. Principles and procedures of statistics. Mc Graw-Hill International Book Company. Singapura.
29) Sunarso, E. 2011. *Pengaruh Ekstrak Kulit Batang Mulitinga calbura Terhadap Kadar Trigliserida Darah Mus musculus Sebagai Sumber Belajar Kimia (LKS) di SMKN 1 Curup*. [Tesis] Prodi Pascasarjana Pendidikan IPA, Universitas Bengkulu.
30) Wan, L., Chen, C., Xiao, Z., Wang, Y., Min, Q., Yue, Y., and Chen J. 2013. *In vitro* and *in vivo* anti-diabetic activity of Swertia kouitchensis extract. *J Ethnopharmacol*., pii: S0378-8741(13)00208-0.
31) X H., Xu, HE., and Ryan, D. 2009. A study of the comparative effects of hawthorn fruit compound and simvastatin on lowering blood lipid levels. *Am J Chin Med*., 37(5):903-8.