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Antihyperglycemic Effect of Propolis Extract from Two Different Provinces in Indonesia

Mahani[1], I.L. Jannah[1], E.S. Harahap[1], M. Salman[2], N.M.F.Habib[2]

[1]*Department of Food Industrial Technology, Faculty of Agroindustrial Technology, Padjadjaran University, Bandung-Indonesia.*
Email: mahanimahani74@yahoo.com

[2]*Faculty of Medicine, Padjadjaran University, Bandung-Indonesia*

***Abstract*— Prevalence of diabetus mellitus (DM) in Indonesia is expected to grow larger, estimated to reach 21,3 million in 2030. The treatments that commonly used for this disease are diet, antidiabetic drug, and insulin replacement, give more burden to the patient caused by its cost. Various studies has been done to find an alternative way by using herbal ingredient, and one of them is bee propolis. Indonesia has a local bee species, Trigona sp, which has great potential to produce propolis. Goal of this study is to determine of the effect of this propolis administration to diabetic model rat. Raw propolis from Java and Sulawesi extracted by using ethanol with the ratio of 1:10 and diluted by prohylen glycol. Five white rats were taken as control negatif group and thirty four more rats induced by alloxan divided into six groups: positive control, insulin, Java propolis 100 & 200 mg, and Sulawesi propolis 100 & 200 mg. Blood glucose level was measured before and after administration of alloxan, and at first & second weeks of the experiment. Result show that propolis from Java and Sulawesi in doses of 100 & 200 mg is effective in decreasing blood glucose for each 244, 282, 427, and 59 mg/dL at first week, and 355, 341, 476, and 84 mg/dL at second week of experiments. The effect in propolis group is larger than control group. Sulawesi Propolis 100 mg show larger effect in decreasing blood glucose than insulin and others propolis groups after two weeks of treatment.**

***Keywords*— diabetes mellitus, insulin, alloxan, propolis, Trigona sp.bees**

I. INTRODUCTION

Prevalence of diabetus mellitus (DM) in Indonesia is expected to grow larger, (Depkes, 2011). It estimated to reach 21,3 million in 2030. The result of Basic Health Research in 2007 shows that the proportion of death caused by diabetus mellitus (DM) in people with age 45-54 years old live at city area reach the second rank, which is 14.7% while for people who live in country area reach the sixth rank which is 5.8% (Depkes, 2011). Generally, diabetus mellitus is a body metabolism disease signed by uncontrolled blood glucose elevation caused by insulin hormone decrease or lack of that hormone effectiveness in human's body (Molina, 2006). Fasting blood glucose level in normal people range from 60 to 120 mg/dL, while in people with diabetes mellitus more than 126 mg/dL (Masharani & German, 2007 ; Molina, 2006).

Propolis has been used in traditional medication for a long time as antibacterial, antifungal, antioxidant, antiinflamation, anticancer, and the other treatment (Marcucci, 1995). Many different current research support those opinion (Bankova, 2005a). Biological activity of propolis caused by bioflavonoid content in it (Marcucci, 1995). Research by Fuliang et al. (2005) and El-Sayed et al. (2009) shows that propolis from Apis mellifera bee has antidiabetic effect.

Approximately two hundreds active compounds in propolis has been identified (Marcucci, 1995; El-Sayed et al., 2009). Chemical compounds in propolis affected by many factors, such as geographic location and condition, the origin of plant, and also the bee species that produce propolis Bankova et al., 1995; Marcucci, 1995; El- Sayed et al., 2009). Differentiation of chemical compositions cause different biological activity of propolis from each area (Kumazawa et al., 2004). Indonesia has a large propolis potention, especially local bee Trigona spp. (Mahani et al., 2011).

This research aim to know the effect of propolis from local bee Trigona spp. treatment comes from Java and Sulawesi in decreasing blood glucose level in diabetic rats model.

II. Materials And Methods

A. Materials

Experimental animals using male white rats (Rattus novergicus) from Wistar groove. Rat's weight range from 150 to 224 grams. Before the research, these animals adapted for seven days. These rats fed by pellet and water in ad libitum way everyday.

Liquid propolis of Trigona spp. bee from Java and Sulawesi. The making of liquid propolis using extraction process. Extraction started by downsizing the size of raw propolis, then added ethanol solvent (1:10) (Krell, 1996). The next step is maseration for 3x24 hours inside watertight and dark place. Propolis filtrate concentrated using rotary evaporator in temperature 600C and 20 rpm speed until reach a concentrated extract. Propylene glycol (PG) added to propolis extract until reach 20% of concentration. The other materials used in this research are : propylene glycol as control treatment substance, insulin Lantus SoloStar® (insulin glargine) as comparison medicion, alloxan as diabetic induce, aquadest and NaCl as solvent, glucose meter and glucose strip to measure glucose level of rats, and than razor blade to taking blood sampel.

B. Alloxan Induce

Two grams of alloxan added with 20 mL of NaCl. Those liquid induced to the rat's back with subcutan method. Fasting glucose blood level measured before alloxan induce. Three days later, fasting blood glucose level re-measured to know successfulness alloxan induce before. Rats with blood glucose level >126 mg/dL considered as diabetic model, while rats with blood glucose level <126 mg/dL re-induced with the same concentration.

C. Grouping

Five normal rats chosen as negative control group (treatment : PG 1 ml/kg Bodyweight/day). Amount 34 diabetic rat models grouped into six groups : positive control group (PG 1 ml/kg Bodyweight/day), insulin (5 IU/kg Bodyweight/day), Java propolis (100 and 200 ml/kg Bodyweight/day, and Sulawesi propolis 100 and 200 ml/kg Bodyweight/day (Al-Hariri et al., 2011, Li et al., 2012). Propylene glycol and propolis are given twice a day, each of them added with aquadest until reach 1 mL of volume . Insulin given once a day and added with NaCl until reach 1 ml of volume. Treatment is given through rat's mouth with spuit and oral sonde for two weeks in a row.

D. Fasting Blood Glucose Level Measurement After the Treatment

Measurement held in first and second weeks after the treatment. Blood sample is taken from rat's tail vein through minor surgery using knife or straight from rat's heart, with surgery fist.

E. Data Analysis

The analysis data is the number of decreases blood glucose after treatment (difference between blood glucose level after alloxan induce and blood glucose after treatment). Data analyzed with SPSS software to know the difference of blood glucose decrease among the groups. Hipothetical test used is Anova test with LSD post-hoc test. If those tests can't be done, then Kruskal-Wallis test will be done continued with Mann-Whitney post hoc test. Test result with $p<0.005$ shows that there is a significant difference among the groups of treatment (Dahlan, 2011).

III. Results And Discussion

After analysis, ANOVA hypothesis test is not possible because the data research results do not have a normal distribution. Therefore, the hypothesis test used is the test of Kruskal-Wallis with post-hoc Mann-Whitney (Dahlan, 2011). The test results along with the decrease in blood glucose levels in each treatment group shown in the figure below.

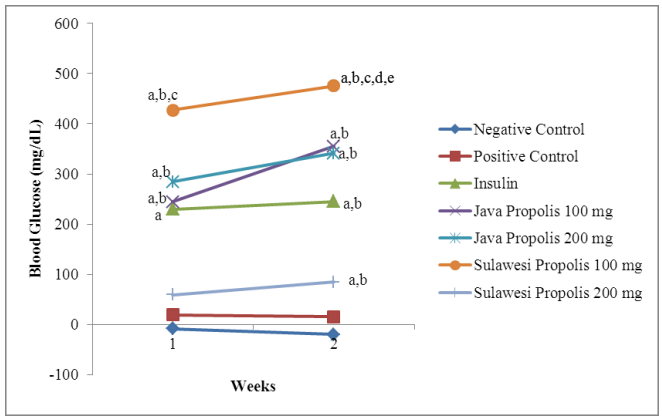

Fig. 1 Reduced blood glucose Levels after treatment

Description: Value represents the median value. The minimum-maksimum value not displayed. Kruskal-Wallis test showed a meaningful value ($p = 0.002$ and $p < 0.001$; after one and two weeks of treatment). Therefore, it needs to be done post-hoc test. Letter a-e is the result of a test post-hoc Mann-Whitney symbolizing the real difference with the negative control group (represented by the letter a), positive control (the letter b), propolis Sulawesi 200 mg (letter c), insulin (d), and Javanese 100 mg propolis (letter e).

A. Comparisons between groups of propolis and control groups In

In the graph shows that all groups of propolis, except Sulawesi propolis 200 mg group, giving the effect of decreasing blood glucose greater than the control group.

Comparisons between groups of propolis and insulin group

In the graph shows that propolis group blood glucose lowering effect similar to the effect of the insulin group. Effect of propolis Sulawesi given 100 mg on 2nd week of treatment was even greater than the standard drug of the type 1 DM

B. Intergroup comparisons propolis

In the graph shows that at first and second week, Sulawesi propolis 100 mg give the effect of decreasing blood glucose greater than 200 mg of propolis Sulawesi. In addition, 100 mg of propolis Sulawesi also gives the effect of lowering blood glucose greater than 100 mg of propolis Java on the second week of treatment.

Diabetes mellitus is a metabolic disease of the body which is generally divided into two katerogori, type 1 and type 2 (Molina, 2006). 1 is characterized by a lack of insulin production or none at all as a result of destruction of pancreatic beta cells. The hormone plays a role in regulating blood glucose levels in the body. Therefore, administration insulin is given standard therapy in patients with DM type 1 (Masharani & amp; German, 2007). Alloxan induce type 1 diabetes condition in mice by removing the free radicals that damage the rat pancreatic beta cells that ultimately lead to impaired insulin production (Szkudelski, 2001).

This study proves that the local bee propolis Trigona sp. from Java and Sulawesi can give the effect of a significant decrease in blood glucose in mice model of type 1 diabetus mellitus. Sulawesi propolis at a dose of 100 mg / kg body weight gives the greatest effect compared to other groups of propolis, even compared with the standard drug insulin after two weeks of treatment. Propolis from Java in a dose of 100 and 200 mg / kg body weight can give the effect of lowering blood glucose equal to insulin.

The influence of the given local propolis can be comparable to the influence of other propolis from different countries which are mostly derived from bees Apis mellifera. Previous research on rat model of diabetes show that propolis origin of northern China in doses of 50-200 mg/kg body weight to control the rise in blood glucose starting at week 6 (Li et al., 2012).

Another study showed that Brazilian propolis did not improve blood glucose levels at doses of 10 and 90 mg/kg after 7 days of treatment (Sartori et al., 2009), but managed at a dose of 100 mg/kg starting at week 3 after treatment (Zhu et al., 2011). Research in Egypt proved that propolis in a dose of 100, 200, and 300 mg/kg can control the blood glucose at day 40 after administration (El-Sayed et al., 2009). As well as research in Saudi Arabia show that propolis in a dose of 300 and 600 mg/kg can lower blood glucose at week 6 after treatment (Al-Hariri et al., 2011).

It is known that the physical properties and chemical composition of propolis each other varies, depending on the origin of plants, species-producing bee propolis, geographical zones, as well as climate and weather conditions (Bankova 2005, Marcucci, 1995). Propolis from Java has dark brown color, whereas propolis from Sulawesi red light. Scent of propolis from Sulawesi stronger than the propolis from Java. Meanwhile, differences in the chemical composition of each propolis affect on the biological activity of each propolis (Kumazawa et al., 2004).

The writer have not been getting the results of the chemical analysis test local content of local bee propolis used in this study. In another study, it was found that the Brazilian propolis compounds containing tri-CQA. These compounds are thought to play a role in controlling blood glucose diabetic rat models by decreasing glucose absorption in the intestine (Matsui et al., 2004). Other compounds are thought to play a role in the antidiabetic effect is luteolin (Mahani et al., 2011). Further tests need to be conducted to determine whether the compounds found in propolis used in this study, and whether these compounds are compounds that play a role in lowering blood glucose levels in diabetic mice models.

IV. CONCLUSIONS

This study demonstrated that local bee propolis Trigona sp. From Java and Sulawesi can give the effect of decreasing blood glucose in mice models of diabetes, and the effect is greater than the negative and positive control group. The effect of propolis equivalent to standard drug insulin, even propolis Sulawesi 100 mg may provide a better effect in the second week of treatment. Compared with other groups of propolis, propolis group Sulawesi 100 mg give the greatest blood glucose lowering effect.

Chemical analysis is needed to identify the content of the active compounds contained in propolis used in this study. In addition, toxicity tests should also be conducted to determine the optimal dose of local bees use propolis origin of this.

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