Assessing the Efficacy of Honey in Diabetes Using SD Rats: By Comparing Acacia Honey, Manuka Honey, and Sugar

Wonsang Gong, Seoyeon Shin, Seongmin Choi, Minjeong Kim, and Hojin Kim
Hankuk Academy of Foreign Studies, Yonginsi, Republic of Korea
Email: {greatday0121, seoyeonshin, dagwon15, mjkim, aoaoao9}@hafs.kr

***Abstract*—Honey is recently being recognized as a natural substance that lowers blood glucose levels in patients with diabetes [1]. To explain this surprising finding, it is hypothesized that the fructose and oligosaccharides present in honey might in some way contribute to the observed hypoglycemic effect [2], [3]. Honey administration was found to increase serum levels of insulin while it reduced serum concentrations of glucose and fructosamine in diabetic rats [4]. Because patients with diabetes also consume various kinds of saccharides through foods, it has come to attention if honey, which also contains glucose, is as effective as sugar in regulating blood glucose levels and blood lipid levels. Therefore, the research utilized Acacia honey and Manuka honey and observed if there is any discrepancy on their effects on diabetes. Acacia honey is one of the most abundantly provided kinds of honey in South Korea and some other Asian counterparts while Manuka honey is commonly known as a functional food effective for diabetes. Originally designed in order to find out if honey has actual effects on regulating blood glucose levels and blood lipid levels, the experiment did not lead to a statistically significant result when comparing the effects of honey with those of the control group. Excluding the control group, however, the three other groups each demonstrated different changes on regulating the blood glucose levels. Hence the results were analyzed excluding the control group, and it was found that Acacia honey had the most positive effect on diabetes by lowering blood glucose levels among the three other groups: Acacia honey, Manuka honey, and sugar.**

***Index Terms*—honey, diabetes, SD rats, HDL-C**

I. Introduction

Honey has antibacterial, hepatoprotective, hypoglycemic, reproductive, antihypertensive, and antioxidant effects [5]. Although medicinal effects of honey are known in public, the mechanism of the effects of honey has not been revealed yet. Since diabetic patients have increased in number, the efficacy of honey on diabetes has gained attention.

A. Honey

Fructose and glucose generally compose honey up to 60% to 70%. Oligosaccharides, proteins, amino acids, organic acids, minerals, and enzymes are contained in honey [6]. Honey can be used on behalf of sugar because it has low Glycemic Index reaction [7].

1) Acacia honey

Acacia honey is made from the blossoms of Robinia pseudoacacia, and has anti-hyperlipidemic effects. Acacia honey also reduces LDL-C (Low-Density Lipoprotein Cholesterol), and increases HDL-C (High-Density Lipoprotein Cholesterol) levels [8].

2) Manuka honey

Manuka honey, which is composed of pinobanksin, pinocembrin, and chrysin, has antioxidizing effects and can treat wounds [9]. It also does not have a detrimental effect on glycation end products.

B. Diabetes

Diabetes has increased in both industrialized and developing countries [10]. Its causes are either when the insulin is not fully produced or when the produced insulin does not function well, leading to increased blood glucose level and thus letting out the glucose through urination. Glucose, however, which is one of the most important energy sources to humans, should be stored in the body.

II. Materials and Methods

A. Materials

Distilled water, white sugar, Acacia honey, and Manuka honey were used. A total 35 Specific Pathogen Free (SPF) rats were prepared; 32 were used and three were left as spare. Blood glucose monitoring devices (Accu Chek-Performa) were used to run blood glucose tests and blood biochemical analyzers (Hitachi 7020) were used to examine blood chemistry.

B. Methods

The rats were put in a 23℃ environment under light stimulation of twelve hours interval and were fed water and fodder. All rats fasted a day before the experiment and their weights were measured once every week. The first 0.5mL of blood sample taken from the jugular veins was examined to obtain the blood glucose level.

Streptozotocin (STZ) was injected twice to induce diabetes into the rats. The second blood sample was taken three days later and was examined to obtain the blood

Manuscript received December 20, 2015, revised July 22, 2016.

doi: 10.18178/ijfe.2.2.147-150

glucose level. The remainder was centrifuged and left for 30 minutes with its serum separated in order to examine the blood chemistry by measuring TC (Total Cholesterol), HDL-C (High Density Lipoprotein Cholesterol, and LDL-C (Low Density Lipoprotein Cholesterol).

The rats which had blood glucose levels of over 220mg/dL were selected and then were separated into four groups. The average blood glucose levels were distributed equally throughout the groups. It is as the following:

- G1: the group that was fed distilled water (control group)
- G2: the group that was fed sugar
- G3: the group that was fed Acacia honey
- G4: the group that was fed Manuka honey

The third blood sample was taken under 8 hours fasting after group segregation and was examined its basal glucose level. Then 1.0g/kg of the designated substance of each group was put through direct oral feeding to G1, G2, G3, and G4 for two weeks. The substances were dissolved in 100mg/mL distilled water.

The fourth blood sample was taken under 8 hours fasting after two weeks of oral feeding and was examined its blood glucose level and chemistry. The fifth blood sample was taken an hour after the rats had received the designated substances, and the sixth blood sample was taken two hours after receiving the designated substances. After the experiment, the rats were euthanized by CO_2 gas.

III. Results

A. Results

1) Weight change

All weights of SD rats were measured once a week. The weights increase consistently in all groups throughout the experiment (Table I).

TABLE I. Weights of SD Rats in Four Groups

Group	Body weights (g)		
	week 0	week 1	week 2
G1	210.6	249.1	257.5
G2	221.8	268.0	295.8
G3	220.5	272.4	295.3
G4	212.3	260.0	276.7

2) Measuring blood glucose levels

The blood glucose level of SD rats was measured six times in total through Accu Chek-Performa (Fig. 1). The first measurement took place before injecting STZ into the rats. Next, the level was measured again three days after the rats received the second STZ. The third measurement was taken four days after the second measurement. Then the rats of G2, G3, and G4 were each given the designated material for two weeks. After that the blood glucose level was measured after fasting the rats for 8 hours. The next blood glucose level was examined an hour after the rats once again received the designated substances, and the last measurement was taken two hours after receiving the substances once more.

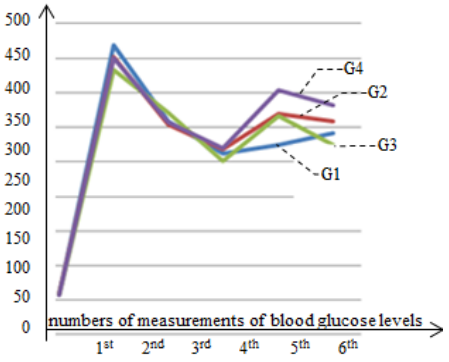

Figure 1. The mean values of blood glucose levels in four groups (G1, G2, G3, G4) throughout the six measurements

It can be notified that before STZ injection, SD rats had normal blood glucose level, ranging from 106.9mg/dL to 109.6mg/dL. The blood glucose level elevated approximately four times from the original level after injecting the STZ twice (Table II).

After the separation into four groups, each labeled as G1, G2, G3, and G4, distilled water was fed in G1, sugar in G2, Acacia honey in G3, and Manuka honey in G4 through oral feeding. It can be notified, by measuring the blood glucose level after two weeks of feeding the designated materials, that in all groups, the levels varied from 300.6mg/dL to 320.1mg/dL and that their values had decreased 15% compared to those of the original levels. An hour after being put the material, the value of G1 was increased by 4% from 312.0mg/dL to 324.3mg/dL, the value of group G2 by 16% from 318.6mg/dL to 370.1mg/dL, the value of group G3 by 22% from 300.6mg/dL to 366.3mg/dL, and the value of group G4 by 25.9% from 320.1mg/dL to 402.9mg/dL. Two hours after feeding the designated substances, only the blood glucose level of group G1 increased slightly and the blood glucose levels of the rest of the groups decreased (Table III).

TABLE II. Blood Glucose Levels before Feeding the Designated Substances

Groups		Blood glucose level (mg/dL)		
		First value	Second value	Third value
G1	mean	109.6	468.6	359.1
G2	mean	109.1	451.4	354.0
G3	mean	107.1	433.9	371.1
G4	mean	106.9	450.5	357.5

TABLE III. Blood Glucose Levels after Feeding the Designated Substances

Groups		Blood glucose level (mg/dL)		
		Fourth value	Fifth value	Sixth value
G1	mean	312.0	324.3	341.0
G2	mean	318.6	370.1	358.3
G3	mean	300.6	366.3	324.0
G4	mean	320.1	402.9	381.5

B. Results Analysis

1) Analysis of the amount of decrease between third and fourth blood glucose levels

In short, the third measurement was taken before feeding the designated substances and the fourth was taken after two weeks of the oral feeding. Hence, comparing the third and fourth glucose levels indicates comparing the blood glucose level before and after the feeding the designated materials. The fourth value of the blood glucose level decreased by 15% compared to the third value partially because of the natural recovery of β-cells from damaged pancreas.

The amount of decrease in blood glucose levels after the oral feeding of each material can also be compared; the more the decrease in blood glucose level, the more the group is effective for diabetes. The variation between the third and the fourth value was 47.1mg/dL for G1, 35.4mg/dL for G2, 70.5mg/dL for G3, and 37.4mg/dL for G4. The values of the four groups indicate that the amount of decrease was largest in G3, demonstrating that G3, which rats were fed Acacia honey, demonstrated the most positive effect in diabetes in lowering blood glucose levels.

Supposing that the amount of decrease due to the natural recovery was identical in all groups, the amount of decrease in blood glucose level after oral feeding of designated materials is G3>G1>G4>G2 in order. Therefore, Acacia honey has the most positive effect on diabetes among other groups in regulating the blood glucose level (Table IV).

TABLE IV. VARIATION BETWEEN THE THIRD AND FOURTH BLOOD GLUCOSE LEVEL

	Third(mg/dL)	Fourth(mg/dL)	Variation(mg/dL)
G1	359.1	312.0	47.1
G2	354.0	318.6	35.4
G3	371.1	300.6	70.5
G4	357.5	320.1	37.4

2) Analysis of the amount of variation for fourth, fifth, and sixth blood glucose level

The slopes of the fifth and sixth values of blood glucose levels were compared (Fig. 2). Because the efficacy of lowering blood glucose level for diabetes is determined by how quickly the blood glucose level goes down to the normal range, food that goes down to the normal range more rapidly is more beneficial for diabetes than food that goes down to the normal range less rapidly. G3, having the steepest slope among the groups, returns to the normal range the most rapidly among the four groups (Table V).

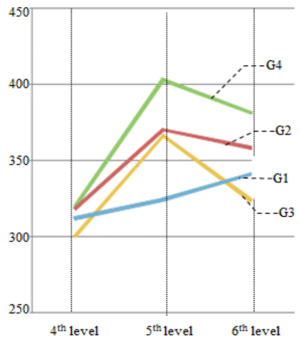

Figure 2. Graph slopes of the amount of variation for fourth, fifth, and sixth blood glucose level

TABLE V. FOURTH, FIFTH, AND SIXTH BLOOD GLUCOSE LEVEL

	Fourth(mg/dL)	Fifth(mg/dL)	Sixth(mg/dL)
G1	312.0	324.3	341.0
G2	318.6	370.1	358.3
G3	300.6	366.3	324.0
G4	320.1	402.9	381.5

Furthermore, G2 takes a longer time in returning to the normal range than other groups since its slope created by the fifth and sixth values is comparatively gradual. Similarly, because G4 has a steeper slope than that of G2 but more gradual than G3, the slope of G4 returns to the normal range more rapidly than G2 while the it returns to the normal range slower than G3. Overall, the groups return to the normal range more rapidly in the order of G3, G4, and then G2. Again, Acacia honey is found to be more effective for diabetes than Manuka honey and sugar.

C. TC and HDL-C Values Analysis

1) TC (Total Cholesterol)

TC does not have a seminal effect on this experiment because both honey and sugar are consisted of neither lipid nor fat. Also the change in TC, which was under 2mg/dL, was far from significant (Table VI).

TABLE VI. BLOOD BIOCHEMISTRY VALUES OF SD RATS

Group		TC(mg/dL)	HDL-C(mg/dL)	LDL-C (mg/dL)
G1	before	90.81	38.66	13.32
	after	88.48	39.14	11.26
G2	before	95.58	38.25	13.75
	after	95.89	39.93	12.58
G3	before	87.44	36.19	13.04
	after	88.70	43.84	11.08
G4	before	92.50	41.55	12.12
	after	92.90	44.23	10.59

2) HDL-C (High-Density Lipoprotein Cholesterol)

High HDL-C value is beneficial for preventing atherosclerosis. The value of HDL-C increased in G1, G2, G4 by 0.5mg/dL, 1.7mg/dL, and 2.7mg/dL respectively. On the other hand, the value of HDL-C in G3 has increased by 7.7mg/dL, showing that Acacia honey can increase the value of HDL-C more than Manuka honey and sugar, helping not only patients with diabetes but also the general public in preventing atherosclerosis.

IV. CONCLUSION

It was found that Acacia honey has a relatively more positive effect on lowering blood glucose level for diabetes than Manuka honey, which is generally known for its effectiveness on diabetes to the public more than other kinds of honey. Comparing the blood glucose variation, the decrease in blood glucose level was the greatest in G3. It was also shown that its blood glucose level has decreased the most when given the same time. Therefore, it can be suggested that Acacia honey has lower Glycemic Index than Manuka honey and sugar. Glycemic Index is the reaction extent of blood glucose level after ingesting standard food. Food with low Glycemic Index increases blood glucose level slowly; thus, foods that have lower Glycemic Index is better for regulating blood glucose level [11]. Meanwhile, TC and LDL-C did not have particular statistical significance, but the value of HDL-C in G3 increased about 3.5 times more than those of G1 and G2, suggesting that Acacia honey will help patients with diabetes as well as the general people in preventing atherosclerosis.

It was hypothesized throughout this paper that the decrease in blood glucose level by the natural recovery of β-cell in pancreas is identical in every group. To prove this, however, measurement of insulin and C-peptide before and after the experiment is required.

Excluding the two weeks of preparatory period, the actual time that the SD rats were fed the designated substances was relatively short. Considering that honey is a food, the research data will gain higher reliability as the time spent on feeding the substances gets longer.

Moreover, it was Type I diabetes, which is created as β -cells are destroyed in the pancreas, which was dealt with throughout the research. It should be noted, however, that Type II diabetes are more common in reality. The data will become more reliable on evaluating the regulation of blood glucose level of honey when deriving the rats into obesity and artificially creating Type II diabetes, or when using actual patients with Type II diabetes.

REFERENCES

[1] M. Abdulrhman, *et al.*, “Metabolic effect of honey in type 1 diabetes mellitus: A randomized crossover pilot study,” *Journal of Medicinal Food*, vol. 16, pp. 66-72, January 2013.

[2] O. Erejuwa, S. Sulaiman, and M. Wahab, “Fructose might contribute to the hypoglycemic effect of honey,” *Molecules*, pp. 1900-1915, February 2012.

[3] O. Erejuwa, S. Sulaiman, and M. Wahab, “Oligosaccharides might contribute to the antidiabetic effect of honey: A review of the literature,” *Molecules*, vol. 17, pp. 248-266, December 2011.

[4] O. Erejuwa, S. Sulaiman, M. Wahab, K Sirajudeen, M. Salleh, and S. Gurtu, “Glibenclamide or metformin combined with honey improves glycemic control in streptozotocin-induced diabetic rats,” *International Journal of Biological Sciences*, vol. 7, pp. 244-252, March 2011.

[5] O. Erejuwa, S. Sulaiman, and M. Wahab, “Honey: A novel antioxidant,” *Molecules*, vol. 17, pp. 4400-4423, April 2012.

[6] S. Bogdanvo, T. Jrendic, R. Sieber, and P. Gallmann, “Honey for nutrition and health: A review,” *Journal of the American College of Nutrition*, vol. 27, pp. 677-689, December 2008.

[7] O. Aqrawal, A. Pachauri, H. Yadav, and J. Urmila, “Subjects with impaired glucose tolerane exhibit a high degree of tolerance to honey,” *Journal of Medicinal Food*, vol. 10, pp. 473-478, September 2007.

[8] A. Farhana, M. Sadiq, and A. Jehangir, “Anti-Hyperlipidemic effect of acacia honey in cholesterol-diet induced hyperlipidemia in rats,” *International Journal of Pharmacy and Pharmaceutical Sciences*, pp. 916-923, January 2013.

[9] M. José, S. Alvarez, G. Massimiliano, and Y. Tamara, “The composition and biological activity of honey: A focus on manuka honey,” *Foods*, vol. 3, pp. 420-432, July 2014.

[10] A. Kar, B. Choudhary, and N. Bandyopadhyay, “Preliminary studies on the inorganic constituents of some indigenous hypoglycemic herbs on oral glucose tolerance test,” *Journal of Ethnopharmacology*, vol. 64, pp. 179-184, February 1999.

[11] O. Erejuwa, S. Sulaiman, M. Wahab, K. Sirajudeen, M. Salleh, and S. Gurtu, “Glibenclamide or metformin combined with honey improves glycemic control in streptozotocin-induced diabetic rats,” *International Journal of Biological Sciences*, vol. 7, pp. 244-252, March 2011.

W. Gong was born in Republic of Korea, on January 21, 1999. He is a twelfth grade senior in the Natural Science course of Hankuk Academy of Foreign Studies in Yonginsi, Republic of Korea.
He has been working as a leader of Biochemisty Seminar Union since 2014.
Mr. Gong wrote “Validation of tissue regeneration effect of melatonin using zebrafish,” (2014) and “Analysis of community characteristics and trend of SNS information using SNAP and SOM algorithm” (2015).

S. Shin was born in Republic of Korea, on December 21, 1998. She is a twelfth grade senior in the International course of Hankuk Academy of Foreign Studies in Yonginsi, Republic of Korea.
She has been working as an intern researcher of DMZ Ecology Research Institute since 2014, researching various floras and faunas in South Korean Demilitarized Zone. She is a journalist of the South Korean Policy Press led by the South Korean government.
Ms. Shin wrote “Developing the optimized ocean current-strengthening desalination semi-permeable membrane distillation based on SVM (Support Vector Machine) model by using GA (Genetic Algorithm) and decision tree,” (2013) “Future prospects and the development of edible insects as provision for climate change” (2014), and “Vegetation classification of DMZ (Demilitarized Zone)” (2015).

S. Choi was born in Republic of Korea, on June 21, 1998. He is a twelfth grade senior in the Natural Science course of Hankuk Academy of Foreign Studies in Yonginsi, Republic of Korea.
Mr. Choi wrote “Comparison between SARS CoV and MERS CoV using Apriori algorithm, decision tree, SVM (Support Vector Machine,” (2016) and “Prediction of SARS coronavirus main protease by artificial neural network” (2016).

M. Kim was born in Republic of Korea, on October 5, 1998. She is a twelfth grade senior in the Natural Science course of Hankuk Academy of Foreign Studies in Yonginsi, Republic of Korea.
Ms. Kim has been studying the way of ensuring the stability of anthocyanins for hair and tendency of mite’s distribution in the skin.

H. Kim was born in Republic of Korea, on April 25, 1998. He is a twelfth grade senior in the Nature Science course of Hankuk Academy of Foreign Studies in Yonginsi, Republic of Korea.
Mr. Kim wrote “A study of Charcoal purification effects on the chemical and biological indicators in Yangjaecheon” (2013) and “Research of anti-spam using a statistical method and Support Vector Machine” (2014).