

## **The role of pure honey in the treatment of diabetes mellitus.**

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### **Abstract**

Today, there are approximately 415 million diabetics worldwide. It is expected to increase to nearly 642 million in 2040. The incidence of type 2 diabetes Mellitus in these patients is 90%. Type 2 diabetes mellitus is a disease could not be provided definite improvement, although there have been numerous scientific studies on its treatment for many years. Recently, similar to the treatment for other diseases, the treatment of type 2 diabetes mellitus is being tested using alternative medicinal methods. One of the alternative methods is the application of pure honey. The main sweeteners in honey are fructose and glucose. The absorption of fructose in the gastrointestinal tract is slower than glucose, and metabolism of fructose occurs independently from insulin. Many studies have shown that honey has antioxidant effects, as well as healing properties for wounds. However, only few studies have examined the effects of honey on the biochemistry values in diabetics. Our aim was to improve the lipid profile and blood glucose regulation in adult patients diagnosed with type 2 diabetes mellitus using metformin, by administering pure honey with appropriate dosage. Three different doses were utilized to determine the optimal dosage and were applied to case groups for 4 months with regular tracking of the parameters. After 4 months, a significant reduction in HbA1c levels was observed in all dosage groups where honey was consumed. Moreover, a decrease in total cholesterol was noted in individuals who consumed honey in doses of 5 to 25 g.

**Keywords:** Pure honey, Diabetes mellitus, Fructose.

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### **Introduction**

Today, there are approximately 415 million diabetics worldwide. This number is expected to increase to nearly 642 million in 2040 [1]. The incidence of type 2 diabetes mellitus in these patients is 90%.

Type 2 diabetes mellitus is a disease could not be provided definite improvement, although there have been numerous scientific studies on its treatment for many years. Therefore, it is an important health problem, which should be investigated through continuous scientific studies. Recently, similar to the treatment for other diseases, the treatment of Type 2 diabetes mellitus is being tested using alternative medicinal methods.

One of the alternative methods is the application of pure honey [2].

The contents of honey vary depending on the plant flora, but the main content of honey remains the same. The main sweeteners in honey are fructose and glucose. The absorption of fructose in the gastrointestinal tract is slower than glucose, and metabolism of fructose occurs independently from insulin [3-5].

Many studies have shown that honey has antioxidant and reduction of oxidative stress effects, as well as healing properties for wounds. However, only few studies have examined the effects of honey on the biochemistry values in diabetics [3,6-8]. In this study, we investigated whether natural honey affects diabetes mellitus treatments. We observed

changes in blood sugar following medication, as well as following the application of both medicine and honey for 4 months in adult patients diagnosed with type 2 diabetes mellitus using metformin.

Our aim was to assess the effect lipid profile and blood glucose regulation in adult patients diagnosed with type 2 diabetes mellitus using metformin, by administering pure honey with appropriate dosage.

## Materials and Methods

### Participants

A total of 64 randomly selected individuals (32 type 2 diabetes mellitus patients using metformin and 32 healthy individuals) from the family medicine polyclinic of The Ministry of Health Ordu University Training and Research Hospital voluntarily participated in the study.

The study was planned as randomized controlled clinical trial.

Pre-tests (fasting-prandial blood glucose, HbA1c, total cholesterol, LDL, HDL, and triglyceride levels) and final test measurements of individuals who were included in the study were taken.

Patients were selected from the outpatient clinic, and consisted of those diagnosed with type 2 diabetes mellitus aged 18-80 years. The number of men and women was equally distributed both in control groups and experiment groups.

Individuals without diabetes identified as the control group, were divided according to the amount of honey administered: 5 g, 15 g, 25 g, and no honey.

Three different doses were utilized to determine the optimal dosage and were applied to case groups for 4 months with regular tracking of the parameters.

The study benefited from repeated measurements using single direction analysis of variance for evaluation of the parameters taken from a total of eight control groups (negative controls). Control groups were given 5 g, 15 g, or 25 g of honey. Case groups were divided into positive control group (only medication) and treatment group which was further divided according to the amount of honey administered (5 g honey/day/

person, 15 g honey/day/person, 25 g honey/day/person). The sample width in each group (control and case groups) is specified as eight individuals. The purity and the quality criteria of the honey were identified in laboratories at the Beekeeping Research Institute of Ordu through various analyses.

### Statistical analysis

First, the data were analysed using Levene's test and the Shapiro-Wilk test for equality of variance and normality assumption, both at  $P > 0.05$ , respectively. According to the test results, data based on biochemistry results (including HbA1c, cholesterol, triglyceride, HDL, and LDL parameters) of the individuals were expressed as the sample size, and mean with standard deviation values. The differences between the pre-test and post-test results in both groups (32 patients and 32 healthy individuals) in terms of the doses applications (0, 5, 15, 25 g/ daily honey consumption) were analysed by using two-way ANOVA with repeated measures, one-way ANOVA with repeated measures and the Tukey test. If the p-value was under 0.05, results were considered statistically significant. All the statistical calculations were made with SPSS 11.0 V. statistical package program.

### Ethical considerations

Before the study, the required ethics committee approval by Ordu University (02/11/2015-2015/4) and written permission by The Ministry of Health Ordu University Training and Research Hospital (01/09/2015-5029) were obtained. The aim of this study was explained to the individuals and informed consent obtained from the participants during the data collection phase.

### Limitations of the study

Patients with HbA1c level of 8 and above were not included in the study.

## Results

Results of the statistical analysis of HbA1c values of the patients and control group before and after 4 months of honey application are shown in Table 1.

**Table 1.** Effects of natural honey on HbA1c values of healthy people and the diabetics.

Measurement Time (A)	Before the application		4 months later		Overall average for C
Application group (B)	Control	Patient	Control	Patient	
Doses (g) (C)					
0	5.15 ± 0.35	7.09 ± 0.91	5.45 ± 0.21	7.79 ± 1.56	6.96 ± 1.43
5	5.37 ± 0.16	6.70 ± 0.90	5.35 ± 0.15	6.66 ± 0.87	6.11 ± 0.95
15	5.14 ± 0.24	6.56 ± 0.77	5.28 ± 0.23	6.34 ± 0.40	5.86 ± 0.78
25	5.69 ± 0.36	6.54 ± 0.77	5.70 ± 0.43	6.40 ± 0.68	6.13 ± 0.71

Overall average for A	6.15 ± 0.94	6.21 ± 1.05					
Overall average for B	Control	Patient					
	5.40 ± 0.34 b	6.72 ± 0.93 a					
<b>Sources of variation</b>							
	A	B	C	A*B	A*C	B*C	A*B*C
P-values	0.361	<0.001	0.306	0.874	0.32	0.157	0.684

The results showed that the HbA1c values differ only in the patient and control groups (P<0.001). When patients are evaluated within their own group, research findings are shown in Table 2.

**Table 2.** Effects of natural honey on HbA1c values of diabetics.

Measurement time (A)	Before application	4 months later	Overall average
<b>Doses (g) (C)</b>			
0	7.09 ± 0.91	7.79 ± 1.56	7.44 ± 1.28 <sup>a</sup>
5	6.70 ± 0.90	6.66 ± 0.87	6.68 ± 0.91 <sup>b</sup>
15	6.56 ± 0.77	6.34 ± 0.40	6.45 ± 0.81 <sup>b</sup>
25	6.54 ± 0.77	6.40 ± 0.68	6.47 ± 0.78 <sup>b</sup>
Overall average	6.70 ± 0.82	6.74 ± 1.04	

<b>Sources of variation</b>			
	A	C	A*C
P-values	0.453	0.002	0.162

It was observed that while the average HbA1c values increased at the end of 4 months for individuals who are not given honey when compared to the first measurements in diabetic group administered honey, the HbA1c values decreased in the group who are given honey. There was also a significant statistical difference between groups who were given honey and those who were not (P=0.002).

Statistical analysis results obtained from cholesterol levels of the patient and control groups before and after 4 months of the application are shown in Table 3.

**Table 3.** Effects of natural honey on cholesterol levels of healthy people and diabetics.

Measurement time (A)	Before the Application		4 months later		Overall average for C		
Application group (B)	Control	Patient	Control	Patient			
<b>Doses (g) (C)</b>							
0	198.7 ± 49.7	257.0 ± 32.9	207.8 ± 44.1	222.0 ± 38.0	228.6 ± 1.43 <sup>a</sup>		
5	184.0 ± 28.6	202.0 ± 21.4	178.4 ± 32.8	189.6 ± 18.4	191.7 ± 0.95 <sup>b</sup>		
15	196.4 ± 39.1	199.9 ± 34.1	194.3 ± 45.7	209.9 ± 31.3	201.7 ± 0.78 <sup>b</sup>		
25	216.5 ± 44.0	194.9 ± 31.9	216.1 ± 37.4	188.7 ± 41.2	199.3 ± 0.71 <sup>b</sup>		
Overall average for A	207.6 ± 39.0		200.6 ± 36.8				
Overall average for B	Control		Patient				
	199.4 ± 40.3		206.1 ± 35.2				
<b>Sources of variation</b>							
	A	B	C	A*B	A*C	B*C	A*B*C
P-values	0.099	0.206	0.021	0.083	0.298	0.028	0.028

Our study showed that cholesterol levels differ in the groups of application (P=0.021). Research findings based on variance analysis to determine whether there were similar findings for the patient group is shown in Table 4.

**Table 4.** Effects of natural honey on cholesterol levels of diabetics.

Measurement time (A)	Before application	4 months later	Overall average
<b>Doses (g) (C)</b>			
0	257.0 ± 32.95	222.0 ± 38.04	239.5 ± 35.50 <sup>a</sup>
5	202.0 ± 21.40	189.6 ± 18.35	195.8 ± 19.88 <sup>b</sup>

15	199.9 ± 34.12	209.9 ± 31.27	204.9 ± 32.70 <sup>b</sup>
25	194.9 ± 31.94	188.7 ± 41.20	191.8 ± 36.57 <sup>b</sup>
Overall average	211.2 ± 38.11	201.1 ± 35.22	
<b>Sources of variation</b>			
	A	C	A^C
P-values	0.004	<0.001	0.001

group who are given honey 15 g per day, the cholesterol values decreased in the group who are given honey 5 and 25 g per day and who are not given honey also found to be significant difference statistically between groups who are given honey and not (P=0.001). Statistical analysis results obtained from triglycerides levels of the patients and the control group before and after 4 months of the application are shown in Table 5.

There was an increase in cholesterol values at the end of 4 months when compared to the first measurements in diabetic

**Table 5.** Effects of natural honey on triglycerides levels of healthy people and diabetics.

Measurement time (A)	Before the Application		4 months later		Overall average for C Control		
Application group (B)	Control	Patient	Control	Patient			
Doses (g) (C)							
0	107.2 ± 72.4	229.7 ± 93.4	109.3 ± 24.7	150.0 ± 66.2	165.4 ± 1.43		
5	101.3 ± 44.2	180.3 ± 71.3	101.6 ± 42.8	179.2 ± 69.1	157.8 ± 0.95		
15	133.9 ± 46.2	159.4 ± 49.8	149.8 ± 46.8	155.1 ± 93.5	152.5 ± 0.78		
25	113.9 ± 43.3	177.3 ± 64.3	129.5 ± 89.1	181.4 ± 86.4	161.3 ± 0.71		
Overall average for A	163.5 ± 70.8		154.5 ± 76.4				
Average for B	Control		Patient				
	119.6 ± 54.3 <sup>b</sup>		175.8 ± 74.1 <sup>a</sup>				
<b>Sources of variation</b>							
	A	B	C	A^B	A^C	B^C	A^B^C
P-values	0.412	<0.001	0.95	0.047	0.094	0.279	0.24

In the study it is determined that triglycerides values differ in the patients and the control group (P<0.001). Therefore, when patients are evaluated within their own, research findings are given in Table 6.

While observing a decrease in triglyceride values at the end of 4 months when compared to the initial measurements in the diabetic group who were not given honey, groups consuming honey at different doses showed that that their triglyceride levels did not change (P=0.922).

**Table 6.** Effects of natural honey on triglycerides values of diabetics.

Measurement (A)	time	Before application	4 months later	Overall average
Doses (g) (C)				
0		193.0 ± 93.38 <sup>a</sup>	137.8 ± 59.40 <sup>b</sup>	165.4 ± 76.39
5		158.2 ± 73.46 <sup>ab</sup>	157.5 ± 71.46 <sup>ab</sup>	157.8 ± 72.46
15		151.6 ± 49.28 <sup>ab</sup>	153.5 ± 81.05 <sup>ab</sup>	152.5 ± 65.16

25	157.8 ± 64.25 <sup>ab</sup>	165.5 ± 88.88 <sup>ab</sup>	161.4 ± 76.57
Overall average	163.5 ± 70.84	154.5 ± 76.39	
<b>Sources of variation</b>			
	A	C	A^C
P-values	0.085	0.922	0.007

Statistical analysis results obtained from HDL values of the patients and control group before and after 4 months of the application are shown in Table 7.

Our study showed that the HDL values differ across all groups before and after the application (P<0.001). When patient group are evaluated within their own group, research findings are shown in Table 8.

While observing a decrease in HDL values at the end of 4 months when compared to the initial measurements of the diabetic group who are given honey at different doses and no honey (P<0.001), groups consuming honey at different doses showed no change in HDL values (P=0.786).

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Statistical analysis results obtained from LDL values of the patients and control group before and after 4 months of the application are shown in Table 9.

**Table 7.** Effects of natural honey HDL values of healthy people and diabetics.

Measurement time (A)	Before the application		4 months later		Overall average for C		
Application group (B)	Control	Patient	Control	Patient			
<b>Doses (g) (C)</b>							
0	46.4 ± 7.54	46.0 ± 12.52	43.4 ± 6.94	43.4 ± 8.34	44.74 ± 9.41		
5	51.9 ± 7.69	47.4 ± 4.39	47.3 ± 6.93	44.1 ± 6.34	46.82 ± 6.12		
15	50.0 ± 11.5	47.5 ± 9.58	45.6 ± 10.8	45.1 ± 8.22	46.75 ± 9.50		
25	52.8 ± 9.18	48.0 ± 10.26	48.2 ± 8.60	43.1 ± 9.81	47.07 ± 9.80		
Overall average for A	48.2 ± 9.28 <sup>a</sup>		44.6 ± 8.21 <sup>b</sup>				
Overall average for B	Control		Patient				
	48.4 ± 8.73	45.6 ± 8.68					
<b>Sources of variation</b>							
	A	B	C	A <sup>∧</sup> B	A <sup>∧</sup> C	B <sup>∧</sup> C	A <sup>∧</sup> B <sup>∧</sup> C
P-values	<0.001	0.168	0.655	0.522	0.753	0.806	0.938

**Table 8.** Effects of natural honey on HDL values of diabetics.

Measurement time (A)	Before application	4 months later	Overall average
<b>Doses (g) (C)</b>			
0	46.0 ± 12.52	43.4 ± 8.34	44.7 ± 9.41
5	47.4 ± 4.39	44.1 ± 6.34	45.8 ± 6.12
15	47.5 ± 9.58	45.1 ± 8.22	46.3 ± 9.50

  

25	48.0 ± 10.26	43.1 ± 9.81	45.5 ± 9.80
Overall average	48.24 ± 9.28 <sup>a</sup>	44.63 ± 8.21 <sup>b</sup>	
<b>Sources of variation</b>			
	A	C	A <sup>∧</sup> C
P-values	<0.001	0.786	0.619

**Table 9.** Effects of natural honey on LDL values of healthy people and diabetics.

Measurement time (A)	Before the application		4 months later		Overall average for C		
Application group (B)	Control	Patient	Control	Patient			
<b>Doses (g) (C)</b>							
0	130.9 ± 53.4	165.2 ± 29.4	142.6 ± 45.1	148.6 ± 38.1	150.8 ± 39.6 <sup>a</sup>		
5	111.8 ± 22.5	118.5 ± 21.4	110.8 ± 28.1	109.6 ± 22.5	113.3 ± 22.5 <sup>b</sup>		
15	119.7 ± 31.3	135.8 ± 35.1	103.6 ± 51.6	127.6 ± 34.1	125.5 ± 37.5 <sup>b</sup>		
25	140.9 ± 33.2	111.5 ± 36.7	142.0 ± 32.2	109.2 ± 47.9	119.9 ± 41.7 <sup>b</sup>		
Overall average for A	129.4 ± 36.11		122.8 ± 39.85				
Overall average for B	Control		Patient				
	125.0 ± 38.9	126.6 ± 37.8					
<b>Sources of variation</b>							
	A	B	C	A <sup>∧</sup> B	A <sup>∧</sup> C	B <sup>∧</sup> C	A <sup>∧</sup> B <sup>∧</sup> C
P-values	0.213	0.664	0.009	0.326	0.729	0.023	0.484

LDL values did not show a change in only the patient and control groups. However, differences in LDL levels were detected in groups where honey was consumed ( $P=0.009$ ). Research findings based on variance analysis in order to determine whether this difference affected the patient group are shown in Table 10.

Our results show that LDL values decreased at the end of 4 months when compared to the first measurements in the diabetic group who are given honey at different doses and no honey. The largest decrease was found to be in patient groups who were not given honey ( $P=0.001$ ).

**Table 10.** Effect of natural honey on LDL values of diabetics.

Measurement (A)	time	Before application	4 months later	Overall average
<b>Doses (g) (C)</b>				
0		165.2 ± 29.35	148.6 ± 38.14	150.8 ± 39.62 a
5		118.5 ± 21.35	109.6 ± 22.49	113.3 ± 22.49 b
15		135.8 ± 35.11	127.6 ± 34.05	125.5 ± 37.48 b
25		111.5 ± 36.72	109.2 ± 47.87	119.9 ± 41.66 b
Overall average		130.84 ± 36.49	122.8 ± 39.85	
<b>Sources of variation</b>				
	A	C	AˆC	
P-values	0.071	0.001	0.813	

## Discussion

Diabetes mellitus is a metabolic disease characterized by chronic hyperglycaemia due to the deficiency or defect in insulin activity. It has been shown that honey cleans up the reactive oxygen radicals and repairs oxidative stress, which decreases blood sugar [6]. While honey repairing renal oxidative stress in diabetic rats was independent of dosage, its hypoglycaemic effect was found to be related with dose [9,10]. This is surprising because honey is sweet and rich in sugar. Fructose and oligosaccharides in honey are thought to be responsible for this hypoglycaemic effect [2].

In an 8 week study by Bahrami, et al., for the group that consumed honey, although a reduction in blood lipid levels and an increase in HbA1c values was detected, cautious administration of honey was recommended for patients with diabetes [3]. In our 16 week study, as a result of repeated measures and analysis of variance with observations of an increase in the HbA1c values at the end of 4 months when compared to the first measurements in diabetic group who are not given honey, the HbA1c values decreased in the group that was given honey at different doses, and there was a significant statistical difference between groups who were given and not given honey. Also, as a result of repeated measures and analysis of variance, while observing an increase in cholesterol values at the end of 4 months when compared to the first measurements in diabetic group who are given honey

15 g per day, the cholesterol values decreased in groups who were given honey between 5 and 25 g per day and no honey [11]. There was also a significant statistical difference between groups who were given honey and those who were not.

Honey is an antibacterial [9], hepatoprotective [12], hypoglycaemic, anti-oxidant [9], and antihypertensive [13] natural substance [14-16]. Honey decreases hyperglycaemia in diabetic rats and humans. However, the mechanism of its effects is still unknown. Honey mainly consists of fructose and glucose. The hypoglycaemic effect of honey is believed to result from fructose. Glucose and fructose impart synergistic effects on the gastrointestinal system and pancreas, and this effect is thought to increase the release of insulin. The results have shown that fructose increase the uptake of hepatic glucose as well as glycogen synthesis and its storage [16].

In studies conducted with healthy people and those with diabetes, foods with low glycaemic index were found to reduce the blood glucose level and to increase insulin secretion. Foods are classified as low (<55), middle (55-69), and high (>70) according to the classification of glycaemic index [17]. The international glycaemic index list also specifies that the glycaemic index of honey vary between 32 to 87. The glycaemic index of honey varies according to their botanical origins as well as the rate of fructose [17,18].

The study that Erejuwa et al. conducted in 2011 using diabetic rats determined that honey combined with oral anti-diabetics provided better glycaemic control and additional metabolic advantages [19]. From our study, it was found that in each of the three different dosage groups of honey, HbA1c values were reduced when compared to the group that was not given honey, and it was statistically significant.

When combining natural honey with glibenclamide or metformin, which are oral anti-diabetics, a significant decrease in blood glucose levels was observed in rats that were made diabetic with streptozotocin [19]. The anti-diabetic effect mechanism of metformin has been documented well [20,21]. However, the mechanism of hypoglycaemic effect of honey is not very clear [19]. It is thought that the biggest component of the hypoglycaemic effect in honey is fructose [22]. Because fructose does not increase the glucose level, insulin secretion during its metabolism is not needed as well [23]. In our study, we showed the synergistic effect of natural honey when used in combination with metformin only in patients who use metformin as anti-diabetic.

While observing an increase in the HbA1c values at the end of 4 months when compared to the first measurements in the diabetic group that was not given honey, the HbA1c values decreased in the group that was given honey at different doses, and there was a significant statistical difference between the groups who were given honey and those who were not.

While observing an increase in cholesterol values at the end of 4 months when compared to the initial measurements of the diabetic group that was given honey 15 g per day, the cholesterol values decreased in groups who were given honey 5 and 25 g per day and not given honey. There was a

significant statistical difference between groups who are given honey and those who were not.

While observing a decrease in triglycerides values at the end of 4 months when compared to the initial measurements of the diabetic group who were not given honey, it was shown that that triglyceride values did not change in the group that was given honey at different doses.

While observing a decrease in HDL values at the end of 4 months when compared to the first measurements in diabetic groups who were not given honey as well as those who were given honey at different doses ( $P < 0.001$ ), it was shown that that HDL values did not change in the group that was given honey at different doses ( $P = 0.786$ ).

There was a decrease in LDL values at the end of 4 months when compared to the first measurements in diabetic groups who were not given honey and also given honey at different doses, the greatest decrease was observed in the patient group that was not given honey.

As it was understood in our study, the use of natural honey in specific doses contributes to the anti-diabetics for the regulation of blood sugar and glycaemic control can be provided well. It is thought to be because of fructose present in honey. In different studies, it is seen that honey affects the other metabolic parameters besides glycaemic control [2,22]. Our study observed that total cholesterol and LDL levels decreased, triglyceride values did not change, but contrary to expectations, decreased the levels of HDL in the group who are given 5 and 25 g of honey. This situation has been interpreted that different results are obtained from natural honey which are obtained from flowers with different flora.

After 4 months, a significant reduction in HbA1c levels was observed in all dosage groups where honey was consumed. Moreover, a decrease in total cholesterol was noted in individuals who consumed honey in doses of 5 to 25 g. An increase in cholesterol levels was observed in groups where 15 g of honey was administered.

In following years, natural honey will be included in the recommended food list of diabetic patients because of this significant decrease in HbA1c values and increase in HbA1c values in the control group. The key takeaway that should be considered that the glycaemic index of honey and the rate of fructose are very important also honey must be completely natural honey.

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