Effects of Bee Propolis on Blood Pressure Record and Certain Biochemical Parameter in Healthy Volunteers

Dhamyaa A. Khalaf, Imad A-J Thanoon
Department of Pharmacology, College of Medicine, University of Mosul, Mosul, Iraq.
Correspondence: Dhamyaa A. Khalaf. dhamyaaahmed@yahoo.com.

(Ann Coll Med Mosul 2018; 40 (1): 20-26).
Received: 20th Apr. 2018; Accepted: 11th Jun. 2018.

ABSTRACT

Objectives: To evaluate the effect of encapsulated bee propolis supplementation 500 mg twice daily for 2 months on blood pressure record, fasting serum glucose, lipid profile and serum uric acid in otherwise healthy volunteers in comparison to controls.

Design: The study was conducted from October 2017 to April 2018, subjects included in the study was healthy non-obese from different areas in Mosul city, so as the control.

Subjects and methods: Forty apparently healthy subjects (Sixteen male and twenty–four female) were included in this study. Blood pressure (BP) were recorded, body weight and body mass index (BMI) were calculated, then a blood sample was taken with assay of fasting serum glucose (FSG), lipid profile {Total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL –C), while serum low density lipoprotein (LDL –C), very low density lipoprotein (VLDL-C) and atherogenic index (AI)} were calculated by using certain equations and serum uric acid (SUA), was measured for both the intervention and the control groups.

After 2 months of supplementation with encapsulated bee propolis 500 mg twice daily, the BP, body weight, BMI, LDL-C, VLDL-C and AI were calculated and FSG, TC, TG, HDL and SUA were measured for the intervention group. All data were presented as means± standard deviation (SD) of mean. Independed t – test of two mean was used. Dependent t – test of two mean was applied for the differences in the intervention group (before and after). Chi square test of independence was used for categorial variables. P–value≤0.05 was considered statistically significant.

Results: Initially, at the start of the study, there was insignificant difference between the interventions and the control groups with regard age, sex, weight, BMI, systolic and diastolic BP, serum TC, HDL- C, LDL –C, AI and SUA, with a significant differences in FSG, TG, and VLDL. By comparison before and after supplementation in the intervention groups, there was a significant decrease in the systolic and diastolic BP record, FSG, TC, TG, LDL –C, AI, SUA, with a significant increase in body weight and HDL –C.

Conclusion: Bee propolis supplementation at a dose of 500 mg twice daily for 2 months carries a beneficial effects on BP record, FSG, lipid profile, and SUA, which should be taken in preventive medicine, since hyperglycemia, hyperlipidemia and hyperureciemia, contributed to the development of atherosclerosis, cardiovascular and cerebrovascular diseases.

Keywords: Propolis, healthy volunteers, FBS, lipid profile, uric acid, blood pressure.

تأثيرات عكبر النحل على قياس ضغط الدم وبعض الفحوصات البايوكيمائيه عند المتطوعين الأصحاء

ضمياء احمد خلف*، عماد عبد الجبار ذنون**
***طالبة ماجستير ، **فرع الادوية، كلية الطب، جامعة الموصل، الموصل، العراق**

الخلاصة

الأهداف: تقيم إعطاء كبسول عكبر النحل بجرعة ٥٠٠ ملغم مرتين يوميا لمدة شهرين على قياس ضغط الدم ومستوى الكلوكوز وصورة الشحوم والحامض البولي في مصل الدم عند متطوعين أصحاء غير بدناء وبالمقارنة مع مجموعة ضبط.

التصميم: تم إجراء الدراسة للفترة من شهر تشرين الأول ٢٠١٧ إلى نيسان ٢٠١٨ وتم تجميع عينة المتطوعين للدراسة وعينة الضبط من مناطق مختلفة لمدينة الموصل.

طرق العمل: إشترك في الدراسة ٤٠ شخصا ١٦ من الذكور و٢٤ من الإناث. تم قياس ضغط الدم، وزن الجسم وحساب دليل كتلة الجسم ثم سحب عينة الدم وقياس مستوى الكلوكوز، الحامض البولي، الكوليستيرول، الشحوم الثلاثية والشحوم عالية الكثافة في مصل الدم مع حساب معدل الشحوم واطئة الكثافة وذلك لأعضاء الدراسة ومجموعة الضبط. بعد مضي شهرين من إعطاء كبسول عكبر النحل تم قياس ضغط الدم وزن الجسم مع حساب دليل كتله الجسم وتم سحب عينة دم لأعضاء مجموعة الدراسة وإجراء نفس الفحوصات المذكورة أعلاه.

النتائج: في البداية كان هنالك اختلافا غير معنوي بين أعضاء مجموعة الدراسة وأعضاء مجموعة الضبط فيما يتعلق بالعمر والجنس، الوزن، معامل كتله الجسم، قياس ضغط الدم الانقباضي والانبساطي وفي مستوى الكوليستيرول، الشحوم عالية وواطئة الكثافة معامل التعصد ومستوى الحامض البولي مع وجود اختلاف معنوي في مستوى الكلوكوز، الشحوم الثلاثية والشحوم واطئة الكثافة جدا. بالمقارنة بين إفراد مجموعة الدراسة قبل وبعد استخدام عكبر النحل ظهر هنالك انخفاض معنوي في معدل ضغط الدم الانقباضي والانبساطي، مستوى الكلوكوز، الحامض البولي والكوليستيرول، الشحوم الثلاثية، الشحوم واطئة الكثافة والشحوم واطئة الكثافة جدا ومعامل التعصد في مصل الدم مع زيادة معنوية في الشحوم عالية الكثافة ووزن الجسم.

الخلاصة: إعطاء عكبر النحل بجرعة ٥٠٠ ملغم مرتين يوميا لمدة شهرين كان له تأثيرات مفيدة على قياس ضغط الدم مستوى الكلوكوز، صورة الشحوم ومستوى الحامض البولي في مصل الدم ممكن الاستفادة منه في تطبيقات الطب الوقائي خاصة إن إرتفاع سكر الدم وإرتفاع مستوى الشحوم والحامض البولي في الدم مرتبط بتطور حدوث تصلب الشرايين وامراض القلب والدماغ الوعائية.

كلمات المفتاح: عكبر النحل، متطوعين أصحاء، مستوى الكلوكوز في حالة الصيام، صورة الشحوم، الحامض البولي وضغط الدم.

INTRODUCTION

In modern primary care, doctors spend considerable time and effort, concentrating on preventive medicine practice.[1] Hyperglycemia, hyperlipidemia and hyperureciemia were considered as main risk factor for developing atherosclerosis and cardiovascular diseases.[2,3,4] Type II diabetes mellitus (DM) is associated with 4 folds increased risk of both coronary and cerebrovascular disease[2] and atherogenic dyslipidemia characterized by abnormal changes in plasma lipid profile as low HDL –C and increased TG[3] and only recently the pathophysiological links between elevated SUA concentration and the risk for atherosclerotic cardiovascular and cerebrovascular disease become clear.[4]

Currently word attention were directed to traditional medicine.[5] Propolis is a resinous material , containing a variety of substances and is used in cosmetics, food supplement and in medicine for centuries in various health problems as treatment and prevention. It exhibit abroad spectrum activities including antibacterial,[6] antifungal,[7] antiviral,[8] anti-inflammatory,[9] antioxidant,[10] immunostimulating[11] and cytostatic proprieties.[12]

In this study we evaluated the preventive effect of encapsulated bee propolis as daily supplement of 500 mg twice daily for 2 months on BP record, FSG, lipid profile, SUA in otherwise non-obese healthy volunteer in comparison to the controls.

SUBJECTS AND METHODS

Forty otherwise healthy non-obese volunteer (sixteen male and 24 female) were included in the study that was conducted from October 2017 to April 2018. Pregnant and lactating women, those with history of allergy, asthma and bleeding disorders were excluded.

Also included in the study 43, age, sex and body weight matched healthy subjects as a control group.

Initially, for both the members of intervention and control groups, BP were recorded, body weight measured, BMI was calculated using following equation:

BMI= Weight (Kg) /Height (m2)[13]

FSG, TC, TG and HDL-C were measured Using kits of Biolabo Company (France).

LDL –C was calculated using the following equation:[14]

TC – HDL – VLDL –C

VLDL level was calculated by the following equation:[14]

TG/5=VLDL

Atherogenic index calculated as:[15]

A.I = TC/HDL-C

Also a kit from Biolabo Company – France was used for measurement of SUA.[16,17]

After 2 months of bee propolis (Forever Company –USA) supplementation in a dose of 500 mg twice daily, BP were recorded, body weight, BMI, LDL-C, VLDL-C and A.I were calculated and serum TC, TG, HDL-C, FSG and SUA were measured.

RESULTS

As shown in **Table 1**, the comparison between the intervention and the control groups with regard to personal characteristics, demonstrated insignificant differences.

Before 2 months of bee propolis supplement, there was a significant higher TG. and VLDL –C concentrationsand lower FSG in the intervention group in comparison to control **Table 2**.

After 2 months of encapsulated bee propolis supplementation and by comparing the intervention and the control groups, there was a significant differences in systolic and diastolic blood pressure record , FSG , TC . LDL –C and A.I (**Table 3, Table 4**).

By comparison before and after supplementation of bee propolis in the intervention group, there was a significant reduction in systolic and diastolic blood pressure (% of improvement: 8.39), diastolic blood pressure (% of improvement: 12.42) with a significant increase in body weight (1.62 %) (**Table 5**).

Also there was a significant reduction in FSG (% of improvement 10.95), SUA (20.64%), TC (15.33%), LDL –C (26.27 %), VLDL –C (34.39%), TG (34.47%) and A.I (34.47%), with a significant increase in HDL-C (8.18%) as shown in (**Table 6**).

Table 1. Comparison between the intervention and control groups with regard personal characteristics.

Characteristics	Intervention group [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
Age (years)	29.9 ± 11.1	29.5 ± 10.5	0.872
Systolic blood pressure (mmHg)	116.8 ± 10.2	113.3 ± 9.4	0.109
Diastolic blood pressure (mmHg)	76.5 ± 5.8	73.6 ± 8.5	0.074
Weight (kg)	59.8 ± 10.5	60.7 ± 9.4	0.662
BMI (kg/m^2)	22.39 ± 2.06	22.35 ± 1.80	0.923
Gender	No. (%)	No. (%)	
Male	16 (40.00)	16 (37.21)	0.794**
Female	24 (60.00)	27 (62.79)	

* Independent T-test of two means was used.

** Chi-square test was used.

Table 2. Comparison between intervention and the control groups with regard to measured biochemical parameters before bee propolis supplementation.

Parameters	Intervention group [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
FSG (mg/dl)	84.9 ± 13.6	93.3 ± 14.8	0.009
SUA (mg/dl)	3.73 ± 1.36	3.34 ± 1.14	0.168
S. cholesterol (mg/dl)	161.8 ± 29.6	155.9 ± 29.5	0.366
HDL (mg/dl)	55.23 ± 8.28	57.16 ± 7.18	0.257
LDL (mg/dl)	90.2 ± 28.4	86.9 ± 26.9	0.592
VLDL (mg/dl)	16.43 ± 7.61	11.86 ± 6.34	0.004
TG (mg/dl)	82.1 ± 38.0	59.3 ± 31.7	0.004
A.I	2.98 ± 0.66	2.76 ± 0.58	0.106

* Independent T-test of two means was used

Table 3. Comparison between the intervention group after bee propolis supplementation and control groups regarding personal characteristic.

Parameters	Intervention group after 2M. [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
Systolic BP (mmHg)	107.0 ± 9.7	113.3 ± 9.4	0.004
Diastolic BP (mmHg)	67.0 ± 7.6	73.6 ± 8.5	0.000
Weight (kg)	60.7 ± 11.3	60.7 ± 9.4	0.999
BMI (kg/m^2)	22.68 ± 2.29	22.35 ± 1.80	0.467

* Independent T-test of two means was used.

Table 4. Comparison between the intervention group after bee propolis supplementation and control groups regarding measured biochemical parameters.

Parameters	Intervention group after 2M. [n = 40] Mean ± SD	Control group [n = 43] Mean ± SD	P-value*
FSG (mg/dl)	75.6 ± 10.6	93.3 ± 14.8	0.000
SUA (mg/dl)	2.95 ± 1.10	3.34 ± 1.14	0.117
S. cholesterol (mg/dl)	137.0 ± 32.2	155.9 ± 29.5	0.006
HDL (mg/dl)	59.73 ± 10.24	57.16 ± 7.18	0.188
LDL (mg/dl)	66.5 ± 31.1	86.9 ± 26.9	0.002
VLDL (mg/dl)	10.78 ± 6.73	11.86 ± 6.34	0.453
TG (mg/dl)	53.9 ± 33.6	59.3 ± 31.7	0.452
A.I	2.34 ± 0.62	2.76 ± 0.58	0.002

* Independent T-test of two means was used.

Table 5. Comparison between the pre and post- supplementation of bee propolis in the intervention group regarding personal characteristics.

Parameters	Base line Mean ± SD	After 2 months Mean ± SD	Before – after	% improvement rate	P-value
Systolic BP (mmHg)	116.8 ± 10.2	107.0 ± 9.7	9.8 ± 1.31	8.39	0.000
Diastolic BP (mmHg)	76.5 ± 5.8	67.0 ± 7.6	9.50 ± 6.77	12.42	0.000
Weight (kg)	59.8 ± 10.5	60.7 ± 11.3	- 0.97 ± 2.04	1.62	0.005
BMI (kg/m^2)	22.39 ± 2.06	22.68 ± 2.29	- 0.29 ± 0.17	1.30	0.092

* Paired T-test of two means was used.

Table 6. Comparison between the pre and post- supplementation of bee propolis in the intervention group regarding measured biochemical parameters.

Parameters	Base line Mean ± SD	After 2 months Mean ± SD	Before – after	% improvement rate	P-value*
FSG (mg/dl)	84.9 ± 13.6	75.6 ± 10.6	9.3 ± 13.0	10.95	0.000
SUA (mg/dl)	3.73 ± 1.36	2.95 ± 1.10	0.77 ± 0.82	20.64	0.000
S. cholesterol (mg/dl)	161.8 ± 29.6	137.0 ± 32.2	24.8 ± 28.1	15.33	0.000
HDL (mg/dl)	55.23 ± 8.28	59.73 ± 10.24	- 4.50 ± 7.91	8.15	0.001
LDL (mg/dl)	90.2 ± 28.4	66.5 ± 31.1	23.7 ± 28.3	26.27	0.000
VLDL (mg/dl)	16.43 ± 7.61	10.78 ± 6.73	5.65 ± 5.59	34.39	0.000
TG (mg/dl)	82.1 ± 38.0	53.9 ± 33.6	28.3 ± 27.92	34.47	0.000
A.I	2.98 ± 0.66	2.34 ± 0.62	0.64 ± 0.65	21.48	0.000

* Paired T-test of two means was used.

DISCUSSION

Propolis is a safe natural resinous product, made by bees from material extracted from plants, flowers and bees wax. It is regarded as a folk medicine possessing a broad spectrum of biological activities including hypoglycemic activity.[18]

This study revealed a significant weight gain in the intervension group after 2 months of bee propolis supplementation at a doses 500 mg twice daily. This is in agreement with study conducted by Denli *et al*, 2005[19], whom reported that the addition of propolis in the diet significantly increase the growth parameter of quail chicks such as body weight gain and feed consumption and improvement feed efficacy compared with controls and they suggested that it could be due to antimicrobial activity of the propolis extract that resulted in improvement of intestinal hygiene that lead to improved digestion and absorption, beside that it has been suggested that bee propolis contain protein, amino acids, vitamins, and flavonoids, for this resinous it has been used by some people as a nutritional supplement. [20]

Also on line with our results, the study conducted by albushabaa (2014)[21] , she reported that propolis extract has antihyperglycemic effect and significantly improved the body weight of diabetic rabbits. Yucel *et al*, (2012)[2], studied the effect of propolis administration on assessement of growth and neonatal diarrhea in calves, they found an improved live weight gain and growth this attributing to the the activity of propolis against many bacterial pathogens, thus preventing calves diarrhea.

Concerning the effect of propolis on blood pressure record, although all of our subject in the study were normotensive, propolis supplement causes a significant reduction in the mean systolic and diastolic blood pressure in comparison to pre-propolis supplementation period and the controls. This is similar to the results of Gogebaken *et al*., 2012[23], whom concluded that propolis decrease tyrosine hydroxylase ,which is the rate limiting enzyme in the biosynthesis of catecholamine in nitric oxide inhibited hypertensive rats.

Talas *et al*, 2013[24] also reported that propolis might be used to protect against the hypertensive effect of nitro L–arginine methyl ester by increasing the generation of vascular nitric oxide.

Concerning the effect of propolis on biochemical parameters under study, this study reported a significant beneficial effects on FSG, lipid profile indices and SUA. This is in agreement with Li *et al*, 2011[25] whom reported that encapsulated propolis can suppress the heightening of FBS in type II diabetic rats, 8 weeks after starting therapy and concluded that encapsulated propolis can improve the insulin sensitivity in type II diabetic rats.

Fuliang *et al*, (2005)[26] also reported that propolis lower FSG and lipids leading to deceased out puts of lipid peroxidation and scavenge the free radicals in rats with diabetes mellitus. Bankova (2005)[27], attributed the hypoglycemic effect of propolis to its flavonoids content. Again our findings were in accordance with study conducted by Zaahkouk *et al*, (2016)[28] reporting a significant lower FSG level and increase in plasma insulin level in streptozotocin induced diabetic rats. Lastly and in a human study conducted by Zhao *et al* (2016)[29] reported that a Brazilian propolis significantly improved FSG level and plasma insulin in human subjects with type II DM.

In contrast to our study finding, Bulalo *et al*, (2009)[30] reported that propolis had no effects on plasma glycemic control and lipid metabolism in diabetic rat model fed on propolis for 28 days, also in contrast to our findings the study conducted by fukuda *et al*, (2015)[31] they concluded that 8 weeks supplementation of Brazillian propolis did not have beneficial effect on serum FSG, although it prevented the action of hyperureciemia and dysfunction of renal glomerular filtrating function that commonly developed in patient suffering from DM.

With regard to lipid profile, Albokhadaim (2015)[32], reported that dietary supplementation of propolis induces a beneficial hypolipidemic effect as hypocholesterlomic and hypotriglyceridemic effect in the sera of rat fed on high cholesterol diet. The effect on serum cholesterol could be attributed to inhibition of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG –COA) reductase, the rate –limiting enzyme that mediates the first step in cholesterol biosynthesis ,while the effect on TG might be attributed to lipase stimulation.

Also in line with our findings, the study conducted by EL-Sayed *et al*, (2009).[33] They conducted that propolis extract offers promising

antidabetic and hypolipidemic effects that might be mainly attributed to its potent antioxidant property.

With regard to effect on SUA, our study reported a significant reduction in SUA after 2 month supplementation of bee propolis, this is in line with the study conducted by Omnia *et al*, (2014) [34], and concluded that propolis act as a protective agent against thioacetamide–induced hyperammonemia in rats and that bee propolis and bee pollen significantly reduces SUA.

In a recent research work Amin *et al*, (2017)[35], studied the reno protective and antioxidant effect of silymarine and propolis on diclofenac sodium induced renal toxicity in rats and concluded that propolis with pollen provide a natural protection against renal toxicity induced by diclofenac sodium and both resulted in a significant decrease in urea, creatinine and SUA level as compared to the group receiving diclofenac only.

In conclusion: Encapsulated propolis supplement for 2 months at dose of 500 mg twice daily in otherwise healthy volunteer, resulted in a beneficial effect on blood pressure record, FSG, lipid profile and serum uric acid which might through a light on the protective effect of propolis against atherosclerosis and cardiovascular diseases in a primary care preventive medicine practice.

REFERENCES

1. Sniplesky D, Careker K, Sundsted K, Burton MC. Primary care physicians practicing preventive medicine in out patient setting. International Journal Preventive Medicine 2016 ; 7 : 5.

2. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ *et al*. Diabetes control and complication trial/epidemiology of diabetes interventions and complication (DCCT / EDIC) study research group. intensive diabetes treatment and cardiovasculare diseases in patient with type I diabetes New England Journal of Medicine. 2005; 353 (25) : 2643 -53.

3. Nelson RH. Hyperlipidemia as arisk factor for cardiovascular disease. Primary Care. 2013 march; 40 (1) : 195- 211 .

4. Krishnan E, Pandya BJ, Chung L, dabbous O. Hyperurecemia and the risk for subclinical coronary atherosclosis. data from a prospective observational cohort study. Arthritis Research and Therapy 2011.13 :R 66 .

5. Cordell GA, C olvard MD. Natural product and tradional medicine : turning on a paradigm. Journal National product. 2012 ; 75 (3) : pp 514 – 525 .

6. Urgur A, Arslan T. An in vitr study on antimicrobial activity of propolis from mugla province of turkey. Journal of Medicinal Food 2004; 7(1) :90 – 4.

7. Ota C, U nterkir cher C, Fantinato V, Shimizu MT. Antifungal activity of propolis on different species of candida. Mycoses 2011;44 (9-10) : 375 – 378.

8. Amaros M, S imoes CMO, Grre L, saurvager F, Cormier M . Comparison of the antiherpes simplex virus activities of propolis and 3 mthyl –butyl – 2- enyl caffeate. Journal National Product 1994; 57: 644- 647 .

9. Miyataka H, Nishiki M, Matsumoto H, Fujimoto T, Matsuka M, Satoh T. Evaluation of propolis. Evaluation of brazilian and chinese propolis by enzymatic and physico-chemical methods. Biological and Pharmaceutical Bulletine 1997 ; 20: 496-56.

10. Nagai T, Inouse R, Inouse H, Suzuki N. Preparation and antioxidant properties of water extract of propolis. Food Chemistry 2003 .80: 29-33.

11. Dimov V, Ivanovska N, Manolova, Bankova V, Nikolov N, Popov S. Immunomodulatory action of propolis. influncing on anti-infectious protection and macrophage function. Apidology 1991 ;22 : 155-162.

12. Banskota AH, Tezuka Y, Midorikawa K, Matsushige K, kadota S. Two novel cytotoxic benzofuran derivative from Brazilian propolis. Journal National product 2000; 63 (9) : 1277- 1279.

13. Blak barn H, Jacobs D. Commentary origins and evaluation of body mass idex (BMI) continuing saga. Interntional Journal of Epidemioloy 2014 ;43(3) :665 - 669 .

14. Friedewald W T, Levy R I, Fredrickson D S."Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge,"Clinical Chemistry, 1972. 18. (6). 499–502.

15. Castelli W.P, Abbott R.D, McNamara PM. Summary estimated of cholesterol used to predict coronary heart disease . Circulation ,67(4):730-734(1983).

16. Burtis C.A, Ashwood E.R, Saunders W.B, Tietz N.W Text book of clinical chemistry, 3rd Edition. (1999). pp. 1245-1250.

17. Fossati P, Prencipe L, and Berti G. Use of 3.5-dichloro-2- Hydroxybenzene sulfonic acid / 4 Amino phenazone chromogenic system in direct enzymatic assays of uric acid in serum and urine. Clinical Chemistry.: 26(227-231) 1980.

18. Abo-Salem OM, El-del RH, Harison G.E.I EL – Halawany N, Ghoraim MM. Expermintal diabetic nephropathy can be prevented by propolis effect on metabolic disturbances and renal oxidative parameter. Pakistan Journal of Pharmaceutical Sciences 2009 ; 22 (2) : pp 205 – 201 .

19. Denli M, Cankaya S, Silici1 S, Okan F, Uluocak A N. Effect of Dietary Addition of Turkish Propolis on the Growth Performance, Carcass Characteristics and Serum Variables of Quail (Coturnix coturnix japonica). Ascian–Australasian Journal of Animal Sciences. 2005;18,(6) : 848-854.

20. Lee SW, Kim HJ, Hwangbo S. Studies on the chemical characteristic of Korean propolis. Korean Journal Society for Food Science of Animal Resources 2001 ;21 :383-388.

21. Albushabaa SHH. Effect of propolis on blood glycemic control and lipid metabolism in diadetic rabbits. International Journal of Sciences and Engineering Research 2014 .5(12) :800-807.

22. Yucel B, Onenc A, Kaya A, Altan O. Effect of propolis on growth performance and neonatal diarrhea of calves. Symbiosis Journal of Veterinary Sciences 2015; 1(1):1-5.
23. Gogebakan A, Talas ZS, Ozdemir I and Sahna E Role of propolis on tyrosine hydroxylase activity and blood pressure in nitric oxide synthase-inhibited hypertensive rats. Clinical and Experimental Hypertension, 2012. 34(6): 424- 428.
24. Talas ZS, Gogebakan A, Onen I. Effect of propolis on blood biochemical and heamaological parameter in nitric oxide synthase inhibited rats by nitro –L – arginine methyl ester . Pakistan Journal of Pharmaceutical Sciences. 2013; 26(5): pp 915-919.
25. Li Y, Chen M, Xuan H, Hu F. Effects of encapsulated propolis on blood glycemic control, lipid metabolism and insulin resistance in type 2 diabetes mellitus rats. Evidence–Base Complementary and Alternative Medicine 2011; 2012 :pp(1-8).
26. Fuliang HU, Hepburn HR, Xuan H,Chen M, Daya S, Radloff SE. Effects of propolis on blood glucose, blood lipid and free radicals in rats with Diabetes mellitus. Pharmacological Research, 2005.51, 147-52.
27. Bankova V .Chemical diversity of propolis and the problem of standardization. Journal of Ethnopharmacology 2005.100(1-2): 114-117.
28. Zaahkouk SAM, Ibrahim DF, Elarabi BE. Antioxidant and hypoglycemic studies on Egyptian propolis and foeniculum vulgare on alloxan induced diabetic rats. International Journal of Animal Biology 2016 ;2:pp1-10.
29. Zhao L, Pu L, Jingyu W, Jinghua L, Jianguan W, Zhonghao X, *et al*. Brazilian green propolis improves antioxidant function in patient with type 2 diabetes mellitus. International Journal of Environment and Public Health.2016;14:pp498-507.
30. Bufalo MC, Barreiro DP, Sartori DRS, Sforcin JM. Absences of propolis effect on plasma glycemic control and lipid metabolism in a diabetic rat model. Journal of Apiprodct and Apimedical Science 2009;1(2) ;pp 51-55.
31. Fukuda T, Fukui M, Tanaka M, Senmaru T, Iwase H, Yamazaki M, *et al*. Effect of brazilian green propolis in patient with type 2 diabetes: A double –blind randomized placebo-controlled study. Biochemical Report 2015;3:pp 355-360.
32. Albokhadam I. Influence of dietary supplementation of proplis on hematology, biochemistry and lipid profile of rats fed high cholesterol diet. Journal of Advance Veterinary Animal Research. 2015 ;2(1) :pp 56-63.
33. El-Sayed el–SM, Abo-Salem OM, Aly HA, Mansour AM. Potential anti diabetic and hypolipidemic effect of propolis extract in streptozotocin- induced diabetic rats. Pakistan Journal of Pharmaceutical Sciences 2009; 22(2) : pp 168-174.
34. Omnia MA, Nabila AM, Nada RR. Biochemical effect of propolis and bee pollen in experimentally – induced hyperammonemia in rats. Benha Veterinary Medical Journal 2014 ;27(1):pp 8-28.
35. Amin KA, Ahmed RR, Hozayen WG, Antar A. Renoprotective and antioxidant effect of silymarin and propolis on diclofenac sodium induced renal toxicity in rats. International Journal of Pure and Applied Biosciences 2017;5 (2):pp 31-42.