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Effects of Cisplatin on Glycemic Control and Lipid Profile in Male Albino Rats Role of Propolis

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Abstract

Aims: This study aimed to investigate the effects of cisplatin on glycemic parameters (fasting blood sugar FBS; glycosylated hemoglobin HbA1c), and lipid profile (total cholesterol TC, triglyceride TG, high density lipoprotein HDL-c, and calculation of low density lipoprotein LDL-c, cardioprotective index HDL/LDL,cardiac risk ratio cholesterol/HDL), with the evaluation of any possible role for propolis in ameliorating adverse effects on these , in comparison to controls.

Materials and Methods: This experimental work takes 6 weeks and involved 60 male albino rats ,weighed 230±40g , divided into 6 groups, each of 10 members.

Group A, received 3 doses of cisplatin at 4 mg/kg intraperitoneally (I.P) at weekly intervals starting by the end of the 2nd week, and killed by the end of the 6th week.

Group B, received propolis at 120 mg /day orally for 6 weeks.

Group C, received propolis 120 mg/day initially then by the end of the 2nd week started cisplatin 4mg I.P weekly for 3 doses.

Group D, received propolis 60 mg/day for 6 weeks.

Group E, received propolis 60 mg daily for 6 weeks, starting cisplatin I.P 4 mg 3 doses by the end of the 2nd week ,one week apart.

Group F, represent the control group, on normal saline orally for 6 weeks.

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At the start the animals in all groups were weighed ,a blood sample was taken then, during the experiment , weighed , physical activity and food intake were recorded, by the end of the experimental duration weight were recorded, a blood sample were taken .The blood samples taken before and after the experiment were for measurement of FBS, HbA1c , TC, TG, HDL-c, and calculation of LDL-c, HDL/LDL, cholesterol/HDL.

Results:

By observation: By comparison of before and 6 weeks after the experiment, there was a significant weight reduction in the group A, with death of 2 members of this group after the 3rd dose of cisplatin. While group B showed a significant weight gain. Clear and significant changes were recorded in parameters of lipid profile , with a insignificant effects of CP on glycemic parameters FBG and HbA1c in group A in comparison to control group with a clear ameliorative effects of propolis on the parameters of lipid profile under study.

Conclusion: CP clearly negatively affects some of the lipid profile parameters and propolis administration clearly ameliorated the adverse effects of cisplatin on the lipid profile under study.

Keywords : Cisplatin , Glycemic Control , Lipid Profile . bee propolis.

INTRODUCTION

Cisplatin (CP) is a commonly used platinum-based chemotherapeutic drug used for the treatment of various types of (1). Its use causes many serious adverse effects, and really it is the drug of choice for the induction of dyslipidemia, liver and kidney injuries in rats (2).Atherogenic dyslipidemia, characterized by high LDL-c/HDL-c ratio and elevated TG, is associated with high cardiovascular risks(3). Komdeur et al has been reported cisplatin-induced hyperglycemia (4) Hyperglycemia , hyperlipidemia and hyperuricemia were considered as main risk factors for developing atherosclerosis and cardiovascular diseases(5).In modern primary care, doctors spend good time and effort,concentrating on preventive medicine practice and the modulations of cardiovascular disease markers by propolis has been shown in several studies, both in vitro and in vivo assays have been developed to elucidate the molecular mechanisms of this beneficial effect, as regulation of glucose and lipoprotein metabolism, decreasing inflammatory cytokines and oxidative stress (6,7,8).Fuliang et al (9), reported that propolis lower fasting glucose and lipids leading to decreased outputs of lipid peroxidation and scavenge the free radicals in rats with diabetes mellitus. This study aimed to assess the effects of CP on glycemic control and lipid profile in male albino rats and studying the possible role of propolis at 2 dose levels in opposing the adverse effects of CP on these parameters.

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MATERIALS AND METHODS:

A total of 60 adult male albino rats weighing 230±40 g ,obtained from the animal house in the College of Veterinary Medicine-University of Mosul, randomly divided into 6 groups each of 10 rats. The animals were housed in metallic cages and subjected to an adaptation period of two weeks ,photoperiod of (12 h:12h light/dark), 25º C± 2 º C temperature and 45-50% humidity , receiving normal amount of water and food. Ethical approval reference number :UOM/COM/MREC/20-21(21).

Group A: received 4 mg cisplatin I.P by the end of the 2nd week for 3 doses one week apart.

Group B: received propolis 120 mg daily orally for 6 weeks.

Group C: Received propolis 120 mg daily orally for 6 weeks and by the end of the 2nd week starting cisplatin I.P 4 mg for 3 doses one week apart between a dose and the other.

Group D: received propolis 60 mg daily orally for 6 weeks.

Group E: received propolis 60 mg daily orally for 6 weeks and by the end of the 2nd week starting cisplatin 4 mg I.P for 3 doses one week apart between a dose and the other.

Group F: Control group receiving normal saline orally.

At the start of the experiment and by the end of the 6th week , a blood samples were taken from all the animals under study, for assessing glycemic control (FBG and HbA1c) with lipid profile parameters as TC, TG, LDL-c, HDL-c, HDL/LDL as a cardioprotective ratio and TC/HDL as a cardiac risk ratio.(10).

By the end of the end of the experiment duration animals were weighed and other blood sample were taken for assay of the same parameters.

Statistical Analysis Of The Data:

The results were expressed as mean± SD; Mann-Whitney test was used to compare of pre and post administration results within the group. Improvement (change) rate was calculated as
Improvement Rate = result of pre-administration – result of after administration/ result of pre-administration x 100.
One-way ANOVA test with Tukey's Pair wise was used to compare results between different groups. The Statistical Minitab version 18 software program was used to perform statistical analysis of the data.

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RESULTS:

1.Observational Results

a. Group A. Two of the members of this group died 3 days after the 3rd I.P dose of cisplatin both showed yellowish discoloration of the whole body , the other members showed clear weight loss ,with decrease in physical activity and food intake.
b. Group B. No death was reported in this group, members of this group looks fully active, with good food intake and obvious weight gain.
c. Group C. No death was reported in this group, with mild decrease in physical activity and food intake and mild weight loss.
d. Group D. No death was reported in this group, physically active with good food intake.
e. Group E. one death was recorded in this group ,with mild reduction in physical activity and food intake, with obvious weight loss.
f. Group F. No losses was reported in this group, all members active physically with good food intake.

Table 1 shows comparison between the 6 groups with regard weight changes before and after the 6 weeks intervention.

2. Biochemical Results

I. Glycemic Control Parameters (FBG, HbA1c):

a. Group A. By comparison of pre and post-administration results, there was an insignificant effects of CP administration on FBG and HbA1c (Table 2).
b. Group B. By comparison of pre and post-administration results , there was a significant reduction in FBG and HbA1c (Table 3).
c. Group C. There was an insignificant reduction in FBG and HbA1c,by comparing pre to post-administration results. (Table 4).
d. Group D. By comparison of the results of pre- and post-administration, there was a non-significant decrease in FBG and HbA1c. (Table 5).
e. Group E. There was a non-significant reduction in FBG and HbA1c on comparing results of pre- to post-administration.(Table 6).
f. Group F. There was a non-significant effects of placebo on the results of pre- and post-administration of placebo. (Table 7).

II. Lipid Profile:

a. Group A. By comparison of pre and post-administration results, there was a significant reduction in HDL-c and cardioprotective index with a significant increase in TC, TG, LDL-c and cardiac risk ratio(Table 8).
b. Group B. By comparison of pre and post-administration results , there was a significant reduction in TC, TG, LDL-c, and cardiac risk ratio with a significant increase in HDL-c and cardiac protection index (Table 9).

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c. Group C. There was an significant reduction in HDL-c and cardioprotective index with a significant increase in TC, TG, LDL-c and cardiac risk ratio,by comparing pre to post-administration results. (Table10).
d. Group D. By comparison of the results of pre- and post-administration, there was a significant reduction in TC, TG, LDL-c, and cardiac risk ratio with a significant increase in HDL-c and cardiac protection index. (Table 11).
e. Group E. There was a significant reduction in HDL-c and cardioprotective index with a significant increase in TC, TG, LDL-c and cardiac risk ratio on comparing results of pre- to post-administration.(Table 12).
f. Group F. There was a non-significant effects of placebo on the results of lipid profile on comparing pre- and post-administration of placebo. (Table 13).

DISCUSSION:

1. Effects On Body Weight

The reduction in body weight observed in this study in the cisplatin group , could be correlated with the reduced food intake noticed during the period of the experiment. Weight gain have been noticed in group C by adding propolis at 120 mg/d, but not at 60 mg/d, this is in agreement with the study conducted by El-Naggar et al., (11). They reported that propolis treatment after cyclophosphamide injection could protect partially the body from weight loss. OrŠolic et al on studying the effect of Croatian propolis on diabetic nephropathy and liver toxicity in mice, reported that body weight was rapidly reduced in animals treated with alloxan alone , the reduction was the greatest between 3 and 10 days and then body weight started to recover especially in diabetic animals treated with water soluble derivative of propolis, which have almost reached a mass of healthy non diabetic mice (12). Rivera-Yanez et al, on studying the hypoglycemic and antioxidant effects of propolis in a model of experimental diabetes, reported that the administration of propolis during the 15 days of treatment showed a considerable effect on the weight loss of diabetic mice (13) Denli *et al*, (14), 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 (15).

2. Effects On The Glycemic Control & Lipid Profile

The link between CP and diabetes mellitus have been suggested by many researchers (5, 10, 11). This study revealed a non-significant effects of CP administration on glycemic control, this is in agreement with the study conducted by Albokhadin (7), while in contrast to our results the study conducted by Komdeur et al (5). With regard the effects of CP on lipid profile. This study revealed a significant increase in TC, TG, LDL-c and cardiac risk ratio and that the co-

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administration of propolis especially at a daily dose of 120 mg ameliorated the adverse effects on these parameters of lipid profile. It could be explained by the fact that the liver plays a major role in controlling plasma levels of TC, thus when there is CP-induced liver impairment (16,17), there will be elevated levels of serum TC and LDL-c (18). The significant increase in serum levels of TC, TG, and LDL-c after exposure of rats to CP might be attributed to hepatocellular dysfunction and impaired lipid metabolism ,which is in agreement with the findings of Akindele et al (19). The marked increase in values of cardiac risk ratio and the reduction in cardioprotective ratio might indicate an increased risk of atherosclerosis and cardiovascular diseases (3,20). The ameliorative effect of propolis reported in this study was in agreement with the study conducted by Khalaf and Thanoon , as they reported that bee propolis supplementation at a total dose of one gram /day for 2 months carries a beneficial effects on many biochemical parameters including lipid profile in healthy volunteers (8), also in accordance with our results, two studies the first study conducted by Eman , who reported that aqueous propolis extract could reduce the hepatotoxicity and hyperlipidemia induced by octylphenol in male albino rats (21)and the recent 2nd study conducted by Salehi-Sahlabadi et al , and they concluded that propolis is associated with a reduction in TG levels and an increase in HDL-c (22).

In Conclusion: CP did not adversely affecting glycemic contro represented by FBG, and HbA1c, but adversely affecting lipid profile parameters to a significant level and propolis especially at a daily dose of 120 mg ameliorated such adverse effects on lipid parameters.

Table (1): Comparison in rate weight and rat`s liver weight among the six groups after 4 weeks of intervention.

Weights	Groups						P-value*
	A Mean ± SD	B Mean ± SD	C Mean ± SD	D Mean ± SD	E Mean ± SD	Control Mean ± SD	
Rate (g)	157.9 ± 17.47 D	241.2 ± 13.32 AB	218.2 ± 20.40 BC	250.9 ± 27.3 A	205.3 ± 28.88 C	217.0 ± 16.73 BC	**0.000**
Liver (g)	5.17 ± 1.13 C	8.21 ± 0.62 A	6.29 ± 0.71 BC	8.50 ± 0.66 A	6.11 ± 1.17 C	7.43 ± 0.61 AB	**0.000**
Liver\body weight ratio	32.90 ± 4.92 A	33.71 ± 2.95 A	33.50 ± 2.66 A	34.06 ± 2.80 A	29.49 ± 5.45 A	34.50 ± 1.85 A	0.070

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Table (2): Effect of cisplatin 4 mg/kg in group A on glycemic control parameters (FBG and HbA1c %).

Parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
B. glucose (mg\dL)	81.40 ± 7.18	83.43 ± 9.46	**- 2.5 %**	0.658
HbA1c %	4.21 ± 0.52	4.28 ± 0.40	**- 1.7 %**	0.995

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

Table (3): Effect of propolis 120 mg in group B rats on the glycemic control

Parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
B. glucose (mg\dL)	93.53 ± 8.02	85.47 ± 6.13	**8.6 %**	**0.042**
HbA1c %	5.10 ± 0.004	4.39 ± 0.280	**13.9 %**	**0.005**

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

Table (4): Effect of propolis 120 mg with cisplatin 4 mg/kg in group C rats on the FBG and HbA1c %

Parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
B. glucose (mg\dL)	91.46 ± 8.73	86.14 ± 6.70	**5.8 %**	0.229
HbA1c %	4.77 ± 0.004	4.35 ± 0.004	**8.8 %**	0.090

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

Table (5): Effect of propolis 60 mg in group D rats on the FBG and HbA1c %

Parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
B. glucose (mg\dL)	93.44 ± 10.86	87.19 ± 8.11	**6.7 %**	**0.285**
HbA1c %	5.08 ± 0.55	4.71 ± 0.32	**7.3 %**	0.172

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100**

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Table (6): Effect of propolis 60 mg with cisplatin 4 mg/kg in group E rats on the FBG and HbA1c %

Parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
B. glucose (mg\dL)	86.10 ± 9.26	85.74 ± 10.67	**0.4 %**	0.691
HbA1c %	4.71 ± 0.53	4.65 ± 0.39	**1.3 %**	0.958

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100**

Table (7): Comparison in blood glucose and FBG and HbA1c % parameters after 6 weeks in control group [group F]

Parameters	Beginning Mean ± SD	After 4 weeks Mean ± SD	% Improvement rate	P-value*
B. glucose (mg\dL)	89.31 ± 9.03	86.63 ± 7.69	**3.0 %**	0.658
HbA1c %	5.07 ± 0.430	4.81 ± 0.30	**5.1 %**	0.291

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100**

Table (8): Effect of cisplatin 4 mg/kg in group A rats on the lipid profile

Lipid profile parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
Cholesterol (mg\dL)	103.33 ± 8.00	191.97 ± 11.02	**- 85.8 %**	**0.001**
TG (mg\dL)	118.84 ± 3.51	149.93 ± 2.17	**- 26.2 %**	**0.001**
HDL (mg\dL)	44.44 ± 3.86	36.33 ± 2.61	**18.3 %**	**0.001**
LDL (mg\dL)	35.13 ± 8.30	124.43 ± 9.13	**- 254.2 %**	**0.001**
HDL\LDL	1.34 ± 0.391	0.29 ± 0.03	**78.4 %**	**0.001**
Chol\HDL	2.29 ± 0.204	5.22 ± 0.473	**- 127.9 %**	**0.001**

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

HDL\LDL → Cardioprotective index, Chol\HDL → Cardiac risk ratio.

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Table (9): Effect of propolis 120 mg in group B rats on the lipid profile

Lipid profile parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
Cholesterol (mg\dL)	117.64 ± 6.18	103.33 ± 8.00	**13.8 %**	**0.006**
TG (mg\dL)	128.15 ± 6.11	118.84 ± 3.51	**7.8 %**	**0.002**
HDL (mg\dL)	39.60 ± 2.42	44.44 ± 3.86	**- 10.9 %**	**0.024**
LDL (mg\dL)	52.20 ± 5.56	35.13 ± 8.30	**48.6 %**	**0.002**
HDL\LDL	0.76 ± 0.12	1.34 ± 0.39	**- 43.3 %**	**0.002**
Chol\HDL	2.97 ± 0.20	2.29 ± 0.20	**29.7 %**	**0.001**

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

HDL\LDL → Cardioprotective index, Chol\HDL → Cardiac risk ratio

Table (10): Effect of propolis 120 mg with cisplatin 4 mg/kg in group C rats on lipid profile.

Lipid profile parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
Cholesterol (mg\dL)	103.33 ± 8.00	172.53 ± 9.14	**- 67.0 %**	**0.001**
TG (mg\dL)	118.84 ± 3.51	147.11 ± 7.41	**- 23.8 %**	**0.001**
HDL (mg\dL)	44.44 ± 3.86	37.94 ± 2.63	**14.6 %**	**0.004**
LDL (mg\dL)	35.13 ± 8.30	105.08 ± 7.65	**- 199.1 %**	**0.001**
HDL\LDL	1.34 ± 0.39	0.36 ± 0.03	**73.1 %**	**0.001**
Chol\HDL	2.29 ± 0.20	4.55 ± 0.30	**- 98.7 %**	**0.001**

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

HDL\LDL → Cardioprotective index, Chol\HDL → Cardiac risk

Table (11): Effect of propolis 60 mg on the lipid profile of group D rats.

Lipid profile parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
Cholesterol (mg\dL)	119.49 ± 8.86	103.33 ± 8.00	**15.6 %**	**0.006**
TG (mg\dL)	130.59 ± 10.64	118.84 ± 3.51	**9.9 %**	0.052
HDL (mg\dL)	40.33 ± 3.00	44.44 ± 3.86	**- 9.3 %**	0.104
LDL (mg\dL)	53.04 ± 8.60	35.13 ± 8.30	**51.0 %**	**0.001**
HDL\LDL	0.77 ± 0.10	1.34 ± 0.39	**- 42.5 %**	**0.001**
Chol\HDL	2.96 ± 0.17	2.29 ± 0.20	**29.3 %**	**0.001**

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

HDL\LDL → Cardioprotective index, Chol\HDL → Cardiac risk ratio

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Table (12): Effect of propolis 60 mg with cisplatin 4 mg/kg in group E rats on lipid profile.

Lipid profile parameters	Before Mean ± SD	After Mean ± SD	% Improvement rate	P-value*
Cholesterol (mg\dL)	103.33 ± 8.00	169.79 ± 10.20	**- 64.3 %**	**0.001**
TG (mg\dL)	118.84 ± 3.51	149.10 ± 3.65	**- 25.5 %**	**0.001**
HDL (mg\dL)	44.44 ± 3.86	36.64 ± 2.54	**17.6 %**	**0.004**
LDL (mg\dL)	35.13 ± 8.30	103.33 ± 9.19	**- 194.1 %**	**0.001**
HDL\LDL	1.34 ± 0.39	0.35 ± 0.04	**73.9 %**	**0.001**
Chol\HDL	2.29 ± 0.20	4.64 ± 0.28	**- 102.6 %**	**0.001**

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

HDL\LDL → Cardioprotective index, Chol\HDL → Cardiac risk ratio

Table (13): Comparison in lipid profile after 6 weeks in control group.

Lipid profile parameters	Beginning Mean ± SD	After 4 weeks Mean ± SD	% Improvement rate	P-value*
Cholesterol (mg\dL)	103.33 ± 8.00	105.73 ± 9.31	**- 2.3 %**	0.793
TG (mg\dL)	118.84 ± 3.51	121.91 ± 5.37	**- 2.6 %**	0.345
HDL (mg\dL)	44.44 ± 3.86	44.27 ± 3.95	**0.4 %**	0.958
LDL (mg\dL)	35.13 ± 8.30	36.46 ± 9.45	**- 3.8 %**	0.942
HDL\LDL	1.34 ± 0.39	1.29 ± 0.38	**3.7 %**	0.928
Chol\HDL	2.29 ± 0.20	2.39 ± 0.30	**- 4.4 %**	0.875

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

HDL\LDL → Cardioprotective index, Chol\HDL → Cardiac risk ratio

Table (14): Comparison in lipid profile among the six groups after 6 weeks of intervention.

Items	Groups						P-value*
	A Mean ± SD	B Mean ± SD	C Mean ± SD	D Mean ± SD	E Mean ± SD	Control Mean ± SD	
Cholesterol (mg\dL)	191.97 ± 11.02 ^{A}	103.33 ± 8.00 ^{C}	172.53 ± 9.14 ^{B}	103.33 ± 8.00 ^{C}	169.79 ± 10.20 ^{B}	105.73 ± 9.31 ^{C}	**0.000**
TG (mg\dL)	149.93 ± 2.17 ^{A}	118.84 ± 3.51 ^{B}	147.11 ± 7.41 ^{A}	118.84 ± 3.51 ^{B}	149.10 ± 3.65 ^{A}	121.91 ± 5.37 ^{B}	**0.000**
HDL (mg\dL)	36.33 ± 2.61 ^{B}	44.44 ± 3.86 ^{A}	37.94 ± 2.63 ^{B}	44.44 ± 3.86 ^{A}	36.64 ± 2.54 ^{B}	44.27 ± 3.95 ^{A}	**0.000**

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LDL (mg\dL)	124.43 ± 9.13 A	35.13 ± 8.30 C	105.08 ± 7.65 B	35.13 ± 8.30 C	103.33 ± 9.19 B	36.46 ± 9.45 C	**0.000**
HDL\LDL	0.29 ± 0.03 B	1.34 ± 0.39 A	0.36 ± 0.03 B	1.34 ± 0.39 A	0.35 ± 0.04 B	1.29 ± 0.38 A	**0.000**
Chol\HDL	5.22 ± 0.473 A	2.29 ± 0.20 C	4.55 ± 0.30 B	2.29 ± 0.20 C	4.64 ± 0.28 B	2.39 ± 0.30 C	**0.000**

*** Mann-Whitney test was used. % Improvement rate = [(before – after) / Before] × 100.**

HDL\LDL → Cardioprotective index, Chol\HDL → Cardiac risk ratio

REFERENCES

1.Lirdi LC, Stupp T, Sasso-Cerri E, Miraglia SM. Amifostine protective effect on cisplatin-treated rat testis. The Anat Rec. 2008;291:797-808.
2. Ogbe RJ, Agbese SP, Abu AH. Protect effect of aqueous extract of Lophira Lanceolata leaf against cisplatin-induced hepatorenal injuries and dyslipidemia in wistar rats. Clinical Phytoscience.2020;6:1-11.
3.Niroumand S, Khajedaluee M, Khadem-Rezaiyan M, Abrishami M, Juya M et al.Atherogenic index of plasma (AIP): A marker of cardiovascular disease .Med J Islam Repub Iran.2015;29:240.
4.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 cardiovascular diseases in patients with type 1 diabetes. New England Journal of Medicine. 2005;353(25):2643-53.
5. Komdeur R, Derksen J, Legdeur MC, Hylkema BS. Cisplatin induces hyperglycemia and hyperosmolar coma. J Med.2007;65(1):37-37.
6. Daleprane JB, Abdalla DS . Emerging roles of propolis: Antioxidant, cardioprotective and antiangiogenic actions. Evidence-Based Complementary and Alternative Medicine.2013;2013: 2-8.
7. Albokhadaim I. Influence of dietary supplementation of propolis on hematology, biochemistry and lipid profile of rats fed high cholesterol diet. J Adv Vet Anim Res. 2015;2(1):56-63.
8. Khalaf DA, Thanoon IAJ. Effects of bee propolis on blood pressure record and certain biochemical parameters in healthy volunteers.Ann Coll Med Mosul;2018;40(1):20-26.
9. 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;51:147-152.
10. OrŠolic N, Jurcevic IL, Dikic D, Rogic D, Odeh D, Balta V et al. Effect of propolis on diet induced hyperlidemia and atherogenic indices in mice .Antioxidents.2019;8(156):1-22.
11. El-Naggar SAA, Elm-Eldeen A, Germoush M, El-Boray K, El-gebaly HA. Ameliorative effect of propolis against cyclophosphamide-induced toxicity in mice. Pharmaceutical Biol.2015;53(2):235-41.

12. OrŠolic N, Sirovina D, Končic MZ, Lackovic G, Gregorovic G. Effect of Croatian propolis on diabetic nephropathy and liver toxicity in mice. BMC Complementary and Alternative Medicine.2012;12:117.
13. Rivera- Yanez N, Rodriguez-Canales M, Nieta-Yanez O, Jimenez-Estrada M, Ibarra-Barajas M, Canales-Martinez MM et al. Hypoglyemic and antioxidant effects of propolis of Chihuahua in a model of experimental diabetes. Evidence-Based Complementary and Alternative Medicine.2018; article ID 4360356
14. 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.
15. 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.
16. Ahmad RA, AL-Jawary AH. Effect of vitamin C on the hepatotoxicity induced by cisplatin in rats. Raf J Sci.2012;23(2):23-33.
17. Mir M, Arab MR, Shahraki MR, Mashhadi MA, Salar MS, Aval FS et al. Toxic effects of cisplatin on hepatocytes and liver enzymes of rats. Anatomical Sciences.2015;12(4):171-175.
18. Atawodi SE, Yakubu OL, Liman ML, Iliemene DU. Effect of methanolic extract of tetrapleura tetraptera (Schum and Thonn) Taub leaves on hyperglycemia and indices of diabetic complications in alloxan-induced diabetic rats. Ascian Pac J Trop Biomed. 2014;4(4):272-278.
19. Akindele JA, Iyamu AE, Dutt P, Satti KN, Adeyeui OO. Ameliorative effect of hydroethanolic leaf extract of Byrsocarpus Coccineus in alcohol and sucrose-induced hypertension in rats. J Tradit Complement Med. 2014;4(3):177-188.
20. .Nwagha UI, Ikekpeazu EJ, Ejezie FE, Neboh EE, Maduka IC. Atherogenic index of plasma as a useful predictor of cardiovascular risk among postmenopausal women in Enugu .Nigeria. Afr Health Sci. 2010;10(3):248-252.
21. Eman SM. Antioxidant effect of aqueous extract of propolis on hepatotoxicity induced by octylphenol in male rats. Acta Toxicol Argent. 2012;20(2):68-81.
22. Salehi-Sahlabadi A, Chhabra M, Rahmani J, Momeni A, Karam G, Nattagh-Eshtirani E et al. The effects of propolis on anthropometric indices and lipid profile: a systemic review and meta-analysis of randomized controlled trials. Journal of Diabetes and Metabolic Disorders.2020;19:1835-1843.