The Protective Effect of Ginkgo Biloba Leaves on Oxidative Stress in Rats with Induced Liver Toxicity

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Abstract

Ginkgo (*Ginkgo biloba* L.) is one of the most distinctive plants, characterized by excellent resistance to various environmental conditions. It is used as a medicinal plant in both traditional and Western medicine. The aim of the present study was to investigate the effect of dried Ginkgo biloba leaves on oxidative stress as well as on liver functions of rats with induced liver toxicity. Thirty adult male albino rats (Sprague-Dawley strain), weighing about 180 ± 10 g,were divided randomly into two main groups as follows: the first group (negative control= 5 rats) was fed on basal diet. The second group (25 rats) was fed a basal diet then these rats were classified as the positive control group fed on basal diet only, however the other rats were fed on basal diet supplemented with dried ginkgo biloba at levels of 2.5%, 5% ,7.5% and 10% , respectively. After four weeks from the start of the experiment, the second groups from 2 to 5 were injected intraperitoneally with CCl_4 1mL/kg BW, a (1:1) mixture with corn oil for 3 days to induce liver toxicity. The existing study illustrated that Ginkgo biloba leaves at the four tested levels could significantly improve ($P<0.05$) the liver functions and lipid profile, increasing the activity of antioxidant enzymes and lowering the oxidative stress by eliminating the deleterious toxic effect of CCl_4, especially with the higher levels of Ginkgo biloba. The findings indicated that ginkgo leaves may have a protective effect role on the oxidative stress in rats with induced liver toxicity.

Keywords: Liver Toxicity , Ginkgo Biloba , Ccl4 **,** oxidative stress, Rats, antioxidants .

INTRODUCTION

The liver is not only the largest organ in the body but also the one playing one of the most important roles in human metabolism as it is in charge of transforming toxic substances in the body **(Lorente *et al* ., 2020)** .The liver is a critical organ in the human body. Although it comprises only about 2% of an adult's body weight, approximately 25% of the total cardiac output goes through the liver (**Bashir *et al* ., 2023)** . The liver is anatomically, histologically, and functionally unique **(Juza and Pauli , 2014)**. It processes blood flowing from the gut through its complex lobular architecture, detoxifying and extracting nutrients from the portal venous blood. It is immunologically unique in the number and types of conventional and nonconventional antigen-processing cells which enable the liver to simultaneously tolerize T cells to the innocuous nutrient and commensal bacteria antigen load from the gut while also **(Andersson, 2021).** Oxidative stress is a causative factor in various types of pathologies, such as cancer, diabetes, neurological disease, and liver illness **(Cichoż-Lach, and Michalak, 2014)** . Plants generally secrete secondary metabolites in response to stress. These secondary metabolites are very useful for humankind as they possess a wide range of therapeutic activities. Secondary metabolites produced by plants include alkaloids, flavonoids, terpenoids, and steroids (**Roy *et al* ., 2022)** .Ginkgo biloba is an ancient plant species that is thought to provide a variety of health benefits to living organisms and contains plenty of bioactive components including terpene trilactones, flavonoids, fatty acids, proanthocyanidins, and polysaccharides , making it a chemically diversified plant (**Ma *et al* ., 2016)** . Mature ginkgo trees typically reach a height of 20 to 40 m and a trunk diameter of one to four meters . They form two types of shoots: long shoots with widely spaced leaves and axillary buds, and short shoots with clustered leaves with no internodes or axillary buds. The leaves have long stalks and a characteristic fan-shape with dichotomously branched veins. They are light green in color and turn golden yellow

in the fall. The tree bark is grey in color, smooth in older trees with longitudinal cracks turning the bark color to brown. The flowers are dioecious and grow only on short shoots (**Šamec *et al* ., 2022)** . Recent research has proven that polysaccharides in G. biloba show various biological activities, such as antioxidant, antitumor, antiinflammatory, hepatoprotective, antidepressant properties, and so on (**Fang *et al* ., 2020)** . CCl4 is a well-known hepatotoxin and has been widely used in inducing acute and chronic liver failure (**Ghasemi *et al* ., 2014) .**

This study was carried out to investigate the protective effect of dried Ginkgo biloba leaves on oxidative stress as well as on liver functions of rats with induced liver toxicity.

MATERIALS AND METHODS

Materials: Dried whole leaves of ginkgo biloba were purchased from the herbalist shops in Cairo, Egypt and was identification at the Agriculture Research Center, Cairo, Egypt. Also, carbon tetrachloride (CCl_4) , chemical kits . Casein, cellulose, sucrose, choline chloride, D-L methionine, vitamins and minerals constituents were purchased from ElGomhoriya Pharmaceutical Company, Cairo, Egypt. Thirty adult male albino rats (Sprague-Dawley strain), weighing about 180±10 g, were obtained from the Animal House of the National Research Center, Dokki, Egypt.

Methods

Preparation of Ginkgo biloba leaves: Dried whole leaves of Ginkgo biloba were cleaned from dust and all invalid parts were removed. Then a grinder mill and sieves were used to obtain a powder particle of less than 0.4mm of all plant parts**.**

Induction of Liver Toxicity in Rats: After the four weeks from the start of the experiment, subgroups from 1 to 5 will be intraperitoneally injected with CCl_4 1mL/kg BW, a (1:1) mixture

with corn oil for 3 days to induce liver toxicity **(karthikeyan and Deepa, 2010)** .

Diet Composition and Experimental Animal Design: The basal diet was formulated according the AIN-93M diet **(Reeves *et al.*, 1993)**. Animals (30 rats) were housed in well conditions in the biological studies lab of Faculty of Home Economics. They were left for seven days as an adaptation period, and they were allowed to feed on standard laboratory food and water. After the period of adaptation, animals were divided into two main groups, as follows: the first group (5 rats) was fed on basal diet and served as a negative control group (-ve), the second group (25 rats) was divided as follows: subgroup **(1)** positive control group was fed on basal diet only. Subgroups (from 2 to 5) were fed on basal diet and supplemented with 2.5, 5, 7.5 and 10% of dried ginkgo biloba, respectively.

After four weeks from the start of the experiment, the second groups from 2 to 5 were injected intraperitoneally with CCl_4 1mL/kg BW, (1:1) mixture with corn oil for 3 days to induce liver toxicity.

At the end of the experimental period (4 weeks), rats were fasted overnight before scarifying and blood samples were collected from each rat and were centrifuged at 3000 rpm for 15 min to obtain the serum for biochemical analysis.

Biological Evaluation: Feed intake (FI), body weight gain percent (BWG%) and feed efficiency ratio (FER) were determined according to **Chapman *et al.*, (1959)** using the following equation:

Biochemical Analysis of Serum: Aspartate aminotransaminase (AST) and Alanine aminotransaminases (ALT) were determined according to the method described by **Young, (2001)**, and Alkaline phosphates (ALP) was determined according to **Roy, (1970)**. Total bilirubin, malondialdehyde (MDA) and glutathione peroxidase (GPx) were determined according to **Young, (2001)**; **Draper and Hadley, (1990)** and **Hissin and Hilf, (1970)**, respectively. Serum

total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) were determined according to **Richmond, (1973)**; **Wahlefeld, (1974)** and **Albers *et al.*, (1983)**, respectively. Regarding serum low density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) were calculated according to **Fridewald *et al.*, (1972)**.

Statistical analysis: All data obtained results were analyzed using Statistical Package for the Social Sciences (SPSS) for Windows, version 20 (SPSS Inc., Chicago, IL, USA). The Analysis of Variance (ANOVA) test was used for determining the significances among different groups according to **(Armitage and Berry, 1987)**. All differences were considered significant if P-values were ($P< 0.05$).

RESULTS AND DISCUSSION

Results recorded in Table (1) showed that the final body weight (FBW) of the positive control group had a significant ($p<0.05$) decrease in FBW as compared to the negative control group.

Regarding to (BWG), the obtained results showed that the positive control group had a significant ($p< 0.05$) decrease in BWG as compared to the negative control group, while supplemented groups with ginkgo biloba leaf powder had a significant ($p< 0.05$) increase in BGW as compared to the positive control.

Concerning (FI), the results obtained showed that the positive control group had a significant decrease ($P< 0.05$) compared to the negative control group

The results obtained showed that the positive control group had a significant ($p< 0.05$) decrease in (FER) as compared to the negative control group In contrast, feeding rats on GBLP caused

significant ($p< 0.05$) increase in FER as compared to the positive control group.

The highest improvements for (IBW, FBW, FI, BGW and FER) were observed at the group that fed on 10% of Ginkgo biloba leaf powder .

The obtained results showed that the positive control group had a significant ($p< 0.05$) decrease in liver weight (LW) as compared to the negative control group, while liver weight increased in groups treated with ginkgo biloba powde

Table (1): The effect of supplemented diet with ginkgo biloba leaves powder on body weight status and relative liver weight in rats with liver toxicity.

Parameters Groups	IBW G	FBW G	FI g/d/rat	BWG G	BWG %	FER	Liver Weight G
Control (-Ve)	185.40±1.72a	239.20±1.88a	**16**	53.80±0.58a	29.02±0.93a	0.080±0.001a	7.23±0.26a
Control (+Ve)	185.80±1.49a	200.60±1.92d	**10**	14.80±0.11e	7.98±0.65e	0.035±0.002d	3.28±0.07d
2.5% GBLP	187.40±1.01a	205.20±1.35cd	**11**	17.80±0.37de	9.49±0.16de	0.038±0.001d	4.83±0.24c
5% GBLP	186.20±1.11a	208.00±1.73cd	**12**	21.80±0.86d	11.70±0.43d	0.043±0.001cd	5.57±0.44bc
7.5% GBLP	185.20±1.18a	212.40±2.01c	**12.5**	27.20±0.97c	14.67±0.51c	0.051±0.001bc	6.27±0.11ab
10% GBLP	186.20±1.86a	221.00±1.04b	**14**	34.81±0.96b	18.96±0.55b	0.059±0.001b	6.84±0.13a

Results are expressed as means ± SD;

values at same column sharing the same superscript letters are not significantly different ($P< 0.05$)

Kim and Go, (2024) showed that some compounds which found in Ginkgo biloba have a promising impact on lipid metabolism, suggesting their significance in addressing obesity-related metabolic disorders. G. biloba seeds contain high levels of vitamin C, carbohy-

drates, riboflavin, proteins, and various other nutrients (**Youdim and Joseph ., 2001).**

Our results showed that the positive control group had a significant decrease in FER, FI, FBW, BWG, BWG% and Liver weight as compared to the negative control group. These findings were consistent **with Chang *et al.* ., (2007).**

The dried leaves of Ginkgo biloba, contain flavonoids, terpene lactones, polyphenols, polysaccharides, and other compositions with a variety of biological functions, such as improving growth performance, nutrient digestibility, and antioxidant activities of animals **(Van and Montoro, 2009).**

Results illustrated in Table (2) liver enzymes were significantly ($P< 0.05$) elevated by CCl_4 injection of the positive control group as compared with the negative control group. Whilst treating rats with (2.5%, 5% , 7.5% and 10%) of GBLP caused significant ($P<0.05$) reductions in the serum of AST, ALT and ALP and total bilirubin levels, compared to untreated liver toxicity rats. However, there are no changes in serum ALT, ALP, or total bilirubin between the groups fed on 2.5 and 5% of Ginkgo biloba leaf powder.. Also, there are no changes in serum ALT, or total bilirubin between the groups fed on 5 and 7.5% of Ginkgo biloba Leaf Powder. The highest improvement in liver functions was observed by the group that fed on 10% of GBLP. There were significant differences for serum AST among the treated rats.

Table (2): The Effect of Supplemented Diet with Ginkgo biloba leaves Powder on Serum Liver Function Enzymes in Rats with Liver Toxicity.

Parameters / Groups	AST μ /L	ALT μ /L	ALP mg/dL	Total Bilirubin mg/dL
Control (-Ve)	21.22±0.16 ^{f}	35.33±0.43 ^{e}	105.28±1.48 ^{e}	0.51±0.06 ^{b}
Control (+Ve)	47.78±0.20 ^{a}	75.43±0.55 ^{a}	169.18±1.25 ^{a}	0.97±0.01^{a}
2.5% GBLP	41.38±0.42 ^{b}	71.63±0.34 ^{b}	165.19±1.92^{ab}	0.85±0.08 ^{ab}
5% GBLP	38.38±0.31 ^{c}	69.31±0.50 ^{bc}	162.98±1.89 ^{b}	0.80±0.06 ^{ab}
7.5% GBLP	34.98±0.24 ^{d}	67.31±0.54 ^{c}	153.79±1.38 ^{c}	0.73±0.09 ^{ab}
10% GBLP	30.78±0.40 ^{e}	63.93±0.57 ^{d}	146.18±1.31^{d}	0.62±0.05 ^{b}

*****Results are expressed as means ± SD;

* Values at same column sharing the same; superscript letters are not significantly different (P< 0.05).

The obtained results are in the same line with **Arab-Nozari *et al* ., (2020)** who demonstrated that G.B treatment led to decreasing the serum levels of ALP, AST and ALT enzymes, which can represent the ameliorative effects of this extract against liver structure damage. **Abdul-Hamid et al ., (2018)** demonstrated that supplementing with grape seed or Ginkgo biloba significantly reduced blood ALT and AST levels after 8 weeks, demonstrating an improvement in enzyme function. The variations in the liver enzymes' activity were improved by ginkgo biloba. The results by **Yang *et al* ., (2011)** indicated that Ginkgo Biloba Powder was able to suppress the hepatotoxicity of CCl4 and the hepatoprotective effect was comparable to the conventionally reputed essential.

Ginkgo biloba has hepatic protective action on the liver and antioxidant defense properties. The leaf extract of G. biloba consists mainly of terpenoids and glycosides that have antioxidant potency **(Raafat et al., 2013).** The combination of ginkgo biloba and bezafibrate significantly decreased AST, ALP, AST/ALT ratio, albumin/globulin ratio, and IL-6 with significant elevations of catalase, and GSH. The combination group produced

more hepatoprotection. This could be attributed to the additive anti-inflammatory and antioxidant effects of the combination **(Zhwan et al., 2023).**

There was a significant decrease in serum SOD, GPX and CAT of the positive control group as compared to the negative control group as seen in Table (3). There was a significant increase in malondialdehyde level of the positive control group as compared to the negative control group. On the other hand, all groups fed on Ginkgo biloba leaf powder had a significant increase in SOD, GPX and CAT while all groups fed on Ginkgo biloba leaf powder had a significant decrease in malondialdehyde level as compared to the positive control group. There was a significant difference in the level of MDA between the group fed on 2.5% and 5% GBLP, while there were no significant changes in the mean of MAD observed between the groups fed on 7.5 and 10 GBLP. Regarding the antioxidant enzymes, it was seen that feeding rats with basal diet supplemented with 2.5 or 5% of GBLP caused a significant increase in in the level of SOD, GPX as well as between the groups fed on 7.5 and 10%. The highest increase in antioxidant biomarkers and the lowest decrease in the oxidative biomarkers was observed at the group fed on 10% GBLP.

Table (3): The Effect of Supplemented Diet with Ginkgo biloba leaves Powder on antioxidant and oxidative biomarkers Levels in Rats with Liver Toxicity.

Parameters / Groups	MDA ng/mL	SOD U/mL	CAT Pg/mL	GPX U/mL
Control (-Ve)	103.83±0.86^{e}	1.77±0.05^{a}	15.77±0.25^{a}	69.70±0.73^{a}
Control (+Ve)	273.98±0.54^{a}	0.54±0.01^{e}	7.60±0.21^{d}	47.95±0.51^{e}
2.5% GBLP	241.81±0.48^{b}	0.61±0.02^{d}	8.16±0.27^{d}	52.87±0.49^{d}
5% GBLP	224.41±0.60^{c}	0.68±0.01^{c}	9.75±0.19^{c}	56.89±0.93^{c}
7.5% GBLP	212.64±0.47^{d}	0.70±0.04^{c}	10.96±0.46^{c}	59.13±0.22^{c}
10% GBLP	206.19±0.67^{d}	0.97±0.08^{b}	13.04±0.25^{b}	63.24±0.55^{b}

Results are expressed as means ± SD;
values at same column sharing the same; superscript letters are not significantly different ($P< 0.05$).

Pretreatment with Ginkgo biloba leaf as well as silymarin prevented the decrease due to CCl_4 and restored the GSH levels to almost normal. Both Ginkgo biloba leaf and silymarin elevated the SOD levels markedly. The CAT activity of liver homogenate in the CCl_4-treated group was measured to be lower in the normal group. Liver CAT activities in Ginkgo biloba leaves and silymarin were higher than those in the CCl_4 toxicant group. Liver GPX activity in theCCl4 group showed a decline as compared withnormal animals. Ginkgo biloba leaf treatment elevated GPX levels **(Naik and Panda 2007)** .

GbE has been used to improve blood circulation without ill effects for centuries in traditional Chinese medicine. GbE contains two groups of major components: flavonoid glycosides and terpenoids. GbE has the property of inactivating oxoferryl radical species, which are more efficient oxidative agents than classical hydroxyl radicals **(Schindowski et al., 2001).** Ginkgo biloba partly promotes anti-oxidative effects by inducing Keap1-Nrf2signaling (which is the major regulator of the cytoprotective Personal non-commercial use only **(Liu et al., 2007).**

The obtained results agreed with **Khattab , (2012)** observed that the levels of MDA in the rats' liver tissue were substantially higher in the CCl_4-intoxicated group than in the control group, according to the results. However, pretreatment of rats with GbE exhibited improvement in hepatic MDA content, as the value of MDA showed much lower as compared to the CCl4 group. Superoxide dismutase has been reported as one of the most important enzymes in the enzymatic antioxidant defense system. It scavenges superoxide anion to form H_2O_2, hence diminishing the toxic effects caused by this free radical **(Parimoo *et al* ., 2014)**

Administration of G. biloba leaves extract reduced the extent and development of fibrous septa, liver cells change, and biochemical alterations in mice exposed to thioacetamide (TAA).

This study showed that G. biloba leaves extract has a potential activity against TAA-induced liver fibrosis and suggested that the chemical constituents of G. biloba are effective in modulation of oxidative stress induced by TAA (**Al-attar**, **2012)**

The effect of a supplemented diet with ginkgo biloba leaf powder on the lipid of hepatotoxic rats was revealed in Table (4). Serum TC, TG, LDL-C and VLDL-C were significantly increased in the positive control group compared with the negative control group. Results also illustrated that all groups that were supplemented with Ginkgo biloba leaves powder decreased significantly (P< 0.05) in serum TC, TG and VLDL-C and LDL-C levels compared to the positive control group, Regarding serum HDL-C level, results showed a significant (P< 0.05) decrease in serum HDL-C level of the positive control group compared to the negative control group. There was a significant change in serum HDL-C level for all supplemented groups with Ginkgo biloba leaves powder compared to negative control groups. The highest improvement for the lipid profile was observed at the group that fed on 10 % of Ginkgo biloba leaves powder

Results of lipid profile were in the same line as **Tabrizi *et al* ., (2021)** demonstrated that GKB administration has been shown to regulate lipid levels mainly by inhibiting adipogenesis and stimulating lipolysis in animal models. also it is likely that the flavonoids in GKB contribute to this beneficial effect by inhibiting HMG-CoA reductase activity as well as modulating hepatocytes gene expression involved in cholesterol metabolism, **Saadallah *et al* ., (2018)** The use of Ginkgo biloba resulted in significant reduction in cholesterol and triglycerides levels, non-significant reduction in LDL-cholesterol. The level of VLDL, which is proportional to triglycerides was also reduced significantly, **Das *et al* ., (2022)** showed that In vitro studies have shown that G. biloba

seeds can impact the synthesis of apolipoprotein B and LDL receptor, modulating the blood cholesterol level of the liver. In vivo, **Hussein *et al* ., (2017)** reported that GB treatment significantly reduced plasma TG and cholesterol levels while increasing HDL-C levels.

Table (4) : The Effect of Supplemented Diet with Ginkgo biloba leaves Powder on lipid profile of Hepatotoxic Rats .

Parameters / Groups	TC mg/dl	TG mg/dl	HDL mg/dl	LDL mg/dl	VLDL mg/dl
Control (-Ve)	153.20±1.73^{d}	82.85±0.37^{e}	38.54±0.81^{a}	98.09±0.41^{f}	16.57±0.07^{e}
Control (+Ve)	178.21±1.43^{a}	125.46±0.69^{a}	24.32±0.31^{e}	128.80±0.67^{a}	25.09±0.13^{a}
2.5% GBLP	169.33±1.35^{b}	122.38±0.95^{a}	25.93±0.22^{de}	119.36±0.57^{b}	24.47±0.39^{a}
5% GBLP	166.47±1.74^{bc}	114.22±0.52^{b}	27.84±0.54^{cd}	115.78±0.39^{c}	22.84±0.10^{b}
7.5% GBLP	162.88±1.38^{c}	108.60±0.59^{c}	29.23±0.23^{c}	111.92±0.36^{d}	21.72±0.11^{c}
10% GBLP	154.13±1.42^{d}	96.86±0.75^{d}	32.77±0.54^{b}	101.98±0.41^{e}	19.37±0.21^{d}

Results are expressed as means ± SD;
values at same column sharing the same; superscript letters are not significantly different (P< 0.05).

Finally, it was observed that the existing study illustrated that Ginkgo biloba leaves at the four tested levels could significantly improve (P<0.05) the liver functions, lipid profile, increasing the activity of antioxidant enzymes and lowering the oxidative stress by eliminating the deleterious toxic effect of Ccl4, especially with the higher levels of Ginkgo biloba. The findings indicated that ginkgo leaves may have a protective effect role on the oxidative stress in rats with induced liver toxicity.

REFERENCES

Abdul-Hamid, M., Galaly, S. R., Mahmoud, H. and Mostafa, F. (2018). The protective effect of grape seed and Ginkgo biloba against hepatotoxicity induced by the antidysrhythmic drug "amiodarone" in male albino rats. Beni-suef university journal of basic and applied sciences, 7(2), 223-230.

Al-attar A. (2012): Attenuating Effect of Ginkgo biloba Leaves Extract on Liver Fibrosis Induced by Thioacetamide in Mice, Journal of Biomedicine and Biotechnology 2012(2):761450

Albers, N., Benderson V. and Warnick G. (1983): Enzaymatic determination of HDL-c, Selected Methods. Clin. Chem., 10: 91-99.

Andersson, E. (2021): In the zone for liver proliferation. *Science*, *371*(6532), 887-888.

Arab-Nozari, M., Ahangar, N., Mohammadi, E., Lorigooini, Z., Shokrzadeh, M., Amiri, F. and Shaki, F. (2020). Ginkgo biloba attenuated hepatotoxicity induced by combined exposure to cadmium and fluoride via modulating the redox imbalance, Bax/Bcl-2 and NF-kB signaling pathways in male rats. Molecular Biology Reports, 47: 6961-6972.

Armitage, G. and Berry, W. (1987): Statistical methods 7th Ed. Ames., Iowa State University. Press.39-63.

Bancroft, J. and Stevens, A. (1996): Theory and practice of histologicaltechnique, Churchill, Livingston, Eden burgh, London, Melhourne and New York.

Bashir A, Hoilat GJ, Sarwal P, et al. Liver Toxicity (2023): . Liver Toxicity. In StatPearls [Internet]. StatPearls Publishing. Available from:https://www.ncbi.nlm.nih.gov/books/NBK526106/.

Chang, H. F., Lin, Y. H., Chu, C. C., Wu, S. J., Tsai, Y. H., and Chao, J. C. J. (2007). Protective effects of Ginkgo biloba,

Panax ginseng, and Schizandra chinensis extract on liver injury in rats. *The American journal of Chinese medicine*, *35*(06), 995-1009.

Chapman, D., Gastilla R. and Campbell J. (1959): Evaluation of protein in foods: 1- A Method for the determination of protein efficiency ratio. Can. J. Biochem. Phys., 37: 679- 86.

Cichoż-Lach, H. and Michalak, A. (2014): Oxidative stress as a crucial factor in liver diseases. World journal of gastroenterology: WJG, 20(25): 8082.

Das, R., Lami, M. S., Chakraborty, A. J., Mitra, S., Tallei, T. E., Idroes, R. and Emran, T. B. (2022). Ginkgo biloba: A treasure of functional phytochemicals with multimedicinal applications. Evidence-Based Complementary and Alternative Medicine, 2022(1), 8288818.

Draper, H. and M. Hadley (1990): Malondialdehyde determination as index of lipid peroxidation. Methods Enzymol, 186: 421-31.

Fang, J., Wang, Z., Wang, P. and Wang, M. (2020). Extraction, structure and bioactivities of the polysaccharides from Ginkgo biloba: A review. International Journal of Biological Macromolecules, 162:1897-1905.

Fridewald, W., Leve R. and Fredrickson D. (1972): Estimation of the concentration of low density lipoprotein separated by three different methods. Clin.Chem., 18: 499-502.

Ghasemi, M., Azarnia, M., Jamali, M., Mirabolghasemi, G., Nazarian, S., Naghizadeh, M. and Tahamtani, Y. (2014): Protective effects of Ephedra pachyclada extract on mouse models of carbon tetrachloride-induced chronic and acute liver failure. Tissue and Cell, 46(1):78-85.

Hissin, P. and Hilf R. (1970): A fluorometric method for determination of oxidized and reduced glutathione in tissues. Anal Biochem., 74(1): 214-26.

Hussein, A., Assad, H. and Rabeea, I. (2017). Antihyperlipidemic, antioxidant and anti-inflammatory effects of Ginkgo biloba in high cholesterol fed rabbits. Journal of Pharmaceutical Sciences and Research, 9(11): 2163-2167.

Juza, R. and Pauli, E. (2014): Clinical and surgical anatomy of the liver: a review for clinicians. Clinical Anatomy, 27(5):764-769.

Karthikeyan M. and Deepa K. (2010): Hepatoprotective effect of premnacorymbosa (Burm f.) Rottl.andwilld leaves extract on CCl4 induced hepatic damage in Wistar albino rat . Asian Pac. J .trop. Med. 3(1):17-20.

Khattab, H. (2012). Effect of Ginkgo biloba leaves aqueous extract on carbon tetrachloride induced acute hepatotoxicity in rats. The Egyptian Journal of Hospital Medicine, 48(1):483-495.

Kim, H., Kang, S., and Go, G. W. (2024). Exploring the multifaceted role of ginkgolides and bilobalide from Ginkgo biloba in mitigating metabolic disorders. Food Science and Biotechnology, 33(13), 2903-2917.

Liu X., Goldring C., Copple I., Wang H., Wei W., and Kitteringham N. (2007): Extract of Ginkgo biloba induces phase 2 genes through Keap1-Nrf2-ARE signaling pathway. Life sciences. 80(17):1586–91.

Lorente, S., Hautefeuille, M. and Sanchez-Cedillo, A. (2020): The liver, a functionalized vascular structure. Scientific Reports, 10(1):16194.

Ma, G., Xiong, J., Yang, G., Pan, L., Hu, C., Wang, W. and Hu, J. (2016): Biginkgosides A–I, unexpected minor dimeric flavonol diglycosidic truxinate and truxillate esters from Ginkgo biloba leaves and their antineuro- inflammatory and neuroprotective activities. Journal of Natural Products, 79(5):1354-1364.

Naik, S. and Panda, V. (2007). Antioxidant and hepatoprotective effects of Ginkgo biloba phytosomes in carbon

tetrachloride-induced liver injury in rodents. Liver international, 27(3):393-399.

Parimoo, H., Sharma, R., Patil, R., Sharma, O., Kumar, P. and Kumar, N. (2014). Hepatoprotective effect of Ginkgo biloba leaf extract on lantadenes-induced hepatotoxicity in guinea pigs. Toxicon, 81:1-12.

Raafat B., Saleh A., Shafaa M., Khedr M. and Ghafaar A. (2013): Ginkgo biloba and Angelica archangelica bring back an impartial hepatic apoptotic to anti-apoptotic protein ratio after exposure to technetium 99mTc. Toxicology and Industrial Health, 29(1): 14–22.

Reeves, P., Nielsen F. and Fahmy G. (1993): AIN-93.Purified diets for laboratory rodents: Final reports of the American Institute of Nutrition adhoe wriling committee of reformulation of the AIN-76 A Rodent Diet. J. Nutr., 123:1939-51.

Richmond, N. (1973): Colorimetric determination of total cholesterol and high density lipoprotein cholesterol (HDL-c). Clin. Chem., 19: 1350- 1356.

Roy, A., Khan, A., Ahmad, I., Alghamdi, S., Rajab, B., Babalghith, A. and Islam, M.(2022): Flavonoids a bioactive compound from medicinal plants and its therapeutic applications. BioMed Research International, (1): 5445291.

Roy, S. (1970): colorimetric method of serum alkaline phosphatase. Journal of Clinical Chemistry, 16:431-432.

Saadallah, L. M. and Thanon, I. A. (2018). Effect of Ginkgo biloba on lipid profile in hypertensive patients on Valsartan monotherapy. Ann Coll Med Mosul December, 40(2):29-33.

Šamec, D., Karalija, E., Dahija, S. and Hassan, S. T. (2022): Biflavonoids: Important contributions to the health benefits of Ginkgo (Ginkgo biloba L.). Plants, 11(10):1381.

Schindowski K., Leutner S., Kressmann S., Eckert A. and Muller W. (2001): Age-related increase of oxidative stress-induced apoptosis in mice prevention by Ginkgo biloba extract (EGb761). J Neural Transm; 108: 969-978.

Tabrizi, R., Nowrouzi-Sohrabi, P., Hessami, K., Rezaei, S., Jalali, M., Savardashtaki, A. and Safiri, S. (2021). Effects of Ginkgo biloba intake on cardiometabolic parameters in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of clinical trials. Phytotherapy Research, 35(1): 246-255.

van Beek, T. A., and Montoro, P. (2009). Chemical analysis and quality control of Ginkgo biloba leaves, extracts, and phytopharmaceuticals. *Journal of chromatography A*, *1216*(11), 2002-2032.

Wahlefeld, A. (1974): Methods of Enzymatic Analysis. Academic Press, Chapter ,5: 1831-1835.

Yang, L., Wang, C., Ye, J., and Li, H. (2011). Hepatoprotective effects of polyprenols from Ginkgo biloba L. leaves on CCl4-induced hepatotoxicity in rats. Fitoterapia, 82(6):834-840.

Youdim, K. A., and Joseph, J. A. (2001). A possible emerging role of phytochemicals in improving age-related neurological dysfunctions: a multiplicity of effects. *Free Radical Biology and Medicine*, *30*(6), 583-594.

Young, D. (2001): Effect of disease on clinical lab Tests, 4th ed. AACC press.

Zhwan A., Asoo N., Ahmed A., Zheen A. and Tavga A. (2023): Study of the effect of bezafibrate with ginkgo biloba extracts in an animal model of hepatotoxicity induced by doxorubicin. Biochemistry and Biophysics Reports. 36:101582.

التأثير الوقائي لأوراق الجنكة بيلوبا على الإجهاد التأكسدي في الفئران المصابة بتسمم الكبد

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الجنكة (Ginkgo biloba L) هي واحدة من أكثر النباتات تميزاً، وتتميز بمقاومتها الممتازة للظروف البيئية المختلفة. ويستخدم كنبات طبي في كل من الطب التقليدي والغربي. كان الهدف من هذه الدراسة هو التحقق من تأثير أوراق الجنكة بيلوبا المجففة على الإجهاد التأكسدي وكذلك على وظائف الكبد لدى الفئران المصابة بتسمم الكبد المستحث. تم تقسيم ثلاثين من ذكور الفئران البيضاء البالغة (سلالة سبراج-داولي) التي تزن حوالي (١٨٠±١٠ جم) عشوائياً إلى مجموعتين رئيسيتين على النحو التالي: المجموعة الأولى (مجموعة التحكم الإيجابي = ٥ فئران) تم تغذيتها على النظام الغذائي القاعدي. المجموعة الثانية (٢٥ جردًا) تم تغذيتها على النظام الغذائي الأساسي ثم صنفت هذه الجرذان كمجموعة تحكم إيجابي تغذت على النظام الغذائي الأساسي فقط، أما الجرذان الأخرى فقد تم تغذيتها على النظام الغذائي الأساسي المضاف إليه الجنكة بيلوبا المجففة بمستويات (٢,٥، ٥ و ٧,٥٪ و ١٠٪) على التوالي. بعد أربعة أسابيع من بداية التجربة، تم حقن المجموعات الثانية من ٢ إلى ٥ داخل البطن بمزيج من 1 (Ccl4) مل/كجم من وزن الجسم (١:١) مع زيت الذرة لمدة ٣ أيام لإحداث سمية الكبد. وقد أوضحت الدراسة الحالية أن أوراق الجنكة بيلوبا بمستوياتها الأربعة المختبرة يمكن أن تحسن بشكل معنوي ($P<0.05$) من وظائف الكبد، وصور الدهون، وزيادة نشاط الإنزيمات المضادة للأكسدة وخفض الإجهاد التأكسدي عن طريق القضاء على التأثير السام الضار لـ Ccl4 خاصة مع المستويات الأعلى من الجنكة بيلوبا. وقد أشارت النتائج إلى أن أوراق الجنكة بيلوبا لها دور وقائي من الإجهاد التأكسدي في الفئران المصابة بتسمم الكبد المستحث.

الكلمات الرئيسية: سمية الكبد , الجنكة بيلوبا , CCL4 , الاجهاد التأكسدي , مضادات الأكسدة.