Hypolipidemic and antioxidant activity of silymarin in streptozotocin-induced diabetic male rats

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Abstract:

The potency of silymarin in ameliorating the lipid peroxidation and antioxidant status has been evaluated in streptozotocin-induced diabetic rats. After induction of diabetes, by single injection of streptozotocin (60 mg/ kg body weight), ninety six (48 intact and 48 diabetic) mature male rats were assigned to 4 equal groups, treated for three periods (15, 25, and 35 days) by drenching intact and diabetic rats with drinking water (C and D groups) and drenching intact and diabetic rats with 200 mg/kg bw of silymarin suspension (SD and S groups). Body weights has been registered at five days interval. After the last day of each period, 8 males from each group were anaesthetized, sacrificed, and blood samples were obtained for assessment of serum lipid profile (total cholesterol; T-c, triglycerides; TG, high density lipoprotein; HDL-c, low density lipoprotein; LDL-c, and very low density lipoprotein; VLDL-c), liver function test (ALT, AST, and ALP concentrations), and oxidant- antioxidants activity (superoxide dismutase; SOD, catalase; CAT, total glutathione; GSH, glutathione reductase; GSH-r, glutathione transferase; GTH-t, glutathione peroxidase; GSH-px and malondialdehyde; MDA). Body weight showed marked increase in control and silymarin treated male rats compared with diabetic control in all periods of experiment. Serum ALT, AST, ALP, T-c, LDL-c, and VLDL-c concentrations decreased significantly in C, DS, and S groups compared with diabetic control (D group) at the end of each period of the experiment, whereas TG and HDL concentration showed significant increase at the same periods. At the end of each period of the experiment, serum oxidant-antioxidant status revealed significant decrease of serum MDA, SOD, CAT, GSH-t, GSH-r and GSH-px activity, whereas total GSH activity was significantly increased. It can be concluded that 200 mg/kg b.w. of silymarin drenching for 15, 25, and 35 days perform positive role in ameliorating the different complications of oxidative stress produced by diabetes mellitus.

Keywords: Silymarin, diabetes mellitus, hypolipidemic, antioxidants.

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Introduction:

Diabetes mellitus is the most important disease involving the endocrine pancreas. Its major manifestations include disordered metabolism and inappropriate hyperglycemia. Recent studies illustrated that uncontrolled hyperglycemia in rats was associated with oxidative stress (1,2). It is well known that in diabetes oxidative stress has been found to be mainly due to an increased production of oxygen free radicals and a sharp reduction of antioxidant defense system. In addition, there is a relationship between diabetes and impairment of lipid metabolism (3).

A number of plants have been shown a free radical scavenging activity in experimental animals, and one of it is the herb milk thistle (*Silybum marianum*). Silymarin is a flavonoid found in the milk thistle. A standardized extract obtained from the seeds of *S. marianum* was found to contain approximately 70-80% of the silymarin flavonolignans and 20-30 % chemically undefined fraction (4). The main component of the silymarin complex is isosilybin (5%), silychristin (20%) and silydianin (10%) (5). Silymarin and its major isomer silybin are used in the manufacture of therapeutic products administered against liver diseases, jaundice and gallstones (6).

Silymarin is a powerful antioxidant said to protect liver cells (and other cells in the body and brain) from toxins. It promotes liver cell protein synthesis and decreases the oxidation of glutathione (7). Apart from its antioxidant properties and its role in stimulating protein synthesis and cell regeneration (8). The extracts prepared from the roots and seeds have been used for liver disorders of bile duct and spleen (9). It has been demonstrated that the protective effect of silymarin is most likely due to its free- radical scavenging activity (5).

The present study aimed to evaluate the potency of silymarin in ameliorating lipid peroxidation and oxidant-antioxidant status in intact and streptozotocin induced diabetic adult male rats.

Materials and methods:

Experimental animals: Mature male Wistar rats has been used in the experiment. Male rats were allowed one week to acclimate to the animal house environment before beginning of experiment. Animals were fed on the standard chow and drinking water *ad libitum* throughout the experiment. Room temperature was maintained at 22±2 °C., the light-dark cycle was on a 12:12 hr with light on at 06:00 a.m. and off at 06:00 p.m. throughout the experimental period.

Induction of diabetes in rats: Twenty four adult Sprague-Dawley rats weighting 240-251 g (56 days old) were used for inducing diabetes. Streptozotocin (STZ) was used to create

animal models of type I diabetes (10). The animals were injected by STZ (60 mg/ kg b.w., i.p.) dissolved in 1M of sodium citrate buffer (pH 4.5). The rats with plasma glucose ≥ 200 mg/ dL were considered as diabetic rats and used for experiment (11).

Experimental Design: After induction of diabetes (more than 200 mg of glucose /dL of blood), 96 (48 intact and 48 diabetic) mature male rats were randomly assigned to 4 equal groups, treated for three periods (15, 25, and 35 days) as follow: control (24 intact rats; C): daily drenched with 0.5 ml of drinking water, D control (24 STZ-induced diabetic rats): daily drenched with 0.5 ml of drinking water, DS treated (24 STZ-induced diabetic rats): daily drenched with Silymarin (Sigma Aldrich Inc., UK) (200 mg/kg, suspended in 0.5 ml of drinking water), S treated (24 intact rats): daily drenched with Silymarin (200 mg/kg, suspended in 0.5 ml of drinking water.

Body weights have been registered at the beginning of the experiment and five days interval for each period of the experiment. Twenty four hours after the last day of each period (On 15^{th}, 25^{th}, and 35^{th} day) of experiment, 8 males from each group were anaesthetized by intraperitoneal injection of 0.3 ml of ketamin and 0.1 ml of xylazin /200 g bw, sacrificed, and blood samples were obtained from abdominal vein for assessment of serum lipid profile (T-c, TG, HDL-c, LDL-c, and VLDL-c), liver function test (ALT, AST, and ALP concentrations), and oxidant- antioxidants activity (SOD, CAT, GSH, GSH-r, GTH-t, and MDA).

Determination of total serum cholesterol: The procedure was described by (12).

Determination of serum triglycerides (TG): The procedure of evaluation of serum triglycerides was described by (13).

Determination of serum HDL-c conc.: The procedure was described by (14).

Determination of serum VLDL-c conc.: VLDL-c concentration was determined by dividing triglycerides values (in mg /dl) on 5 (15).

Determination of serum LDL-c conc.: when TG concentration not exceeds 400 mg/dl, the following formula is only valid (15):

LDL-c conc. (mg/dL) =total cholesterol – Triglycerides/5 + HDL

Assessment of ALT and AST enzymes activity: Assessment has been performed by using the colorimetric method of Reitman and Frankel (16).

Assessment of total GSH: The absorbance of the reduced chromagen was measured at 412 nm and was directly proportional to the GSH conc.(17).

Assessment of superoxide dismutase (SOD) activity in liver subcellular fluid: By using the modified photochemical Nitroblue tetrazolium (NBT) method in utilizing sodium cyanide as peroxidase inhibitor, SOD levels were assessed (18).

Determination of catalase (CAT) activity: According to Aebi (19) and Kakkar *et al*. (20), CAT activity was assessed by measuring the degradation rate of H_2O_2. The rate of disappearance of H_2O_2 was monitored spectrophotometrically at 230 nm.

Estimation of lipid peroxidation: The level of peroxidation product viz. Malondialdehyde (MDA) was measured according to Dillard and Kunnert (21).

Glutathione reductase activity: was measured by the method of Carlberg and Mannervik (22).

Glutathione-transferase activity: was measured by the method of Habig *et al*. (23). Protein was estimated by the method of Lowry *et al.* (24).

Statistical Analysis: All the values are expressed as mean ± SD. Data of the experiment were analyzed using one way analysis of variance (ANOVA 1), using F-test (25). Least significant difference; LSD was carried out to estimate the significance of difference between individual groups. P value less than 0.05 was considered significant.

Results:

Body weight:

Results of body weight (5 days intervals) clarified in figure (1A) revealed significant differences ($P<0.05$) between experimental groups. Diabetic non treated group (D) showed significant decline ($P<0.05$) in its body weight gain starting on the 5^{th} day and continued throughout the following days of the experiment. At the end of 1^{st} stage of experiment (15 d. stage), results showed significant decline in body weight gain of diabetic (D), diabetic silymarin treated (DS), and non diabetic silymarin treated (S) groups when compared with control. At 25^{th} day stage, body weight gain of S group increased to be not significant in comparison with control. Also DS group increased but still significantly ($P<0.05$) lower than control, whereas D group remained significantly lower than other three groups. These changes continued throughout the 35^{th} stage of experiment (figure 1B).

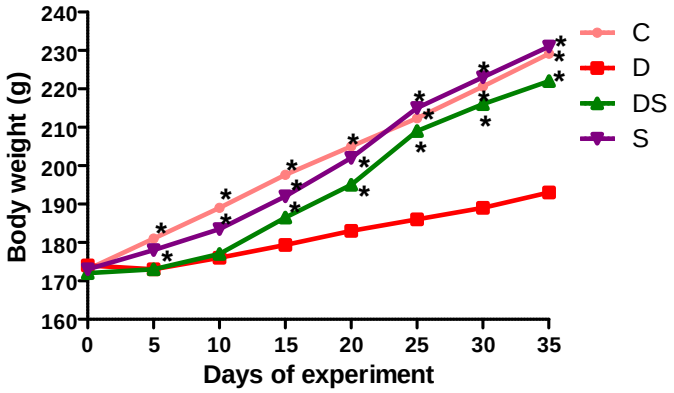

Figure (1A): effect of Silymarin on body weight (g) in Streptozotocin- induced diabetic mature male rats.

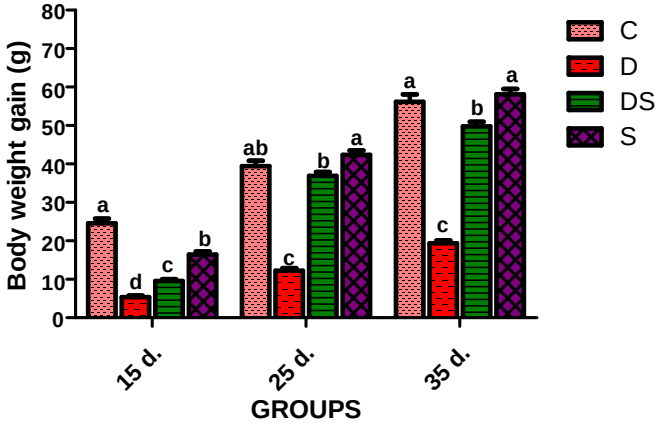

Figure (1B): effect of Silymarin on body weight gain (g) in Streptozotocin- induced diabetic mature male rats.

Numbers represent mean ± standard deviation.
* Significantly higher than control (P<0.05).
Different letters represents significant (P<0.05).
C: Intact rats: drenched with drinking water daily for 15,25,&35 days.
D: Diabetic rats: drenched with drinking water daily for 15,25,&35 days.
DS: Diabetic rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.
S: Intact rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.

Liver function tests:

ALT activity: The results of first stage of experiment (figure 2), revealed significant increase (P>0.05) of ALT activity in diabetic non-treated male rats (D group) compared other three groups. Diabetic silymarin treated (DS group) and intact silymarin treated (S group) male rats registered activities similar to that of control. These differences continued in the second and third stages of the experiment.

AST activity: As shown in the results of ALT, AST activity was significantly higher in D group, whereas that recorded in S group was significantly the lowest among the experimental groups in all of the three stages of experiment (figure 2).

ALP activity: In diabetic non treated rats, serum ALP activity registered the highest level ($P<0.05$) among the experimental groups at the three stages of experiment. At the 1st stage of experiment, diabetic silymarin treated (DS group) rats recorded activity significantly ($P<0.05$) higher than that of control, whereas intact rats treated with silymarin (S group) registered no significant differences ($P>0.05$) compared with control. During 2nd and 3rd stages of experiment, D group remained significantly ($P<0.05$) higher than other groups, which registered no significant differences ($P>0.05$) when compared with each other (figure 2).

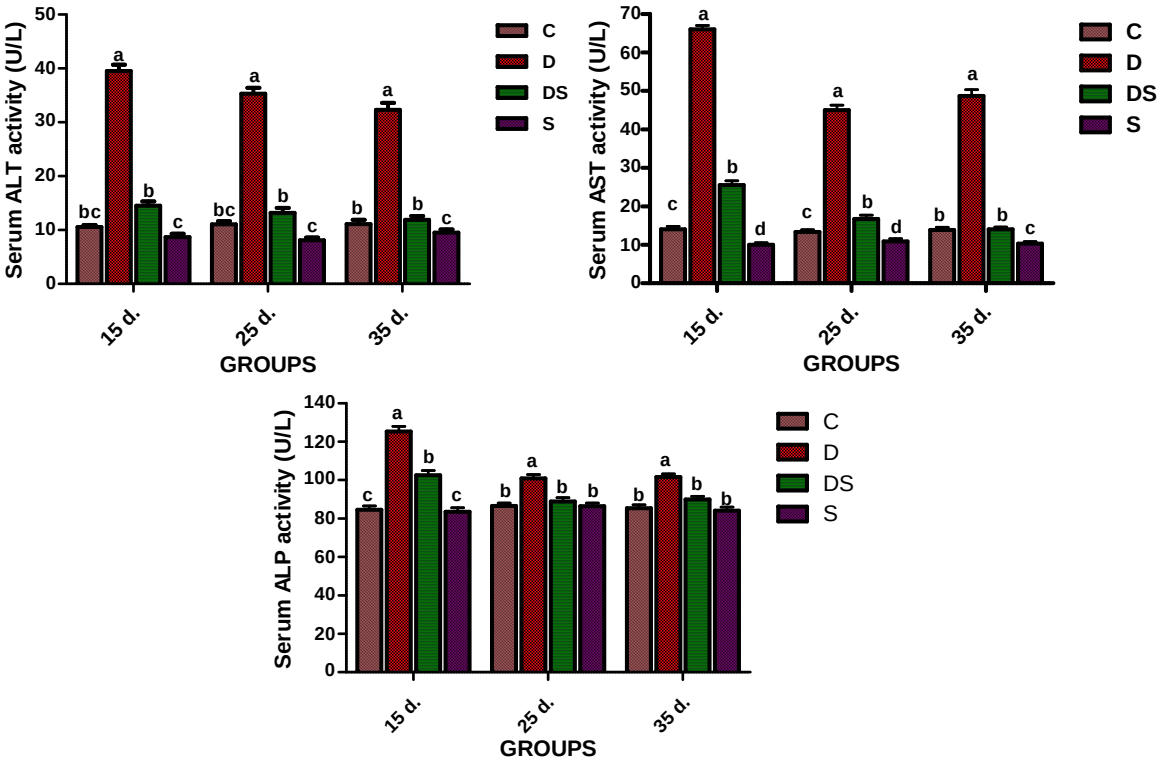

Figure (2): effect of Silymarin on serum ALP, AST, and ALP activity (IU/L) (g) in streptozotocin- induced diabetic mature male rats.

Numbers represent mean ± standard deviation.
Different letters represents significant ($P<0.05$).
C: Intact rats: drenched with drinking water daily for 15,25,&35 days.
D: Diabetic rats: drenched with drinking water daily for 15,25,&35 days.
DS: Diabetic rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.
S: Intact rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.

Serum lipid profile:

Triglycerides: Figure (3) illustrate serum concentrations of triglycerides in experimental groups at the end of each of the three stages of experiment. At the end of all stages, intact

silymarin treated male rats (S group) showed no significant (P>0.05) difference in comparison with control, whereas diabetic non treated (D group) and diabetic silymarin treated male rats revealed significant (P<0.05) decline compared with control.

Total cholesterol: Statistical comparison between treated and control male rats revealed significant decline (P<0.05) of total cholesterol concentration in intact silymarin treated male rats (S group) compared with control and diabetic groups (D and DS groups) in all stages of experiment. Diabetic silymarin treated male rats (DS group) registered significant decline (P<0.05), in all stages of experiment, in comparison with diabetic non treated male rats (D group), but still significantly higher (P<0.05) than that of control in 1st stage, then recorded no significant difference (P<0.05) in 2nd stage, and significant decline (P<0.05) in 3rd stage (figure 3).

High density lipoprotein: High density lipoprotein concentration in intact male rats treated with silymarin (S group) showed significant increase (P<0.05) early in the 1st stage of experiment and continued in increment during 2nd and 3rd stages of experimental period. Diabetic male rats (in D and DS groups) revealed significant decline (P<0.05) in their serum HDL concentrations in comparison with control in all stages of experiment. But male rats of DS group registered concentrations significantly higher (P<0.05) than that of male rats of D group (figure 3).

Low density lipoprotein: Figure (3) illustrate serum low density lipoprotein concentrations of experimental groups in the three stages of experiment. At the end of all stages, intact silymarin treated male rats (S group) showed significant (P>0.05) decline of LDL concentrations in comparison with control, whereas diabetic non treated (D group) and diabetic silymarin treated male rats revealed significant (P<0.05) elevation compared with control. On the other hand, statistical comparison showed significant difference (P<0.05) between D and DS groups.

Very low density lipoprotein: Statistical comparison between treated and control male rats revealed significant decline (P<0.05) of serum very low density lipoprotein concentration in intact silymarin treated male rats (S group) compared with control and diabetic groups (D and DS groups) in all stages of experiment. Diabetic silymarin treated male rats (DS group) registered significant decline (P<0.05), in all stages of experiment, in comparison with diabetic non treated male rats (D group), but still significantly higher (P<0.05) than that of control (figure 3).

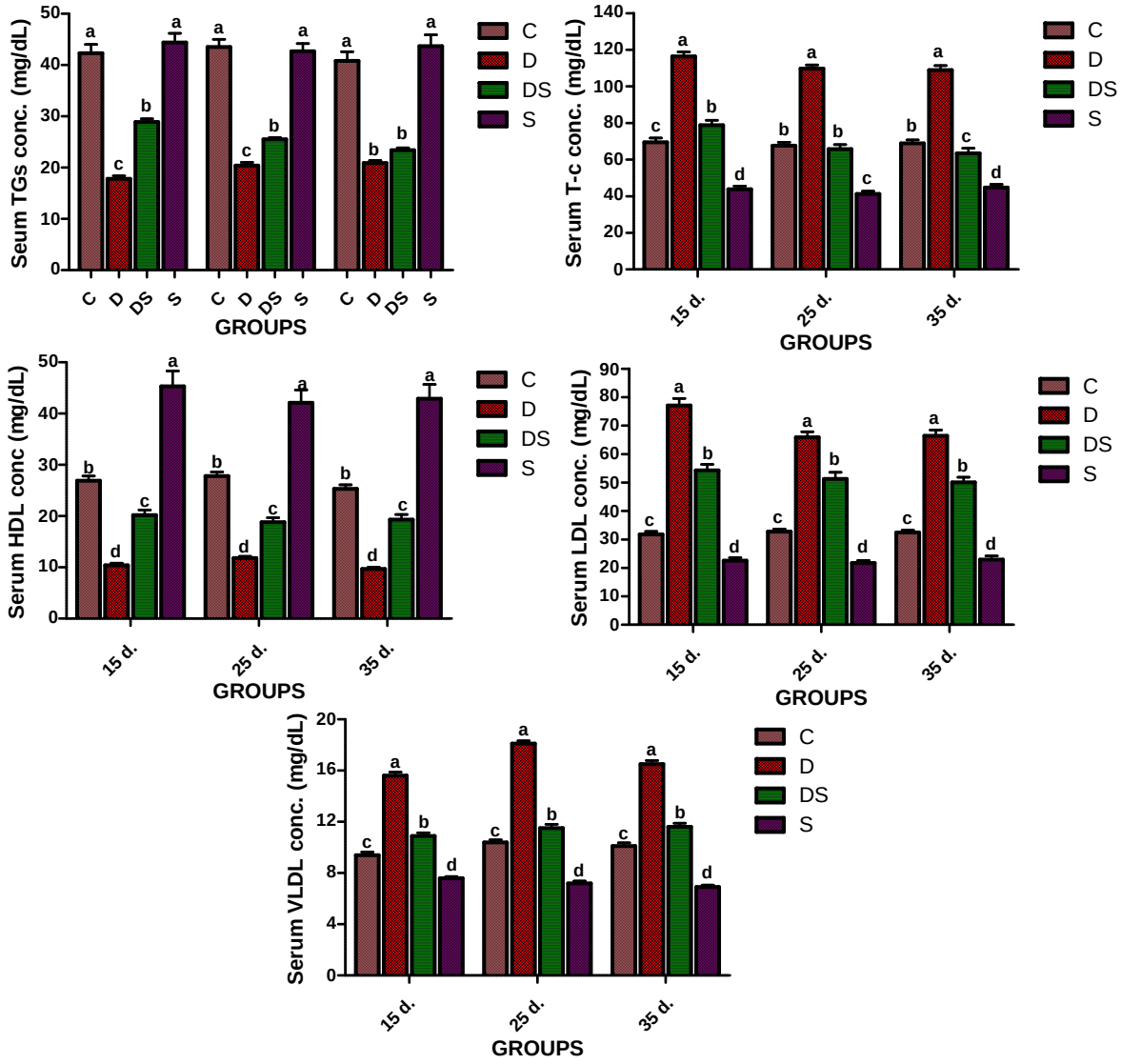

Figure (3): effect of Silymarin on serum TG, total cholesterol, HDL-c, LDL-c, and VLDL-c (mg/dL) in streptozotocin- induced diabetic mature male rats.

Numbers represent mean ± standard deviation.
Different letters represents significant (P<0.05).
C: Intact rats: drenched with drinking water daily for 15,25,&35 days.
D: Diabetic rats: drenched with drinking water daily for 15,25,&35 days.
DS: Diabetic rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.
S: Intact rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.

Serum oxidant – antioxidant status:

Malondialdehyde (MDA): The results clarified in figure (4) revealed significant increase (P<0.05) of serum MDA concentration in non-treated diabetic rats (D group) among the experimental groups in stages of experiment. In spite of the significant decrease (P<0.05) in MDA concentration of silymarin treated diabetic rats (DS group) compared with D group, but still significantly (P<0.05) higher than control and silymarin treated (S group).

Superoxide dismutase: As shown in figure (4), the results revealed significant increase ($P<0.05$) of SOD activity in non-treated (D group) compared with other groups, in all stages of experiment. Silymarin treated diabetic male rats (DS group) was significantly ($P<0.05$) higher than that of control in all stages of experiment, whereas silymarin treated intact male rats (S group) registered insignificant difference ($P>0.05$) in comparison with control.

Catalase: The results revealed significant increase ($P<0.05$) of CAT activity in non-treated (D group) compared with other groups, in all stages of experiment. Silymarin treated diabetic rats (DS group) was significantly ($P<0.05$) higher than that of control in all stages of experiment, whereas silymarin treated intact rats (S group) registered insignificant difference ($P>0.05$) in comparison with control (figure 4).

Glutathion: In comparison with control, statistical comparison revealed significant elevation ($P<0.05$) of serum GSH concentration in silymarin treated intact rats (S group) in 1^{st} and 2^{nd} stages of experiment, whereas, non treated diabetic rats showed significant decline ($P<0.05$) in all stages of experiment. GSH activity in silymarin treated diabetic male rats (DS group) was significantly ($P<0.05$) lower than that of control at the end of 1^{st} and 2^{nd} stages but recorded no significant difference at the end of 3^{rd} stage of experiment (figure 4).

Glutathion transferase: At the end of all stages, intact silymarin treated rats (S group) showed significant ($P>0.05$) decline of GSH-t activity in comparison with control, whereas diabetic non treated (D group) and diabetic silymarin treated rats revealed significant ($P<0.05$) elevation compared with control (figure 4).

Glutathion reductase: The results clarified in figure (4) showed significant increase ($P<0.05$) of serum GSH-r activity in non-treated diabetic rats (D group) among the experimental groups in all of the three stages of experiment. In spite of the significant decrease ($P<0.05$) in GSH-r activity of silymarin treated diabetic rats (DS group) compared with D group, but still significantly ($P<0.05$) higher than control and silymarin treated rats (S group).

Glutathion peroxidase: The results clarified in figure (4) showed significant increase ($P<0.05$) of serum GSH-px activity in non-treated diabetic male rats (D group) among the experimental groups in all of the three stages of experiment. In spite of the significant decrease ($P<0.05$) of GSH-px activity in silymarin treated diabetic male rats (DS group) compared with D group, but still significantly ($P<0.05$) higher than control and silymarin treated groups, in all stages of experiment, whereas silymarin treated group) showed no significant difference ($P>0.05$) compared with control.

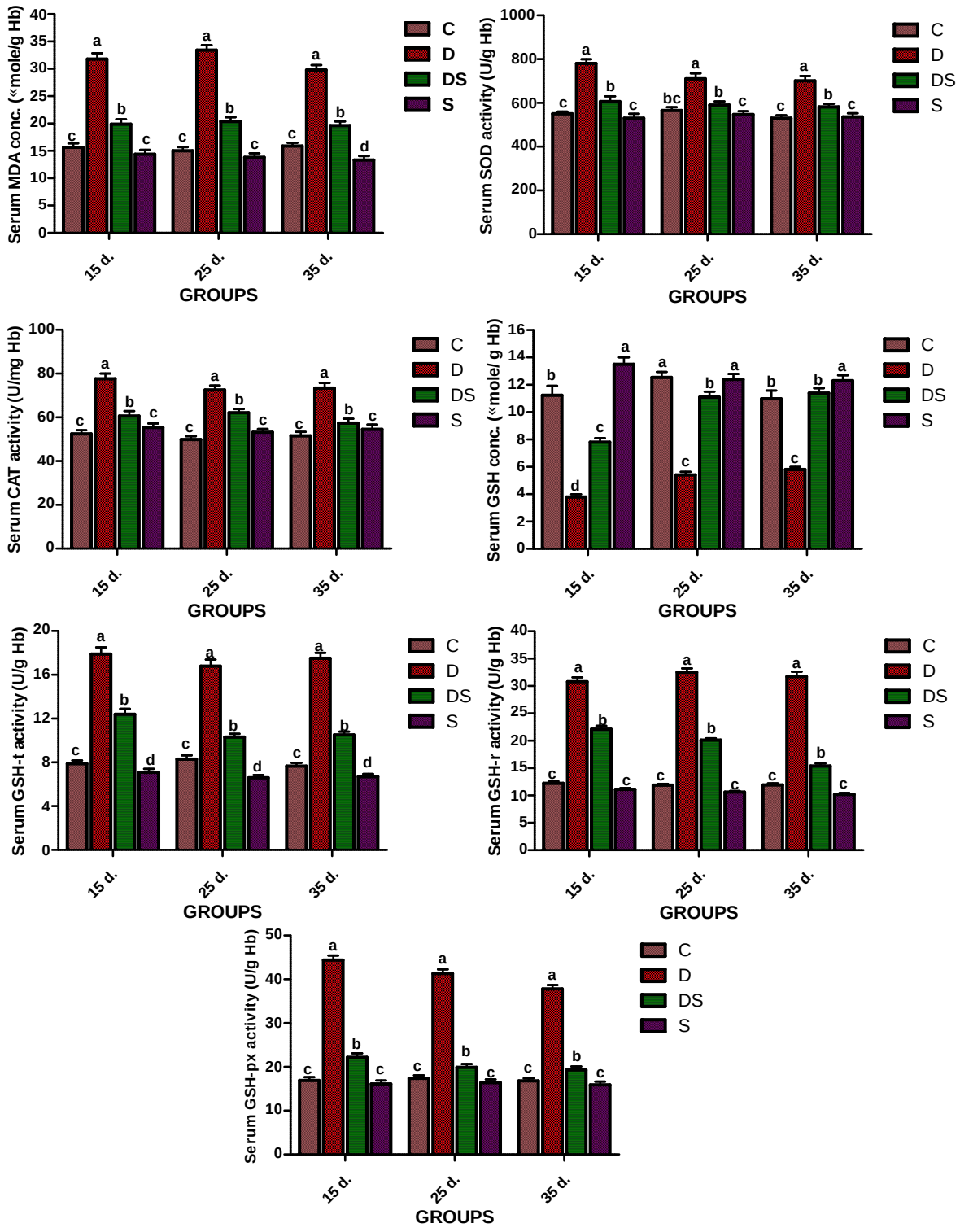

Figure (4-17): effect of Silymarin on serum MDA (µmole/g Hb), SOD (U/g Hb), CAT (U/mg Hb), GSH (µmole/g Hb), GSH-t (U/g Hb), GSH-r (U/g Hb), and GSH-px (U/g Hb) activities in streptozotocin- induced diabetic mature male rats.

Numbers represent mean ± standard deviation.

Different letters represents significant (P<0.05).

C: Intact rats: drenched with drinking water daily for 15,25,&35 days.

D: Diabetic rats: drenched with drinking water daily for 15,25,&35 days.

DS: Diabetic rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.

S: Intact rats: drenched with Silymarin (200 mg/kg, suspended in 500 µl) daily for 15,25,&35 days.

Discussion:

Throughout the three periods of the present experiment, all male rats showed normal activity and body health. This revealed that silymarin drenching at the given dose (200 mg/kg b.w.) and given periods (15, 25, and 35 days) has no harmful effect on body function in normal rats, but instead, has a positive beneficial effect in ameliorating side effects of streptozotocin-induced diabetic male rats. In the present study, we tried to find out how oxidative stress could be reduced with pharmacological intervention. The present results showed that silymarin plays potent role as a pharmacological agent in reducing the complications of oxidative stress accompanied diabetes mellitus, since free radicals are formed disproportionately in diabetes by glucose oxidation, nonenzymatic glycation of proteins, and the subsequent oxidative degradation of glycated proteins. Changes in oxidative stress biomarkers, found in non treated diabetic male rats (group D) included decrement the activity of superoxide dismutase, catalase, glutathione reductase, glutathione peroxidase, glutathione transferase as well as lipid peroxidation indicated by decrement of MDA. As it has been found that antioxidant therapy may be of great value in diabetic patients. However, the classic antioxidants, like vitamins E and C, do not seem to be helpful (26). Using silymarin, in the present study, consider as one of new insights to counteract the mechanisms leading to the generation of oxidative stress in diabetes, as our findings showed significant increase of antioxidant molecules, such as SOD and CAT. So, silymarin may hopefully inhibit the mechanism leading to diabetic complications at an early stage.

In the present study, glucose control did not differ between therapeutic groups, which supports the hypothesis that the effect results from silymarin itself, rather than from a general improvement in metabolic control. The role of silymarin in diabetes may attributed to its antioxidant, anti-glycation and anti- inflammatory properties. It has been evidenced that a significant factor associated with hyperglycemia in diabetics is the resultant nonenzymatic glycation of biological proteins (27), with the irreversible formation of advanced glycation end products (AGEs) (28). Also it has been found that silymarin reduced the production of advanced glycation end products in diabetes (29).

Drenching of rats with silymarin has been caused significant changes in body weight gain between groups throughout the experimental periods. It can be suggested that these difference was time dependant which may attributed to the duration of the treatment, particularly it has been found a significant decrease of body weight in the first period in our experiment, which further increased to reach the insignificant level when we extend the duration of the treatment in comparison with control. The increment of body weight in silymarin treated groups

compared with non treated diabetic group may results from the beneficial effect of silymarin on the metabolic processes, as a result of increased insulin concentration and glucose utilization by body cells. As, it is well known that body mass gain and loss is a complex process involving numerous interactions among the endocrine regulatory systems and other contributing factors such as genetic, nutritional and environmental **(**30). Silymarin can enter into the nucleus and act on RNA polymerase I enzymes and the transcription of rRNA, resulting in increased ribosomal formation. This in turn hastens protein and DNA synthesis, which enhances the biosynthetic apparatus in the cytoplasm, thus leading to an increase in the synthesis rate of both structural and functional proteins. At least conceptually, this stimulation may enable cells to counteract the loss of transporters and enzymes occurring under many pathological conditions. This action has important therapeutic implications in the repair of damaged hepatocytes and restoration of normal functions of liver (31).

Improved liver function leads to improved diabetes control, as the liver is the first and most important tissue involved with insulin utilization. The reduction in lipid peroxidation produced by silymarin can lead to improved metabolic control and a reduced requirement for endogenous insulin. Diabetes causes hepatic damage which is known to have a profound effect on metabolism of lipids and lipoproteins. Moreover, the present results in accumulation of hepatic lipids as well as lipid peroxides which lead to autooxidation of hepatic cells by disrupting the balance between the levels of pro-oxidants and antioxidants (32, 33). Therefore, this leads to oxidative stress in the hepatic cells which is the most striking initial manifestation of diabetes induced liver injury. When there is damage to the liver cell membrane, the cytosolic enzymes are leaked into the blood stream (34). Therefore, the elevation of these cytosolic enzymes in the blood stream is a needful quantitative marker of the extent of hepatic damage. The elevated levels of the ASP, ALT, and ALP indicate the hepatocellular damage and alterations in the membrane permeability. Our results demonstrated that streptozotocin-treated rats revealed significant changes in serum concentrations of ALT, AST, and ALP. While silymarin treated male rats showed significant decrease in the concentrations of these enzymes. On the other hand, the present study revealed that the silymarin at the given dose has no harmful effect on liver function in normal rats. Treatment with silymarin attenuated the elevated levels of ASP, ALT, and ALP. However, liver has a number of mechanisms to keep itself away from the toxic effects of free radicals generated by diabetes.

The present study showed that silymarin had favorably modified serum lipid profile in male rats with significant decreases in total cholesterol, triglycerides, LDL-cholesterol and VLDL-

cholesterol and increased HDL-cholesterol. The lowering of total cholesterol concentration in blood serum may results from the obvious different (inhibitory and stimulatory) effects on many enzymes at the absorption, production and elimination of cholesterol itself or its containing compounds. At the absorption level, the effect of the extract may be on the Acyl-CoA-cholesterol esterase enzyme that responsible for the absorption of cholesterol in the small intestine (35). Or, the effect of silymarin in acceleration of cholesterol elimination by its stimulatory effect on 7-α-hydroxylase which responsible for the conversion of cholesterol into bile acid in the liver (36). On the other hand, the present results can be attributed to the effect of silymarin on cholesterol production through decreasing the activity of β-hydroxy methyl glutaryl-CoA reductase enzyme which responsible for the production of cholesterol in the liver and other body tissues, by converting it into mevalonic acid. This inhibition results in the decrease of the inhibitory effect of cholesterol on protein kinase and the phosphoprotein phosphatase enzymes that responsible for binding of sterol-regulatory element binding protein with the DNA (36).

The obvious significant increase of HDL-cholesterol and significant decrease of LDL-c and VLDL-c levels compared with the baseline values in our study, refers to the positive efficial role of silymarin as hypolipidemic agent. These effects may result from the seed-contained compounds such as monoterpenoids and sequiterpenoids that have hypolipidemic effects (37). As well as its contents of antioxidants such as gamma selenine, 2-methyl propanol, and octa decenamide that responsible for stopping the action of free radicals and prevention the oxidation of linoleic acid (38).

The antioxidant defense system has been studied in the present study, both the enzymatic (SOD and catalase) and non enzymatic (glutathione) antioxidants. The increment of serum glutathione content in the liver of the rats treated with silymarin may be one factor responsible for inhibition of lipid peroxidation. Glutathione, a major non protein thiol involving in many aspects of cellular metabolism and regulation, plays a crucial role in the cellular antioxidant defense system by scavenging free radicals and other reactive oxygen species, removing hydrogen and lipid peroxides and preventing oxidation of bimoleculs (39). Under in vivo conditions, glutathione acts as an antioxidant and its decrease was reported in diabetes mellitus (40). We have observed a significant decrease in glutathione levels in liver during diabetes (D group). The decrease in glutathione levels represent increased utilization due to oxidative stress (41). The depletion of glutathione content of liver may lower the antioxidant activity as glutathione is required as a substrate for this activity (42). The enzymatic antioxidant status was measured in the present study by determination of

superoxide and catalase enzymes in the serum level. It has been shown that SOD and catalase enzymes increased in streptozotocin-induced diabetic male rats. Our results evidenced a parallel increase in both SOD and CAT in streptozotocin-induced diabetic rats in response to oxidative stress. These results were reversed with silymarin treatment to a level comparable to that recorded with control rats. SOD and CAT are the two major scavenging enzymes that remove toxic free radicals. Previous studies have reported that the activity of SOD is low in diabetes mellitus (43). Reduced activities of SOD in serum have been observed during diabetes and this may result in a number of deleterious effects due to the accumulation of free radicals (44). Administration of silymarin increased the activity of this enzyme and may help to control free radical, as silymarin has been reported to be well known antioxidant (45), which scavenge the free radical generated during diabetes.

In conclusion, the present results demonstrated that silymarin showed a protective effect, probably as flavonoids. A hepatoprotective effect of silymarin has been observed in rats treated with paracetamol and thioacetamide (46). Flavonoids can act in the initiation stage of peroxidation interfering with the metabolism oxidative agent either by scavenging the free radicals or by impairing the microsomal enzymatic system needed for this metabolism. Besides, it can scavenge lipoperoxides and their radicals or act as chelating agents for Fe^{+2} ion, interrupting the Fenton reaction.

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فعالية السليمارين الخافضة للدهون والمضادة للأكسدة في ذكور الجرذان المستحدث فيها داء السكري باستخدام الستربتوزوتوسين

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الخلاصة:

تم تقييم فعالية السليمارين في تخفيف أثار الأكسدة الفوقية للدهون والفعالية المضادة للأكسدة في ذكور الجرذان المستحدث فيها داء السكري تجريبياً. بعد استحداث داء السكري، باستخدام حقنة واحدة من الستربتوزوتوسين (60 ملغم/كغم من وزن الجسم)، تم تقسيم 96 جرذا ذكرا (48 سليمة و 48 مصابة بالسكري) على أربع مجموعات متساوية عولجت على ثلاث مراحل (15 و 25 و 35 يوما) بتجريع مجموعة سليمة (C) ومجموعة مصابة (D) ماء الشرب ومجموعة سليمة (SD) ومجموعة مصابة (S) بمعلق السليمارين (60 ملغم/ كغم من وزن الجسم). تم تسجيل وزن الجسم كل 5 أيام. بعد نهاية كل مرحلة من مراحل الدراسة، تم تخدير 8 ذكور من كل مجموعة ، وشرحت وأخذ منها عينات دم لغرض تقدير مستوى الدهون (الكولستيرول الكلي T-c و الكليسيريدات الثلاثية TG و البروتينات الدهنية عالية الكثافة HDLP و البروتينات الدهنية واطئة الكثافة LDLP و البروتينات الدهنية ذات الكثافة الواطئة جدا vLDLP) وفحوصات وظائف الكبد: الانزيم الناقل للألانين (ALT) والانزيم الناقل للأسبارتيت (AST) والفوسفاتيز القاعدي (ALP) ومضادات الأكسدة (Super-oxide dismutase; SOD و Catalase; CAT و Glutathione; GSH و Glutathione reductase; GSH-r و Glutathione transferase; GSH-t و Glutathione peroxidase; GSH-px و Malon-dialdehyde; DA).

أظهرت أوزان الجسم ارتفاعا ملحوظا في مجموعتي السيطرة والمعالجة بالسليمارين مقارنة مع المجموعة المصابة وغير المعالجة في جميع مراحل الدراسة. بينت النتائج انخفاضا معنويا في تركيز كل من ALT و AST و ALP و T-c و LDL-c و VLDL-c في مجموعات C و DS و S بالمقارنة مع مجموعة D في نهاية كل مرحلة من مراحل التجربة، بينما ارتفع معنويا تركيز كل من TG و HDL في نفس المراحل. أظهرت نتائج حالات الأكسدة ومضاداتها في نهاية كل مرحلة من مراحل الدراسة انخفاضا معنويا في فعالية كل من MDA و SOD و CAT و GSH-t و GSH-r و GSH-px بينما ارتفعت معنويا فعالية GSH الكلي. يستنتج من الدراسة الحالية أن تجريع 200 ملغم من السليمارين لكل كغم من وزن الجسم لمدة 15 و 25 و 35 يوما يؤدي فعالية في تلطيف الآثار الجانبية للفعالية التأكسدية المصاحبة لداء السكري.