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Effect of Oral Silymarin on Liver Function, Antioxidants Activity and Blood Lipid Profile of Induced Hepatic Injury Growing Rabbits

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Abstract

OBJECTIVE: This work explored the HPLC method of silymarin in preventing CCl_4 induced hepatotoxicity in New Zealand albino rabbits in an aspect of its anti-inflammatory and lipid-lowering effects.

Methods: Seventy-five NZW male rabbits, aged eight weeks, were randomly assigned into five equal groups. The first group served as the control and did not receive any treatment, while the other four groups were administered a subcutaneous injection of CCl4 (0.5 ml) twice weekly for three weeks. After CCl4 administration, the treated groups were provided with the basal control diet supplemented with silymarin at doses of 25, 50, or 75 mg/kg body weight for six weeks.

Results: Oral silymarin at 50 and 75 mg/kg improved hepato-testicular weights compared to this study's CCl4-induced liver injury group. Among these three doses, the dose of 50 mg/kg enhanced the highest level in total serum proteins such as total protein, albumin, and globulin as well as in thyroid proteins. Additionally, the dose of the extract within the current experiment also exhibited a relatively significant antioxidant impact that enhances liver functions by reducing the content of ALT, AST, and ALP. Also, in the group treated with silymarin at 50 mg/kg, there was a hypocholesterolemic action manifesting reduced serum cholesterol, LDL, and triglyceride while elevated HDL cholesterol compared to other groups.

Conclusion: Dietary silymarin supplementation, particularly at 50 mg/kg, appears to be a promising strategy for improving antioxidant activity, liver function, and blood lipid profile in rabbits experiencing CCl_4-induced hepatic injury. This suggests its potential for alleviating these conditions.

Keywords: Silymarin, hypocholesterolemic, liver function, antioxidant and IL-6.

Introduction

Of late, there has been a keen interest in the literature on inflammation as a complication of liver failure. As for the exact pathways through which CCl_4 causes hepatotoxicity with substantial hepatic toxicity, cirrhosis, and inadequate liver function, the exact mechanisms remain poorly understood, but multiple investigations have proved that exposure to CCl_4 results in cell injury, including hepatocytes [1-6]. Prior research indicates that, while CCl4 is not inherently cytotoxic, it can induce cellular damage by triggering the assembly of the species rich in oxygen. These free radicals originate oxidative stress by producing ROS and in the process cause organ dysfunction [7, 8].

The reactions caused by CCl_4 can be followed by a chain of processes that cause cell damage. Based on free radicals, CCl_4 can catalyze lipid peroxidation

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and hurt both the intracellular and membrane lipids [9]. This can affect normal lipid metabolism and results in over accumulation of lipid droplets of hepatocytes. At the same time, CCl_4 can interfere with protein synthesis which results in members of the protein classes which determine the structure and function of the cell. These combined effects can lead to cell death from steatosis to apoptosis and fatty liver disease [1-3, 10].

The liver usually contains or/eliminates oxidative stress through the antioxidant system pathway [7, 8]. Nonetheless, enhanced production of ROS may upset this equation by suppressing the antioxidant system [7, 8]. At present, further consideration has been given to the use of ecological antioxidants for protecting against toxicities caused by chemicals. Those administered from natural plant sources have been used in the management of numerous clinical conditions. Phenolic components, compounds from plant sources consumed in fruits, vegetables, and grains, have notable therapeutic potential and antitumor effects. Therefore, non-conventional anti-inflammatory plants, such as photogenic plants, have received relatively higher consideration when it comes to realistic sources of several phytochemicals such as *Silybum marianum* [11, 12]. The flavonoid silymarin, extracted from milk thistle (*Silybum marianum*), has demonstrated antioxidant activity [13-15]. It scavenges ROS and prevents lipid peroxidation that shields cells from oxidative damage. Furthermore, silymarin suppresses the formation of TNF-α generated reactive oxygen metabolites and lipid peroxidation in cellular membranes and affects T-cell function [16, 17].

Silymarin was used in treating different forms of liver pathology revealed by progressive tissue damage and non-function [18-20]. It has various pharmacological actions; it inhibits neutrophil migration, reduces the activity of Kupffer cells, decreases the production of leukotriene, and affects prostaglandin synthesis [21-24]. Silymarin can modify membrane lipid composition, particularly cholesterol and phospholipids, which may influence lipoprotein metabolism and reduce hepatic LDL and triglyceride synthesis [25].

Alternatively, this study aims to assess the hepatoprotective impacts of silymarin against CCl4-prompted liver damage in NZW rabbits. The research delved into various aspects of silymarin's potential benefits, including (1) Determining if silymarin can effectively reduce inflammation in the liver, a key factor in CCl_4-induced hepatic injury. (2) Investigating silymarin's ability to defend liver cells from damage and promote liver regeneration. (3) Assessing silymarin's potential to reduce abnormal lipid profiles, comprising total cholesterol, LDL cholesterol, and triglycerides, while increasing beneficial HDL cholesterol. (4) Evaluating silymarin's antioxidant properties and ability to counteract oxidative stress, a major contributor to CCl_4-induced liver damage. (5) Examining the potential impact of silymarin on testicular health and reproductive function, as liver damage can affect overall health and well-being. By exploring these various aspects, the objective of this work is to deliver an inclusive understanding of silymarin's potential therapeutic benefits for liver diseases connected with oxidative stress and inflammation.

Material and Methods

The supplementary file includes the location of the experiments, the support provided, and the ethical guidelines.

Rabbits Management

A total of 75 New Zealand White rabbits, aged 8 weeks, were randomly divided into 5 experimental groups. The rabbits were housed individually in controlled environmental conditions and fed a standard diet. To enrich their environment, cardboard boxes were provided [26]. After the CCl4 exposure (3 weeks), the rabbits were then fed the basal diet supplemented with silymarin at 25, 50, and 75 mg/kg body weight for 6 weeks. Therefore, the total experimental feeding period was 6 weeks, starting after CCl4 exposure. All procedures were conducted in accordance with ethical guidelines [27].

Experimental Design

The experiment employed five groups of rabbits to appraise the defensive effects of silymarin towards liver damage induced by CCl4 [28]. The control group received only the basal diet for the entire twelve-week duration of the study. This diet provided the rabbits with their essential nutrients, detailed in Table 1, and served as a baseline for comparison. The remaining four groups were designed to evaluate the impact of silymarin on liver damage induced by CCl4. Rabbits in these groups received a single subcutaneous injection of CCl_4 (0.5 ml/rabbit) in the neck region twice a week for three weeks. This CCl_4 treatment aimed to induce liver damage in these animals. Following the three weeks of CCl_4 injections, the four treatment groups transitioned to a modified diet. They continued to receive the basal diet as their foundation, but it was now supplemented with varying amounts of silymarin. Group 2 received the basal diet with no added silymarin (0 mg/kg).

Groups 3, 4, and 5 received the basal diet supplemented with silymarin at increasing doses: 25 mg/kg, 50 mg/kg, and 75 mg/kg respectively. This six-week period with silymarin supplementation

allowed researchers to investigate its potential protective impacts against induced liver damage. The silymarin employed in this experiment was commercially obtained from Sigma-Aldrich Co. (Product No: S0292, 98%). By incorporating this detailed structure, the paragraph provides a clearer picture of the experimental design and how the researchers aimed to test silymarin's effectiveness.

Measurements

Following the 8-week feeding trial, five rabbits from each group were randomly selected for slaughter. These rabbits were chosen to represent the average body weight of their respective groups. Before and after complete bleeding, the individual live weights of the rabbits were recorded. Subsequently, the carcasses were skinned and eviscerated. The liver and testes were weighed and articulated as a percentage of the total body weight.

Blood samples collection

Three milliliters of venous blood were gathered from each of the five rabbits in the two different experimental groups and the blood was then separated into two equal fractions. In the primary aliquot, hemoglobin concentrations in the patient were determined using the electrochemical analyzer. The second aliquot was centrifuged to provide serum this serum was stored at -200 ^{o}C and was used for biochemical tests. The samples of blood were also retrieved from all the used rats and the different serum biochemical tests which were also run include total proteins, albumin, cholesterol, triglycerides, LDL, HDL, ALT, AST, ALP, GGT, total bilirubin, IgG, IgM, TAC, CAT, SOD, GPx, MDA, T3, T4 and CRP were determined using commercial kits. Additionally, to estimate inflammation we measured the interferon-γ and interleukin-6 concentrations utilizing ELISA.

Biochemical assay

Liver tissues were collected, homogenized, and analyzed for markers of oxidative stress, including MDA, GPx, and SOD (For detailed protocols, *c.f.* Supplementary file) [29].

Histological Observation

Immediately following slaughter, liver tissue samples were collected and fixed in a 10% formalin-saline solution. The tissues were then processed for histological analysis, which included dehydration, paraffin embedding, sectioning, and staining with hematoxylin and eosin. The stained slides were examined microscopically and photographed [30].

Statistical Analysis

The statistical analyses were performed by one-way ANOVA [31].

Results and Discussion

Body and Organ Weights

Table 2 summarizes the effects of CCl_4 and silymarin supplementation on body weight and the relative weight of the liver and testes. Compared to the control group, rabbits treated with CCl_4 alone (CCl_4 group) experienced significant weight loss ($p \leq 0.0001$). This suggests that CCl_4 exposure negatively impacted their overall growth. Interestingly, rabbits in the silymarin-supplemented groups (25 mg/kg, 50 mg/kg, and 75 mg/kg) were able to maintain their body weight to a superior extent relative to the CCl_4 group.

The treatment with CCl_4 expressively amplified the comparative liver weight relative to other groups ($p \leq 0.0001$), this increase likely reflects liver damage rather than healthy growth. Silymarin supplementation, however, helped to normalize the relative liver weight in these groups (CCl_4 + Silymarin groups). In contrast to the liver, the virtual weight of the testes was considerably lower in the CCl_4 group compared to the control and silymarin-supplemented groups ($p \leq 0.0001$). This suggests a potential negative effect of CCl_4 on testicular development. Notably, silymarin supplementation, particularly at higher doses (50 mg/kg and 75 mg/kg), led to a noteworthy increase in relative testes weight compared to the CCl_4 group ($p \leq 0.0001$) (Table 2).

The significant weight loss observed in the CCl_4 group specifies that CCl_4 exposure negatively impacted overall growth and development. The increased relative liver weight in the CCl_4 group is likely indicative of liver damage caused by CCl_4 toxicity [32]. The decreased relative testes weight in the CCl_4 group recommends that CCl_4 may have adverse impacts on testicular improvement and function. Silymarin supplementation helped to mitigate the negative effects of CCl_4 on body weight, suggesting its potential to protect against CCl_4-induced growth retardation [33]. Silymarin effectively normalized the relative liver weight in the CCl_4-treated groups, indicating its hepatoprotective properties [34]. Silymarin supplementation, particularly at higher doses, significantly increased the comparative testes weight in the CCl_4-treated groups, suggesting its potential to counteract the negative effects of CCl_4 on testicular development. The results recommend that the protective effects of silymarin may be dose-dependent, with higher doses demonstrating more significant benefits. Silymarin is known to have anti-oxidant and anti-inflammatory features [35]. These properties may participate to its protective effects

against CCl_4-induced toxicity. Silymarin can also interact with cellular signaling pathways involved in liver and testicular function, potentially mitigating the negative effects of CCl_4 [36].

Hepatoprotective Effects of Silymarin on CCl_4 Toxicity

As publicized in Table 3, CCl4 treatment noticeably increased the serum levels of ALT, AST, and ALP compared to the control group. However, silymarin supplementation considerably diminished the CCl4-induced increase in these liver enzymes. This indicates liver damage caused by the CCl_4 treatment. Interestingly, even the group receiving the lowest silymarin dose (CCl_4 + 25 mg silymarin) showed significantly higher ALT, AST, and ALP levels in comparison with the control and higher dose silymarin groups (CCl_4 + 50 mg/kg and CCl_4 + 75 mg/kg). Furthermore, CCl_4 treatment caused a substantial reduction in total protein and globulin concentrations compared to other groups. This suggests impaired protein synthesis, potentially due to liver damage.

Silymarin supplementation, particularly at higher doses (50 mg/kg and 75 mg/kg), helped to normalize the elevated levels of ALT, AST, and ALP, suggesting its hepatoprotective effects. Silymarin supplementation also helped to restore total protein levels to near-control values, indicating its potential to mitigate the undesirable impacts of CCl_4 on protein synthesis. CCl_4 is known to induce oxidative stress and liver damage through the formation of ROS [37]. Silymarin, with its antioxidant properties, can help neutralize these ROS, protecting the liver from damage [38]. Silymarin may also have anti-inflammatory activity, which can support diminish the inflammation associated with CCl_4-induced liver injury [39]. Additionally, silymarin has been shown to have hepatoprotective effects through its aptitude to restrain various signaling paths involved in liver function and regeneration [40]. In conclusion, the data presented in Table 3 provide indication for the protective impacts of silymarin against CCl_4-induced liver damage. Silymarin supplementation can help mitigate the negative impacts of CCl_4 on liver enzymes and protein levels, suggesting its impending as a therapeutic agent for liver diseases.

Silymarin Protects Against CCl4-Induced Liver Damage in Rabbits

Interestingly, serum protein, albumin, and globulin levels were significantly elevated in both the control and CCl4+50 mg silymarin groups. This suggests that silymarin supplementation at a dose of 50 mg/kg may mitigate the CCl4-induced decrease in serum protein levels. These findings indicate that chronic liver disease was effectively decreased when treated with silymarin. All levels of dietary silymarin supplementation expressively raised serum levels of thyroid hormones (T3 and T4) and hemoglobin (Hb) in comparison to the control group (Table 4). In disparity, CCl4-induced cirrhosis escorted to a substantial decrease in serum T3, T4, and Hb levels. Silymarin treatment significantly ameliorated the reduction in T3 and T4 levels caused by CCl4, with a more pronounced effect on T3. Furthermore, a positive correlation was observed among serum T3 levels and the severity of liver dysfunction.

Lung fibrosis due to CCl_4 decreased the antioxidant enzymes and also caused the elevations in serum total cholesterol, triglyceride, and LDL cholesterol. These lipid parameters (Table 4) were subsequently well improved by silymarin level, especially with a concentration of 50 mg/kg, thus establishing the lipid-reducing property of Silymarin. Alternatively, the findings specified that silymarin significantly elevated the levels of HDL-cholesterol particularly, in the 50 mg/kg treated group. These observations indicate that silymarin, in the research context examined here, has a positive effect on lipid metabolism, by means not yet known, which could involve the inhibition of lipid synthesis and enhancement of lipid degradation.

Silymarin exerts its hepatoprotective effects by scavenging ROS, including hydroxyl radicals and superoxide anions, thereby preventing lipid peroxidation and oxidative damage to cellular components [41]. Silymarin inhibits the production of pro-inflammatory cytokines and mediators, reducing inflammation and tissue damage [38]. Silymarin verified anti-inflammatory behavior by controlling the pro-inflammatory cytokines production and activating the Nrf2 pathway [42]. Silymarin can activate the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, leading to increased expression of antioxidant genes and reduced oxidative stress [43]. It can also inhibit the activation of the nuclear factor-κB (NF-κB) pathway, which is involved in inflammation and cell death [44]. Silymarin has been shown to promote hepatocyte proliferation and regeneration, aiding in liver repair and recovery [45]. Silymarin may interact with the metabolism of CCl_4, potentially reducing the formation of toxic metabolites [46]. These mechanisms collectively participate to the hepatoprotective effects of silymarin, highlighting its impending as an effective therapeutic agent for liver diseases.

Silymarin Protects Against CCl4-Induced Liver Damage

Table 5 demonstrates that CCl4 treatment significantly increased oxidative stress, as signposted by raised MDA levels and diminished levels of

antioxidant enzymes (TAC, SOD, and GSH-Px) in both serum and liver tissue. Silymarin supplementation, particularly at doses of 50 mg/kg and 75 mg/kg, ominously attenuated CCl4-induced oxidative stress by reducing MDA levels and levitating the activity of antioxidant enzymes.

CCl4 treatment led to an extensive decrease in IgG and IgM levels in comparison with the control group and silymarin-treated groups. However, silymarin supplementation, particularly at a dose of 50 mg, expressively amplified immunoglobulin levels closer to normal values. While the 75 mg silymarin group showed a slight decrease in antioxidant enzyme activity and immunoglobulin levels in comparison with the 50 mg group, both doses effectively mitigated the negative effects of CCl4. TNF-α, a key inflammatory cytokine, plays a significant role in CCl4-induced liver damage. Silymarin treatment suggestively inhibited TNF-α levels, suggesting its potential to alleviate liver injury. Additionally, CCl4 treatment considerably compact serum levels of IL-6, TNF-α, and IFN-γ compared to the control and silymarin groups. Nevertheless, the 50 mg silymarin group exhibited expressively reduce levels of these cytokines in comparison to other silymarin groups (Table 5).

Silymarin can control the immune response by influencing the production of immunoglobulins and inflammatory cytokines [47]. As demonstrated in Table 5, silymarin supplementation can mitigate CCl4-induced oxidative stress, inflammation, and immune dysfunction, emphasizing its prospective as a therapeutic agent for liver diseases.

Our results are reliable with previous studies demonstrating the hepatoprotective impacts of silymarin against liver damage induced by treatment with CCl4. As reported previously [48], Cirsium species extracts exhibited similar protective impacts in a mouse model of CCl4-induced liver injury. Additionally, silymarin's immune-modulatory effects were conveyed in other researches. El Elaimy et al. [49] found that silymarin protected towards chlorpyrifos-induced immunotoxicity in rats. Silymarin's antioxidant properties are well-documented in the literature. A review by Saller et al. [50] highlighted the utility of silymarin in treating liver diseases, emphasizing its antioxidant effects. In brief, the findings of this study support the existing body of evidence on silymarin's hepatoprotective and immunomodulatory properties. These results highlight the impending of silymarin as a therapeutic agent for liver diseases, particularly those associated with oxidative stress and immune dysfunction.

Liver Histology

Fig. 1, shows histological sections of liver tissue from different groups. The control group exhibited normal liver architecture with intact hepatocytes, blood sinusoids, central veins, and Kupffer cells. In contrast, the CCl_4-treated group displayed severe liver damage characterized by hepatocyte necrosis, inflammation, fatty changes, and congestion. Silymarin treatment demonstrated varying degrees of protection against CCl_4-induced liver damage, with reduced hepatocyte necrosis, decreased inflammation, improved fatty changes, and a more normalized liver architecture in the treated groups compared to the CCl_4-only group.

The findings of our work confirm that CCl4 exposure causes substantial liver damage, including necrosis, inflammation, and fatty degeneration. Silymarin treatment significantly alleviated these pathological changes, with a dose-dependent response. The hepatoprotective effects of silymarin are likely ascribed to its antioxidant, anti-inflammatory, and liver regenerative properties.

The histological examination demonstrates the severe damage caused by CCl_4 exposure to the liver, characterized by hepatocyte necrosis, inflammation, fatty changes, and congestion. Silymarin treatment was shown to mitigate these harmful effects, with a dose-dependent response. The protective effects of silymarin are likely attributed to its antioxidant, anti-inflammatory, and hepatoprotective properties, which may help prevent or reduce hepatocyte necrosis, inflammation, and fatty changes. The findings of this study recommend that silymarin could be a favorable therapeutic agent for treating liver diseases caused by oxidative stress and inflammation. Its potential benefits include the prevention of liver damage, promotion of liver regeneration, and reduction of inflammation.

Our findings are consistent with previous research, such as that convoyed by Elmahdy et al. [51], who explored the anti-fibrotic potential of stem cell therapy in CCl4-induced liver fibrosis. While the experimental approach differed, the results underscore the severity of CCl4-induced liver damage and the potential for therapeutic interventions. Karakus et al. [52] examined the protective effects of Panax ginseng towards CCl_4-induced liver damage. Similar to our findings, the study demonstrated the ability of a natural compound to mitigate liver damage affected by CCl_4. Sabry et al. [53] investigated the therapeutic potential of mesenchymal stem cell-derived microvesicles for CCl_4-induced liver fibrosis. While the approach was different, the findings support the notion that stem cell-derived therapies can be beneficial for liver diseases. In brief, the results reported herein are consistent with the accessible literature on the hepatoprotective effects of silymarin and other therapeutic interventions for CCl_4-induced liver damage. These findings underscore the potential of natural compounds and stem cell-based therapies as promising therapeutic strategies for liver diseases.

Conclusion

The current work investigated the hepatoprotective impacts of silymarin towards CCl_4-induced liver damage in rabbits. The results demonstrated that CCl_4 exposure significantly increased liver enzymes, decreased protein levels, and disrupted thyroid hormone levels. Additionally, CCl_4 induced oxidative stress, impaired immune function, and increased inflammatory markers. Silymarin supplementation effectively mitigated the negative effects of CCl_4 on liver enzymes, protein levels, thyroid hormones, oxidative stress, immune function, and inflammatory markers. These findings suggest that silymarin has privileged antioxidant, anti-inflammatory, and immunomodulatory properties. The study highlights the prospective of silymarin as a therapeutic agent for liver diseases caused by CCl_4 exposure or other toxic substances. Further work is warranted to explore the specific mechanisms of action of silymarin, including its effects on various signaling pathways and cellular processes. Additionally, clinical trials are needed to evaluate the efficacy of silymarin in treating specific liver diseases and to better understand its therapeutic potential in human patients.

Author contributions statement

Eman A. El-Said designed and supervised the animal experiments, contributed to data collection, and participated in drafting the manuscript, focusing on animal procedures and results. Khaled M. Elattar conducted biochemical data analysis, prepared figures and tables, drafted relevant sections of the manuscript, and provided critical revisions. Ayman Y. El-Khateeb designed the study, supervised silymarin supplementation, contributed to data analysis, drafted key sections of the manuscript, and provided critical revisions. Sahar E. Hamed conducted histological analysis, prepared images, and contributed to manuscript revisions related to histological observations.

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TABLE 1. Calculated analysis of a basal diet

Calculated analyses (NRC, 1994)	**Growing diet (8-14 weeks)**	**Nutrient**	**Amount (mg) per kg Premix**	**Nutrient**	**Amount (mg) per kg Premix**
Digestible energy (kcal/kg)	2512	Vitamin D3	1,000,000 IU	Vitamin B12	10
Crude protein %	18.02	Vitamin E	10,000	Biotin	50
Crude fiber%	15.30	Vitamin K3	1,000	Folic acid	30,000
Ether extract%	2.87	Vitamin B1	1,000	Choline chloride	50,000
Calcium%	1.30	Vitamin B2	4,000	Iron	30,000
Non-phytate P%	0.71	Vitamin B6	1,500	Manganese	40,000
Lysine%	0.88	Vitamin A	10,000,000 IU	Copper	3,000
Methionine%	0.23	Nicotinic acid	20,000	Iodine	450 mg
Meth. + Cyst.%	0.54	Pantothenic acid	10,000	Zinc (Selenium)	45,000 (100)

TABLE 2. Effect of dietary supplementation of silymarin on live body weight, relative weight of liver and testes of growing rabbits.

Treatments	***Items***		
	LBW (g)	**Liver %**	**Testes %**
Control	2250^{a}	2.320^{c}	0.451^{a}
CCl_4	1250^{b}	3.788^{a}	0.172^{d}
CCl_4+ Sily. 25 mg/kg	2111^{a}	3.018^{b}	0.345^{c}
CCl_4+ Sily. 50 mg/kg	2130^{a}	2.882^{b}	0.409^{ab}
CCl_4+ Sily. 75 mg/kg	2106^{a}	2.922^{b}	0.395^{bc}
SEM	58.82	0.082	0.018
p-value	<.0001	<.0001	<.0001
LSD 0.05	173.53	0.243	0.052

^{a,b,c} Indicate statistically significant differences ($p \leq 0.05$).

TABLE 3. Effect of dietary supplementation of silymarin on serum liver enzymes activity and protein of growing rabbits.

Items	Control	*CCl_4*	*CCl_4+ Sily. 25 mg/kg*	*CCl_4+ Sily. 50 mg/kg*	*CCl_4+ Sily. 75 mg/kg*	SEM	*p*-value	*LSD 0.05*
ALT(IU/L)	23.08^{c}	82.11^{a}	49.16^{b}	23.48^{c}	24.38^{c}	1.149	<.0001	3.389
AST(IU/L)	42.78^{c}	111.45^{a}	59.63^{b}	45.21^{c}	45.60^{c}	1.427	0.0022	4.211
ALP (U/10ml)	10.36^{c}	38.16^{a}	13.03^{b}	11.67^{bc}	11.94^{bc}	0.549	<.0001	1.618
γ-GT (U/L)	7.18^{d}	25.86^{a}	18.70^{b}	10.88^{c}	12.92^{c}	1.263	0.002	2.425
T.Bili (mg/dl)	0.309^{c}	0.688^{a}	0.490^{b}	0.362^{bc}	0.428^{bc}	0.031	0.001	0.1378
TP (mg/dl)	6.27^{a}	3.97^{d}	5.07^{c}	6.13^{ab}	5.96^{b}	0.084	0.0209	0.249
Alb(mg/dl).	3.21^{a}	2.45^{c}	3.06^{b}	3.17^{ab}	3.25^{a}	0.049	0.699	0.146
Glob(mg/dl).	3.07^{a}	1.51^{d}	2.01^{c}	2.96^{a}	2.71^{b}	0.040	<.0001	0.119
A/ G ratio	1.05^{c}	1.61^{a}	1.52^{ab}	1.07^{c}	1.20^{b}	0.016	<.0001	0.046

[a,b,c] Values within the same row differ significantly ($p < 0.05$).

TABLE 4. Effect of dietary supplementation of silymarin on serum thyroid hormones, hemoglobin and lipids profile of growing rabbits.

Items	Control	*CCl_4*	*CCl_4+ Sily. 25 mg/kg*	*CCl_4+ Sily. 50 mg/kg*	*CCl_4+ Sily. 75 mg/kg*	SEM	*LSD 0.05*	*p*-value
T4(ng/ml)	19.66^{a}	13.50^{c}	17.55^{b}	19.26^{ab}	18.64^{ab}	0.600	1.769	0.0022
T3(ng/ml)	5.26^{a}	2.30^{d}	3.81^{c}	4.86^{b}	3.87^{c}	0.111	0.326	0.0001
Hb	13.16^{c}	18.20^{a}	15.28^{b}	13.14^{c}	12.52^{c}	0.284	0.839	0.0001
Chol. (mg/dl)	87.40^{d}	174.92^{a}	129.72^{b}	89.50^{d}	108.16^{c}	1.411	4.164	0.0001
TG. (mg/dl)	77.41^{d}	129.92^{a}	109.72^{b}	76.50^{d}	90.16^{c}	1.404	4.143	<.0001
HDL (mg/dl)	28.96^{a}	12.11^{d}	18.44^{c}	29.10^{a}	21.12^{b}	0.550	1.623	<.0001
LDL (mg/dl)	42.96^{d}	136.82^{a}	89.34^{b}	45.10^{d}	69.01^{c}	1.429	4.216	<.0001

[a,b,c] Values within the same row differ significantly ($p < 0.05$).

TABLE 5. Effect of dietary supplementation of silymarin on serum antioxidant activity and some immunological responses hormones of growing rabbits.

Items	Control	*CCl_4*	*CCl_4+ Sily. 25mg/kg*	*CCl_4+ Sily. 50mg/kg*	*CCl_4+ Sily. 75 mg/kg*	SEM	*p*-value	*LSD 0.05*
TAC(mmol/ml)	1.840^{a}	0.786^{d}	1.120^{c}	1.694^{ab}	1.496^{b}	0.067	<.0001	0.199
CAT(u/ml)	69.44^{a}	29.71^{d}	39.48^{c}	56.32^{b}	52.62^{b}	2.568	<.0001	2.866
MDA (nmol/ml)	37.87^{c}	117.64^{a}	70.80^{b}	38.68^{c}	53.68^{c}	5.147	<.0001	15.184
Liver MDA (nmol/g)	24.00^{d}	$86..32^{a}$	51.62^{b}	29.64^{d}	40.38^{c}	3.178	.0012	9.376
SOD (ng/ml)	27.90^{a}	16.28^{e}	19.72^{d}	25.66^{b}	21.98^{c}	0.719	<.0001	2.120
Liver SOD(ng/g)	41.10^{a}	14.80^{d}	27.16^{c}	38.78^{a}	31.28^{b}	0.914	0.0001	2.695
GSH-Px (U/L/h)	0.586^{a}	0.204^{d}	0.271^{cd}	0.404^{b}	0.341^{bc}	0.033	0.001	0.098
Liver GSH-Px (ng/g)	24.51^{a}	13.18^{c}	17.28^{b}	22.66^{a}	19.82^{b}	0.872	0.0031	2.571
IgG (mg/dl)	547.60^{a}	410.60^{c}	473.40^{b}	534.60^{a}	506.60^{ab}	13.634	0.034	40.219
IgM (mg/dl)	156.00^{a}	85.60^{e}	103.00^{d}	134.40^{b}	114.20^{c}	1.718	<.0001	5.067
TNF-α(pg/ml)	26.80^{e}	114.08^{a}	64.16^{b}	38.40^{d}	51.80^{c}	2.679	0.0012	7.906
IL-6 (pg/mL)	123.80^{d}	198.00^{a}	181.00^{b}	152.40^{c}	183.00^{b}	3.633	<.0001	10.501
IFN-γ (pg/mL)	20.00^{d}	58.20^{a}	38.20^{b}	29.80^{c}	32.60^{bc}	2.024	<.0001	5.970
CRP (ng/ml)	2.81^{d}	16.68^{a}	8.17^{b}	3.42^{d}	5.13^{c}	0.967	0.001	1.535

[a,b,c] Values within the same row differ significantly ($p < 0.05$).

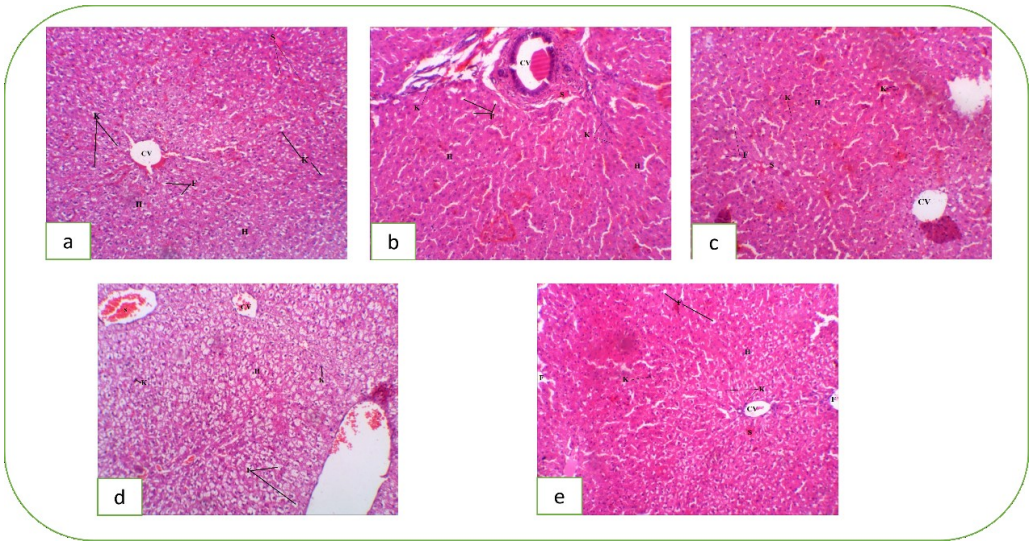

Fig. 1. Microscopic histological examination of CCl_4-induced acute liver injury. (a) Control group; (b) Group injected with CCl_4; (c) CCl_4+ 25 mg silymarin;(D) CCl_4+ 50 mg silymarin and (e) CCl_4+ 75 mg silymarin H= hepatocytes; s= blood sinusoids; cv= central vein; K= Kupffer cells and F= fatty cirrhosis.

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تأثير السليمارين على التأثيرات الفسيولوجية وخفض نسبة الكوليسترول في الأرانب النامية

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الملخص

الهدف: بحثت هذه الدراسة في قدرة السليمارين على مقاومة الإصابة الكبدية الناجمة عن رباعي كلوريد الكربون في أرانب نيوزيلندا البيضاء ((NZW، مع التركيز على تأثيراته المضادة للالتهابات ومضادات ارتفاع نسبة الدهون في الدم.

الطرق: تم تقسيم خمسة وسبعين أرنبًا ذكرًا من أرانب نيوزيلندا البيضاء إلى خمس مجموعات (ن = 15 أرنب / مجموعة) بعد الفطام. عملت إحدى المجموعات كمجموعة تحكم، ولم تتلق أي علاج. تلقت المجموعات المتبقية حقنة واحدة تحت الجلد من (0.5 مللى CCl4 / ارنب). تم تقسيم هذه المجموعات بحيث تلقت كل منها إما نظامًا غذائيًا قياسيًا أو نظامًا غذائيًا مكملًا بالسليمارين بجرعات 25 أو 50 أو 75 مجم/كجم لمدة ستة أسابيع.

النتائج: أثرت مكملات السيليمارين بجرعات 50 و75 مجم/كجم بشكل إيجابي على الوزن النسبي للكبد والخصيتين مقارنة بالمجموعة الضابطة. بالإضافة إلى ذلك، أسفرت جرعة 50 مجم/كجم عن أعلى مستويات الكسور البروتينية (البروتين الكلي والألبومين والغلوبيولين) وهرمونات الغدة الدرقية. كما أدى السيليمارين بهذه الجرعة إلى تحسين نشاط مضادات الأكسدة في مصل الدم وعلامات وظائف الكبد (ALT وAST و ALP) بشكل ملحوظ. وعلاوة على ذلك، أظهر تأثيرًا خافضًا للكوليسترول في الدم، حيث انخفض الكوليسترول والكوليسترول الضار والدهون الثلاثية بينما ارتفع بشكل ملحوظ في الكوليسترول الجيد مقارنة بالعلاجات الأخرى.

الاستنتاج: يبدو أن مكملات السليمارين الغذائية، وخاصة بجرعة 50 مجم/كجم، تشكل استراتيجية واعدة لتحسين نشاط مضادات الأكسدة، ووظائف الكبد، ومستوى الدهون في الدم لدى الأرانب التي تعاني من إصابة الكبد الناجمة عن رباعي كلوريد الكربون. وهذا يشير إلى إمكاناتها في تخفيف هذه الحالات.

الكلمات الدالة: السيليمارين، خافض للكوليسترول في الدم، وظائف الكبد، مضادات الأكسدة، و.IL-6