ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Histopathological and Biochemical Investigation of Silymarin's Inhibitory Effect on the Formation of Obesity Induced by High Fat Diet in Rats

Ratlarda Yüksek Yağlı Diyetle İndüklenen Obeziteye Karşı Silymarin'in Önleyici Etkisinin Histopatolojik ve Biyokimyasal Olarak İncelenmesi

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ABSTRACT

Aim: *Obesity is a health problem caused by excessive fat accumulation in the body and can lead to many health complications. Nurses play an important role in managing the care of patients struggling with obesity. This study investigated the restorative effect of silymarin on obesity induced by a high-fat diet (HFD).*

Materials and Methods: *In this study, 32 rats were randomly divided into four groups (n=8). Control: no action. Obesity: was fed with HFD. Silymarin: 3 mg/kg silymarin was given by orogastric gavage daily. Obesity+silymarin: 3 mg/kg silymarin daily was given in addition to HFD. Liver function tests and lipid profile values were measured in serum samples, and the liver was examined histopathologically.*

Results: *Macro-microvesicular fatty changes and coagulation necrosis were observed in centrilobular hepatocytes in livers of the obesity group, while a normal histological appearance of the liver was viewed in the obesity+silymarin group. In the obesity group, ALP and LDH activities in addition to triglyceride levels were significantly higher than control, while these values in the obesity+silymarin group were similar to control.*

Conclusions: *Silymarin largely prevented fatty liver changes and significantly restored impaired lipid profile and liver function tests in rats fed with HFD.*

Key words: *liver function tests; lipid profile; histopathology; nurse care; obesity; silymarin*

ÖZET

Amaç: *Obezite vücutta aşırı yağ birikmesinden kaynaklanan ve birçok sağlık komplikasyonuna yol açabilen bir sağlık sorunudur. Hemşireler obezite ile mücadele eden hastaların bakımının yönetilmesinde önemli bir rol oynamaktadır. Bu çalışmada, silimarinin yüksek yağlı diyet (HFD) ile indüklenen obezite üzerindeki onarıcı etkisi araştırılmıştır.*

Materyal ve Metot: *Bu çalışmada 32 rat rastgele dört gruba ayrılmıştır (n=8). Kontrol: hiçbir işlem yapılmadı. Obezite: HFD ile beslendi. Silimarin: 3 mg/kg silimarin orogastrik gavaj yoluyla günlük olarak verildi. Obezite+silymarin: Günlük 3 mg/kg silimarin HFD'ye ek olarak verildi. Serum örneklerinde karaciğer fonksiyon testleri ve lipit profili değerleri ölçüldü ve karaciğer histopatolojik olarak incelendi.*

Bulgular: *Obezite grubunun karaciğerlerinde sentrilobüler hepatositlerde makro-mikroveziküler yağ değişiklikleri ve koagülasyon nekrozu gözlenirken, obezite+silimarin grubunda karaciğerin normal histolojik görünümü izlendi. Obezite grubunda ALP ve LDH aktiviteleri ile trigliserid düzeyleri kontrole göre anlamlı derecede yüksekken, obezite+silimarin grubunda bu değerler kontrole benzerdi.*

Sonuçlar: *Silimarin, yağlı karaciğer değişikliklerini büyük ölçüde önlemiş ve HFD ile beslenen sıçanlarda bozulmuş lipit profili ve karaciğer fonksiyon testlerini önemli ölçüde düzeltmiştir.*

Anahtar kelimeler: *karaciğer fonksiyon testleri; lipit profili; histopatoloji; hemşirelik bakımı; obezite; silimarin*

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Introduction

Obesity is defined by the World Health Organization as abnormal or excessive fat accumulation in adipose tissues. This abnormality is one of the most common global health problems for all age groups[1,2]. The prevalence of obesity is increasing worldwide and is becoming one of the important health problems among children and adolescents as well as the adult population[3]. Industrialization and urbanization are indicated as the major changes in people's lifestyle that may predispose to obesity. In addition, the fact that food items contain high amounts of fat and sugar and are abundant and cheap, increased ready-eat, and rapid eating habits, and decreased physical activity, and excessive calorie intake contributes to the increase in obesity[4]. Nurses can provide both preventive and therapeutic care related to obesity. The role of nurses in obesity treatment begins with informing and directing patients about options such as diet, exercise, medication, and surgical treatment. Additionally, nurses are an important part of the multidisciplinary team by assessing patients' nutrition habits and physical activity levels, ensuring correct use of medications, and collaborating with other healthcare professionals[5]. According to the data of the World Health Organization, obesity has been reported to be one of the most important factors in the occurrence of chronic diseases such as diabetes, heart disease, chronic respiratory diseases, stroke and cancer, which are responsible for approximately 60% of all deaths in the World[6,7]. Recently, the search for preventive measures and treatments to reduce the risk of obesity, hypertension, type 2 diabetes mellitus, hypercholesterolemia, hyperlipidemia, and thrombosis has increased. In line with these searches, nurses have an important role in the management of obesity-related health problems. Methods such as diet and medical applications (statins) are frequently used to prevent high blood cholesterol and related pathologies. Accordingly, two different medicines named as orlistat and sibutramine, are recommended by the American Food and Drug Administration (FDA). Of these two drugs, orlistat reduces the absorption of fat in intestinal by suppressing the pancreatic lipase enzyme, and sibutramine also reduces appetite by suppressing the deactivation of neurotransmitters such as dopamine, serotonin and neurosephrine in brain. However, these two different drugs can reduced whole body weight moderately[8–11]. Today, pharmacotherapy is recommended as a second-line therapy for weight management after the lifestyle change. In fact, for the long-term management of obesity have been developed a large number of drugs that can provide a positive energy balance, target various pathways through various different mechanisms, and affect various factors. Especially in recent years, some anti-obesity medications have been used to treat morbid obesity; however, most of these drugs have been removed from the market due to their serious cardiovascular side effects[12]. For this reason, as in many diseases, herbal and preventive medicine is among the methods used for the prevention and treatment of obesity and they are very popular[13]. Herbal products in Türkiye and in the world is the most popular form of complementary and alternative Medicine[14]. International studies have perceived herbal and traditional therapies such as the consumption of "organic" and "unprocessed" foods that do not contain toxins or additives as harmless, while for their drugs they are "chemicals" that should be avoided[15]. Silymarin that is a natural flavonoid, is a thistle (*Silybum marianum*) component. It is a metabolic regulator known to have anti-oxidant, anti-inflammatory, anti-cancer, anti-mutagenic, anti-bacterial and anti-virus effects. In addition, silymarin has more than one pharmacological activity and its components include silibinin, silenanine and silistristin. Silymarin metabolically stimulates liver cells and activates ribosomal RNA synthesis to stimulate protein Formation[16]. Non-alcoholic fatty liver disease that is a chronic liver disease, is found mostly in obese people who are fed high-fat diets and have sedentary lifestyles[17]. Silymarin is used in the treatment of many liver disorders characterized by functional impairment or degenerative necrosis. Also, it has preventive and curative effects on prevention of various diseases such as Alzheimer, and insulin resistance especially in cirrhotic patients, cancer and cardiovascular diseases. In addition, silymarin has many of activities such as delaying aging, increasing life time, increasing movement speed and stimulation, renal protection, hypolipidemic and anti-atherosclerosis activities[18]. Silymarin can play an important role as an antioxidant as it prevents their absorption and biological activation by increasing the metabolism and excretion of polyunsaturated fatty acids and mycotoxins[19]. Silymarin is a well tolerated active ingredient and no drug interaction has been reported. The most common problems as a side effect are digestive system disorders. However, the incidence of these disorders is the same as placebo[20]. In this study, the protective effect of silymarin on liver tissue, was investigated by liver function tests, lipid profile values and histopathologically in rats with experimental obesity induced with a high-fat diet.

Material and Methods

Experiments

Ethical approval was obtained for the study from the Van Yüzüncü Yıl University Experimental Research Local Ethics Committee (Ethics committee Decision No: 2018/02). In the study, 32 male Wistar Albino rats were used at 3 months old and weighing 200–280 g. The rats were fed with tap water and standard pellet rat food (for the control and slymarin groups) at a temperature of 22±2° C, at a rhythm of 12 hours light and 12 hours dark in rooms with 60% humidity. Feed and water intake was left free (adlibitum) for all groups. The rats were weighed at the beginning of the study and randonmly assigned into groups to be as evenly distributed in weight as possible.

Preparation of High Fat Diet (HFD)

After the standard pellet feed from a private commercial feed manufacturer was milled, 300 g/kg of butter was melted and added to the feed. With this method, a fatty diet pellet feed with a high energy value (over 4000 kcal / kg) consisting of 60% saturated fat was obtained. The average amount of feed that the rats could eat for a week was calculated, and high-fat diets were prepared fresh weekly[21]. Also, silymarin was purchased commercially and was administered to rats at a daily dose of 3 mg/kg by orogastric gavage.

Creating Groups

Thirty-two rats were divided equally and randomly into four groups (n=8). Groups were created as follows.

Control Group: The rats were fed with standard pellet feed.

Obesity Group: The rats were fed with high-energy dietary pellet feed.

Obesity+Silymarin Group: The rats were fed with dietary pellet feed with high energy value, and 3 mg/kg of silymarin daily was given by orogastric gavage.

Silymarin Group: The rats were fed with a daily 3 mg/kg silymarin orogastric gavage in addition to the standard pellet feed.

The study was continued for 8 weeks. The weight changes were determined by weighing the rats in all groups on the 0, 15, 30, 45 and 60 days of the experiment. At the end of the study, after the rats anesthetized with a mixture of 0.5 mg/kg Ketamine + 0.1 mg/kg Xylazine, intracardiac blood and other tissue samples were taken for histopathological and biochemical examinations.

Biochemical Analysis

After the blood taken into yellow capped biochemistry tubes was centrifuged at 3000 *xg* for 10 minutes, the serum samples in upper phase were transferred to another tube and stored at -80° C until they were studied. Measurement of AST, ALT, GGT, LDH, alkaline phosphatase, HDL, LDL, cholesterol, triglyceride and glucose values in serum samples were measured using the chemiluminescence immunoparticle method by the Architect SystemAbbott Plus CI 16200® (AbbottDiagnostic Plus CI 16200, USA) analyzer.

Histopathological Examination

At the end of the experimental application, all animals were anesthesied and tissue samples were taken from the livers. Macroscopic findings observed in internal organs including the liver, were recorded. After the liver tissue samples were fixedin 10% buffered formalin, 4 μm sections were taken with a microtome (Leica RM2235), embedded in paraffin blocks, stained with hematoxylin-eosin (HE) and Oil Red O (for fatty changes) for histopathological examination and examined under a light microscope (Nikon Eclipse 80*i, DS-Ri2*). Liver tissues; it was examined in terms of inflammation, steatosis, degeneration, and fibrosis.

Statistical Analysis

Results are expressed as mean and standard deviation. IBM Statistical Package for Social Sciences (SPSS) program (version 20) was used for analysis. The Shapiro Wilks test was used to check whether the data were normally distributed or not. Since the data were distributed normally, whether there was any difference between the groups, was determined by the Kruskal-Wallis test. Posthoc was performed to determine from which group the differences originated. Averages with a p value of 0.05 or less were considered significant relative to each other. In addition, correlation analysis between parameters was also performed.

Results

Biochemical Findings

During the study, the results of the increase in the average weight of the animals by groups and days were shown in detail in Table 1. There were no significant differences between the weight averages of the groups at the beginning and 15th day of the study, and all the group values were similar (p>0.05). However, it was observed that the weight averages of other groups other than the control group increased considerably from the 30th day (p<0.009). But there was no significant difference between the obesity and obesity + silymarin groups of the 60th day (p>0.05). Also, comparing the time-dependent group weight averages within the same group depending on the age increase in the control group from the starting day until the 60th day, the other groups showed increases due to age and diet.

Results of Liver Function Tests

Results of AST, ALT and LDH values from liver function tests are shown in detail in Table 2 and Fig. 1. In the obesity group, LDH values increased significantly compared to the control group (p<0.05), while ALT values decreased (p<0.05). There was no significant difference in AST values (p>0.05). Also, LDH values in the obesity+silymarin and silymarin groups were quite low compared to the obesity group (p<0.05). In addition, ALT values in the control and silymarin group were higher than in the obesity group (p<0.05). There was no significant change in GGT values and the values of all groups were similar (p>0.05).

When lipid profile values were examined in Table 2 and Fig. 2, interestingly, total cholesterol values in the obesity group were not significant, but were low compared to the control group (p>0.05), while obesity+silymarin and silymarin were high (p<0.05). Also, HDL values were lower in the obesity group compared to the control and obesity+silymarin groups, while the highest LDL and HDL values were observed in the obesity+silymarin group (p<0.05). There was no significant difference between the LDL values of the other groups. Also, triglyceride values were highest in the obesity group, while the lowest was in the silymarin group (p<0.05). There was no significant difference between the obesity+silymarin and silymarin groups (p>0.05).

Table 1. *Live weight average and standard deviation values according to groups and days*

	Control	Obesity	Obesity+Silymarin	Silymarin	P value (time)
Baseline	155.17±17.46	162.86±9.99	174.00±9.17	168.29±19.85	0.155
15 thday	187.67±12.48$^{\neq}$	199.43±11.65$^{\neq}$	209.71±11.40$^{\neq}$	204.57±21.09$^{\neq}$	0.077
30th day	196.17±13.03$^{*\neq}$	218.57±11.18$^{\neq}$	219.43±13.45$^{\neq}$	218.29±13.24$^{\neq}$	0.009
45th day	212.67±13.84$^{\neq}$	223.14±11.25$^{\neq\phi}$	237.43±18.17$^{*\neq\varphi}$	223.14±10.06$^{\neq}$	0.028
60 thday	216.67±17.47$^{\neq\phi}$	250.86±19.18$^{\theta\neq\varphi}$	250.00±20.07$^{\theta\neq\varphi}$	238.71±15.01$^{\neq\phi}$	0.009
Pvalue (group)	0.011	0.020	0.001	0.001	

*p: Significant compared to the other groups on the 30th or 45th days (p <0.05), †p: significant compared to control and Silymarin groups on the 60th day (p <0.05), ≠p: significant according to the starting day in the same group (p <0.05), ϕp: significant according to day 15th in the same group (p <0.05), φp: significant according to the 15th and 30th days within the same group (p <0.05).

Table 2. *Mean and standard deviation values of some liver function tests and lipid profile values at the end of study*

	Control	Obesity	Obesity+Silymarin	Silymarin	P values
AST	107±11	104±9	104±9	115±10	0.076
ALT	45±5	27±3$^{\neq}$	28±4$^{\neq}$	37±2	0.001
LDH	295±21	1084±83*	601±36$^{\theta}$	596±42$^{\theta}$	0.001
GGT	2.92±0.12	3.10±0.12	3.08±0.15	2.98±0.14	0.109
Alk-P	186±20	203±13	177±14	235±43*	0.004
Cholesterol	53±4	48±4	67±3*	55±8$^{\phi}$	0.001
HDL	37.3±3.6	30.9±2.8*	48.5±2.4*	40.1±6.6	0.001
LDL	10.2±0.9	9.6±0.9	13.5±1.7*	10.4±1.8	0.009
Triglyceride	111±9*	128±8*	84±6*	69±5*	0.001
Glucose	126.5±9.5	116±18	87.5±7$^{\theta}$	88±6$^{\theta}$	0.002

AST: aspartattransaminase, ALT: alanintransaminase, LDH: lactatedehydrogenesis, GGT: gammaglutamyltransferase, AlkP: alkalenfosfataz, HDL: high-density lipoprotein, LDL: low-density lipoprotein, *p: Significant according to other groups (p<0.05), ϕp: Significant according to control and Silymarin groups (p <0.05), θp: significant according to obesity and obesity + Silymarin groups (p <0.05), θp: significant according to control and obesity groups (p <0.05).

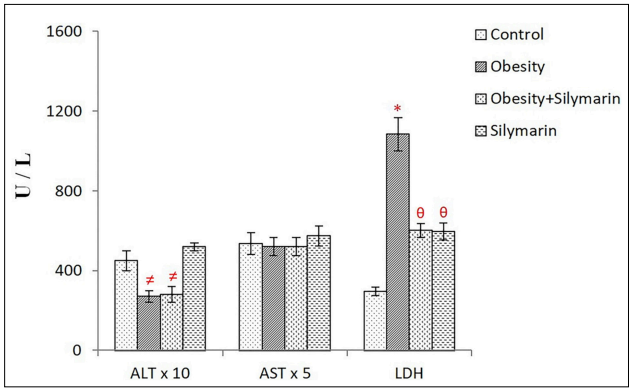

Figure 1. *Comparison of AST, ALT and LDH values from liver function tests *p: Significant compared to other groups (p <0.05), ≠p: Significant compared to other groups (p <0.05), θp: Significant compared to control and obesity groups (p <0.05).*

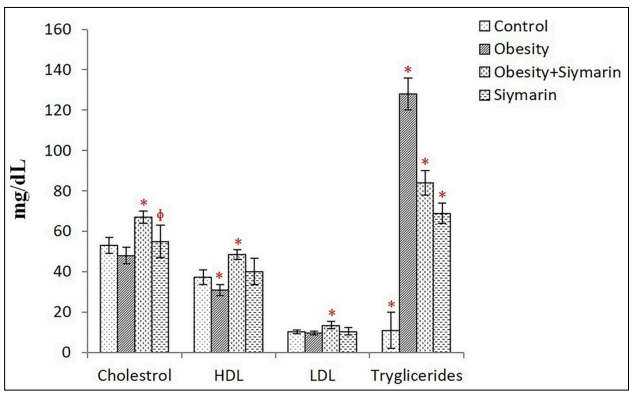

Figure 2. *Collective comparison of lipid profile values.*p: Significant compared to other groups (p<0.05), ≠p: Significant compared to control and Silymarin groups (p <0.05), θp: Significant compared to obesity and obesity + Silymarin groups (p <0.05).*

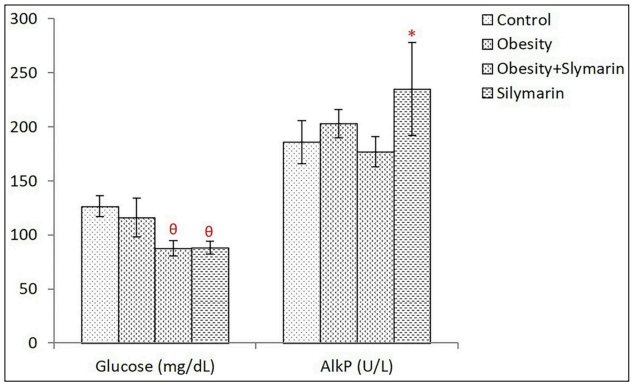

Figure 3. *Comparison of glucose and AlkP values *p: Significant compared to other groups (p <0.05),θp: Significant compared to control and obesity groups (p <0.05).*

Alkaline phosphatase values from parameters associated with bone development during development were higher in the silymarin group than in other groups (p<0.05). There was no significant difference between the other groups (p>0.05). Also, glucose values of silymarin and obesity + silymarin groups were lower than control and obesity groups (p <0.05, Table 1 and Fig. 3). Also, the Pearson-correlation coefficients and degrees of importance of the groups according to the parameters and between the parameters are given in detail in Table 3. A positive value indicates that the parameters are positively correlated and the negative value parameters are negatively correlated. Correlations are expressed as percentages. The results showed a positive correlation between ALT and AST values, while there was a significantly negative correlation between LDH and ALT and HDL values. When cholesterol values were examined, there

Table 3. *Collective display of values for correlation between groups and parameters*

Correlations										
	Groups	AlkP (U/L)	ALT (U/L)	AST (U/L)	Cholesterol (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	Glucose (mg/dL)	LDH (U/L)	Triglyceride (mg/dL)
Gruplar	1									
AlkP (U/L)	0.415*	1								
ALT (U/L)	0.205	0.302	1							
AST (U/L)	0.464*	0.286	0.85**	1						
Cholesterol (mg/dL)	0.341	-0.084	-0.237	-0.204	1					
HDL (mg/dL)	0.392*	-0.086	-0.118	-0.135	0.927**	1				
LDL (mg/dL)	0.248	-0.144	-0.348	-0.301	0.862**	0.825**	1			
Glucose (mg/dL)	-0.797**	-0.200	-0.117	-0.310	-0.511**	-0.551**	-0.453*	1		
LDH (U/L)	0.111	0.144	-0.428*	-0.077	-0.337	-0.430*	-0.240	0.045	1	
Triglyceride (mg/dL)	-0.801**	-0.250	-0.335	-0.359	-0.528**	-0.610**	-0.387*	0.701**	0.443**	1

*p: The correlation is significant to the 0.05 value (2-tailed), **p: The correlation is significant to the 0.01 value (2-tailed),

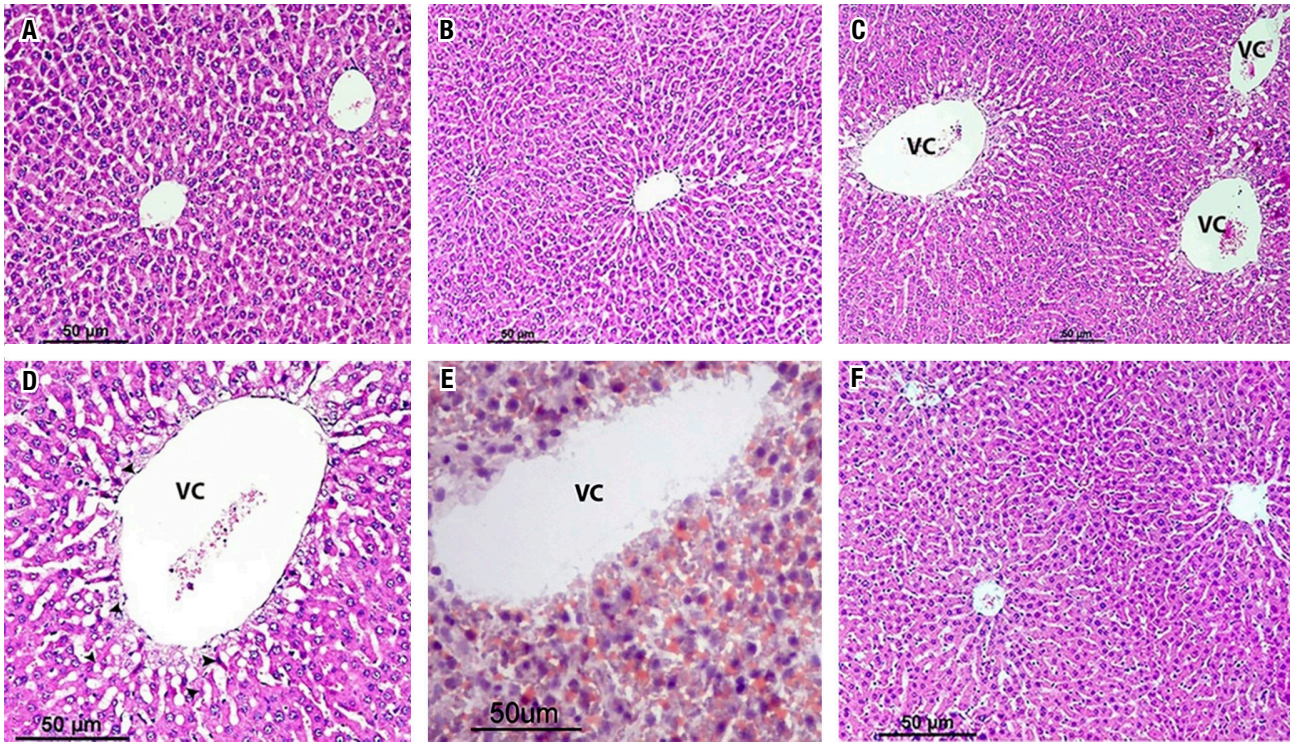

Figure 4. *Collective demonstration of histopathological images for all groups. A: Control group, the normal microscopic view of liver tissue is observed (H.E.). B: Silymarin group, the normal microscopic view of liver tissue is observed (H.E.). C: Obesity group; vacuoles degeneration is observed in centrilobular hepatocytes (VC) in liver tissue (H.E.). D: Obesity group; in the liver tissue, sharp limited vacuoles of different sizes in centrilobuler hepatocytes (VC) and coagulation necrosis (arrowheads) are observed in some of these hepatocytes (H.E.). E: Obesity group; fat deposits in orange color are observed in centrilobular hepatocytes (Oil Red O satining). F: Obesity + Silymarin group; the normal histological appearance is observed in the liver tissue (H.E.) (Bar: 50 µM).*

was a positive correlation between cholesterol and HDL and LDL values, while there was a negative correlation between glucose and triglyceride values. Also, there was a positive correlation between HDL values and LDL values, while there was a negative correlation between glucose, LDH, and triglyceride values. Also, there was a negative correlation between LDL values and glucose and triglyceride values, while there was a positive correlation between glucose and LDH values and triglyceride values.

Macroscopic Findings

No morphological changes were detected in the macroscopic examination of the organs in the necropsies of the control and experimental group rats.

Histopathological Findings

Control: Microscopically, it was observed that the liver had a normal histological appearance. The structures of the hepatocytes and portal areas appeared normal. The hepatocytes formed regular remark cords around the vena centralis and the sinusoids between the remark cords were normal (Fig. 4A).

Obesity: Almost similar morphological changes were observed in the livers of all rats in this group. These changes were especially localized in hepatocytes in the periacinar and intermediary regions of the lobules. It was determined that the cytoplasm of hepatocytes in these regions had sharp limited vacuoles of different sizes and it was determined in Oil Red O staining that these vacuoles were related to fatty changes (Fig. 4E). This **steatosis** (macrovesicular or microvesicular) was one of the commonest morphological of hepatocytes. Macrovesicular steatosis, in which the nucleus of the hepatocyte is displaced by one or more fat vacuoles easily visible by light microscopy. Also, coagulation necrosis was observed in some of these hepatocytes. The nucleus of necrotic hepatocytes were generally the dark stained, picnotic and flattened in appearance (Fig. 4C-D). Inflammatory reactions consisting of focal mononuclear cell infiltrations were seen in the portal regions. However, there was no increase in connective tissue in these areas. The congestion and dilatation were observed in sinusoids around of some vena centralis (Fig. 4C-D).

Obesity+Silymarin and Silymarin groups: In the livers of all rats in these groupswere observed to have the normal histological appearances as in the control group (Obesity+Silymarin: Figures 4F; Silymarin: Figures 4B).

Discussion

Current treatments for obesity include dietary changes, psychotherapy and various pharmaceutical interventions for people with eating disorders, surgical interventions for patients with complications, and nursing care is required for this condition[5,8]. Also, current anti-obesity treatments are limited due to the high cost and numerous side effects[22]. Current medications and toxic chemicals have been reported to cause liver damage and may even cause liver cirrhosis and cancer[19]. Anti-obesity drugs such as rimonabant, fenfluramine and sibutramine have been withdrawn from the market for serious adverse effects such as increased cardiovascular risks, mood disorders and even suicidal sensitivity[23]. These drug treatments can cause numerous side effects such as depression, anxiety, headache, dizziness, nausea, and fatigue[8]. Therefore, the development of new types of anti-obesity drugs is an urgent need[24]. Natural anti-obesity products are gaining popularity in recent years[25]. Natural products are promising alternatives due to their effective biological activity and potentially less serious side effects[24]. Since current anti-obesity drugs have strong side effects, it is necessary to develop functional foods as adjuvant therapies[22]. Recently, algae are recognized as a good source of anti-obesity substances[26]. Supportive therapies such as herbal remedies may be required for individuals who do not respond to lifestyle changes[27]. Therefore, herbal prescriptions with relatively few side effects, which offer the advantage of being useful for a variety of indications, have been recently re-investigated[8]. As an alternative approach, many researchers have focused on the anti-obesity effects of natural ingredients consumed daily. Because these ingredients are generally considered less toxic than synthetic drugs[28]. Dietary supplements based on thistle (silymarin) are among the most common preparations used by the EU and US adult population[18]. Thistle is one of the oldest medicinal plants and has been used for centuries to treat many diseases[29]. Silymarin, the effective ingredient of thistle seeds, is one of the medicinal plants specific to chemotypes used in drug production for liver diseases[30]. In a study investigating the effect of silybum marianum extract on obesity, it was reported that silymarin prevented liver damage by regulating lipid metabolism, leptin and insulin levels and parameters related to obesity in the blood in rats fed with HFD[31]. Another study showed that silymarin increased hepatocyte membrane permeability to glucose in streptozotocin-induced diabetes. It has also shown that silymarin not only reduces hyperglycemia but also acts as a protector against the stresses associated with high glucose to increase insulin resistance[32]. A study by Sung-Hyun Kim et al., Showed that silymarin is highly promising for the development of gastric cancer drugs, as it inhibits cell growth and tumor formation by inducing apoptosis in human gastric cancer cells both in vitro and in vivo[33]. In a study conducted to determine whether long-term treatment with silymarin is effective in reducing lipoperoxidation and insulin resistance in diabetic patients with liver cirrhosis, it was shown that silymarin effectively neutralizes superoxide radicals and reduces systemic signs of inflammation. In addition to reducing membrane peroxidation, silymarin also significantly reduced glycosylated hemoglobin and insulin requirements[34]. In a study, it was reported that silymarin has a protective effect depending on the dose in the indomethacin-induced ulcer model and that silymarin at a dose of 100 mg/kg accelerates the healing process. In addition, it has been determined that silymarin, indomethacin or other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) may have beneficial effects in preventing gastric damage[35]. Hepatic steatosis induced by excessive lipid deposition in the liver is highly associated with obesity and associated complications[24]. Obesity leads to metabolic stress resulting in liver damage, including nonalcoholic fatty liver disease (NAFLD)[22]. It has been proven that silymarin has a healthy effect on the liver and prevents liver damage histopathologically when given with a drug that causes hepatotoxicity such as isoniazid[36]. In this study, there were no macroscopic differences between the control group and the experimental groups in the liver of rats, but microscopically, the liver was in normal histological appearance in the control group and the silymarin group, and but there were sharply limited vacuoles of different sizes (fatty changes) in the centrilobular hepatocytes of the liver in the obesity group fed with HFD. In addition, it was determined that some of these hepatocytes had coagulation necrosis. However, in the group fed with silymarin together with HFD, despite HFD, it was observed that silymarin prevented the fatty changes of liver and degenerative necrotic changes.

Plasma or serum levels of ALT, AST, GGT and ALP enzymes, key biomarkers in the diagnosis of liver diseases, are crucial indicators of liver damage or injury. The increase in serum levels of these enzymes is caused by the damage to the structural integrity of the hepatocytes and their mixing into the bloodstream. It was reported that silymarin and naringin reduce liver damage caused by methotrexate with antioxidant effects[37]. Another study reported that silymarin, which is given for treatment against ethanol-induced liver toxicity in mice, increases antioxidant enzyme activity and GSH levels[37,38]. In another study, it was reported that in rats treated with CCl4 at a dose of 50 and 200 mg/kg milk thistle, increased liver ALT and AST levels with CCl4 were significantly reduced and brought closer to control group values[39,40]. Previous studies reported that milk thistle significantly decreased ALT and AST values, which were increased compared to the control group, in rats treated with 0.5 mL/kg CCl4 twice a week for eight weeks[40,41] reported that the increased serum ALT, AST, and ALP values in rats with liver damage with anti-tuberculosis decreased with the administration of 200 mg/kg of milk thistle and approached the control group values. In this study, no significant difference was found between the groups in serum GGT and AST levels. However, LDH, triglyceride and serum glucose values were found to be low, and total cholesterol and HDL values were found to be high in the experimental groups receiving silymarin. These results are also in keeping with the previous studies mentioned above. However, we think that the reason why silymarin increased total cholesterol levels as an unexpected effect in the group given slymarin may be related to the dose and duration of treatment used in our study.

Conclusion

In the obesity group, it was noted that fat degeneration and necrotic changes occurs in hepatocytes around the vena centralis, while in the obesity + silymarin group, an almost normal appearance of liver is observed. It is thought that this hepatoprotective effect is due to the positive effects of silymarin on the antioxidant and circulatory system, as well as the regulating effects of blood triglyceride levels. The likely cause of fat degeneration, especially in hepatocytes around vena centralis; due to the histological structure of the liver, hepatocytes in these regions are thought to be most susceptible to hypoxia and are related to the circulatory disorder, which can be caused by feeding on a high-fat diet. As a result, it has been determined that silymarin significantly prevents liver fatty changes and damage, at the same time significantly regulates blood glucose and triglyceride levels, and also increasing HDL levels, called good cholesterol. Moreover, nurses play a crucial role in combating obesity and liver diseases by providing education and counseling to patients on the use of herbal products, diet, exercise, and lifestyle habits, as well as ensuring the proper use of medications and managing health problems associated with obesity. In this regard, it is known that silymarin has beneficial effects against fatty liver and obesity, however we believe that more studies high-quality value are needed to apply it in clinics.

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Declaration of Interest

The authors have no conflicts of interest associated with publication of this article.

Data Availability Statement

Data available on request due to privacy/ethical restrictions (The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions)

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