RESEARCH ARTICLE

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Investigation of the effect of Thermolife Ixir product on weight loss and some biochemical parameters in rats

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Abstract

The purpose of this study is to investigate the effect of 2017-0730 Patent Number Thermolife Ixir product on weight loss and some biochemistry values in obese rat with fatty liver. Thirty male Wistar albino rats fed a high-fat diet were the material of the study. An obesity model was created in rats fed a special high fat diet. *Ad libitum* feeding was applied to rats with a special diet and water. These rats were randomly divided into 3 groups consisting of 10 rats in each group. Group B was given 1 gram of the product daily, and 1.5 grams of the product was given to group C while group A was served as control. All rats were fed a high-fat diet. Before the study, the body weight was measured and blood was drawn for serum parameters. The test mixture was administered orally for a month, the same parameters were measued periodically and differences were determined. After the study, it was observed that the body weight of the rats in group B and C decreased significantly compared to group A. It was determined that there was a decrease in cholesterol and triglyceride values, an increase in HDL values and, the changes in other parameters were not statistically significant. At the end of the study (the 30th day), it was observed that the adipose tissues in the body appearred normal and lower in the rats in group B and C which were fed without a diet change. The rats in group A had appearent fatty tissues in abdomen and aroud the different areas of the body. In histopathological examination, the liver in group A rats was associated with hepatic steatosis, which covered approxiamtely 10% of the liver, due to excessive fatty nutrition. In a dependent manner, the rats in groups B and C had lower triglyceride and glucose levels and higher HDL levels. In conclusion, the Thermolife Ixir productcauses weight loss and fat burning in rats in a dose dependent manner that is also associated with increase in HDL as well decrease in triglyceride and glucose levels.

Keywords: Rat, liver, steatoz, thermolife ixir, obesity.

INTRODUCTION

Resveratrol (3,4 ', 5-trihydroxy-stilbene), discovered in the medicinal plant of *Veratrum grandifolium Loes fil* for the first time in the early 1930's, is a compound of the stylbene group and showing a high phytoalexin property (Creasy and Creasy, 1998; Keskin et al., 2009;). The term phytoalexin (Phytoalexin) comes from the combination of the words phyton, meaning plant in ancient Greek, and alexein, which means protective (Bavaresco and Vezzulli, 2006). Resveratrol, which has an important place in the protection of plants against diseases with its phytoalexin property, has also been proven that it does not lose its protective properties such as antimicrobial, antifungal, antioxidant and anticancer in humans and other living things (Zgoda-Pols et al., 2002; Ito et al., 2003; Tedesco et al., 2000). Biochemical and molecular mechanisms of action of resveratrol have been studied. It can bind to a wide variety of cell signal proteins such as DNA polymerase, topoispmerase II, tubulin, F1-ATP. It suppresses anti-apoptotic gene products by activating various transcription factors, inhibits protein kinases, increases the effect of antioxidant enzymes, suppresses the activity of angiogenic and metastatic gene products with inflammatory markers, and acts on genes that regulate the cell cycle (Keskin et al., 2009).

Resveratrol stops or suppresses cancerous cells at different stages and helps control of gastritis and ulcer formation with the development of Helicobacter Pylori in the stomach. It reduces the risk of coronary heart diseases and has a healing effect in Alzheimer's disease. Furthermore, it strengthens the immune system with its high antioxidant effect and has antiallergic effect. It has a protective effect in some lung diseases and prolongs life (Park et al., 2001; Fulda and Debatin , 2004; Mahady and Pendland, 2000; Delmas et al., 2005; Marambaud et al., 2005; Celotti et al., 1996; Cheong et al., 1999; Huang et al., 2001; Culpitt et al., 2003). Another remarkable effect of resveratrol is that it decreases cholesterol and prevents or regresses fat in the liver (Keskin et al., 2009; Kimura et al., 1983).

Hepatic lipidosis can be defined as the vacuolization of hepatocytes, which are the functional cells of the liver, largely with triglycerides or fat accumulation in the parenchyma (Holan, 2009). Although many of them have not been proven yet, many different factors can be involved in the etiology of the disease (Schaer and

Gaschen, 2019). Stress, obesity, prolonged fasting, changes in the gut microbiome or hormones, alcohol and drug use, exposure to toxins, and pancreatectomy are among the factors that cause or predispose to hepatic lipidosis (Scherk and Center, 2010; Burrows, 2003; Turgut and Ok, 2001). Hepatic lipidosis is the most common chronic liver disease in humans (Mahmoud et al., 2016). Affecting 70-80% of obese individuals, the disease threatens 20% of the population in western countries (Chitturi et al., 2007; Radcke et al., 2015). It is common among animals, especially in cats (Gümüşü et al., 2013). Hepatic lipidosis in cats, first described by Barsantive et al. In 1977, constitutes approximately 50% of all liver diseases (Gül et al., 2006; Barsantive et al., 1977). Triglyceride accumulation occurs in more than 80% of hepatic lipidosis hepatocytes, or more than 5% of the total weight of the liver (Pazak et al., 1998; Schaneider, 2019). Affected individuals are often obese or have a recent source of stress in the anamnesis (Schaneider, 2019). Weight loss, hepatomegaly, diarrhea, vomiting, icterus, depression, dehydration, ptyalism and ceruical ventroflexion are common clinical findings (Gümüş et al., 2013). Ultrasound, Doppler, Magnetic Resistance Imaging and Computed tomography techniques can be used to measure the size by imaging the liver in diagnosis, while increases in liver enzyme activities are made by blood biochemical analysis (Fusai et al., 2005; Isselbacher and Podolsky, 1998). Definitive diagnosis can be made by histopathological examinations. In treatment; Elimination of the factor that triggers hepatic lipidosis, treatment of the primary disease, if any, and supportive therapy are performed (Schnaider, 2019). Balanced electrolyte fluids and non-glucose fluids are preferred in fluid treatment, taurine, L-carnitine and vitamin applications are applied to aid fat mobilization (Holan, 2009; Turgut and Ok, 2001; Farina, 2005). The purpose of this study is to investigate the effect of 2017-0730 PATENT NUMBER THERMOLIFE İXİR product on weight loss and some biochemistry values in obese rat with fatty liver.

MATERIALS AND METHODS

The study was approved by the Kırıkkale University Local Ethics Committee for Animal Experiments (2019-2 / Decision number: 17). In the study, 30 healthy adult male albino wistar rats weighing between 300-350 g were used. Rats were fed *ad libitum* for 8 weeks with a commercial special diet containing 35% fat (Arden, Ankara) and an obesity model was created. After all rats included in the study were fed with a fatty diet, abdominal ultrasound examinations were performed just before the product trial started. The adipose tissues of all rats, for which the presence of fat was checked, was viewed with the help of ultrasound. These rats were randomly divided into 3 groups including 10 animals in each one. While 1 gram of "Thermolife Ixir" product was given to group B and 1.5 grams of product "Thermolife Ixir" daily to lose weight, group A was separated as the control group. The content of the product Thermolife Ixir in a mass of 5 g containing1500 mg L-Arginine HCL (1485 mg Arginine BRD: 29.7%), L-Methionine (910 mg BRD: 100%), Vitamin C (L-Ascorbic Acid 750 mg BRD: 75%), Vitamin B3 (Nicotinamide 150 mg NE BRD: 75%), Resveratrol (117.5 mg BRD: 2.35%), Coenzyme Q10 (100 mg BRD: 50%) and Sodium Selenite 0.44 mg (corresponds to 0.198 mg elemental Selenium BRD: 99%). It also contains acidity regulators and flavors. All groups were fed a high-fat diet throughout the study. Body weight measurements of all rats were made once a week from the 0^{th} day of the study until the end of the study, and their serum was removed by taking a blood sample every 15 days and centrifuging at 3000 rpm. It was stored at -20 ºC until analysis in the laboratory. Triglyceride, cholesterol, glucose, LDL, HDL, AST and ALT values of the samples taken were analyzed with Mindray brand BS300 fully automatic biochemistry device using Relassay commercial kits. For histopathological analysis, at the end of the study, the livers of all rats were removed and the specimens prepared after routine determinations were stained with hematoxylin eosin and checked. The differences between them were compared statistically.

STATISTICAL ANALYSIS

Statistical Analysis method was performed using SPSS (version 16.0 Chicago, IL USA). All results are presented as mean ± standard deviation. The paired student *t* test was used to show the differences within the group with normally distributed and by using the Mann Whitney U test to evaluate the differences between the groups which are not normally distributed. A *P* value of 0.05 for all analyzes was considered significant.

RESULTS

On Weight Loss

During the study, rats were fed with a special diet (35% fat content) for the last 30 days. The average body weight of the control group (A group) was 661.37 ± 50.2 grams, and the average body weight of the group B given 1 gram of Thermolife ixir per day was 602.71 ± 22.56 grams. In group C rats given 1.5 grams of Thermolife Ixir Daily, the average body weight was determined as 600.78 ± 15.32 grams. The difference among groups was signicifant ($p<0.001$) (Table 1).

Table 1. The effect of Thermolife İxir usage on body weight in rats fed with special diet.

	Control	Thermolife Ixir 1 gr	Thermolife Ixir 1,5 gr
Body weight (gr)	661,37±50,2 [a]	602,71±22,56 [b]	600,78±15,32 [b]

(a and b represent similar and different statistical values)

Glucose values

At the end of the study, glucose levels were measured as 143.2 ± 28.8 mg / dl, 117.75 ± 13.02 mg / dl and 116.78 ± 12 in the control, groups using 1 g of product per day and 1.5 g of product, respectively. It was determined that the blood glucose levels among the control and experimental groups were significantly different ($p<0.05$) (Table 2).

Total Cholesterol values

At the end of the study, the total cholesterol level was measured as 55 ± 24 mg / dl, 51 ± 22 mg / dl and 51 ± 22 mg / dl in the control, daily 1 g product and 1.5 g product groups, respectively. A decrease in total cholesterol was observed with the use of the product, but this decrease was not significant ($p>0.05$) (Table 2).

Triglyceride values

The mean Triglyceride level was 128,75±48,25 mg/dl, in the control group while the mean Triglyceride level of the group given 1 gram of Thermolife ixir per day was 112,5±23,5 mg/dl. The Triglyceride level of the group given 1.5 grams of Thermo İxir per day was found to be

99,3±22,7 mg/dl. Statistically, a difference was found among groups p<0.01 (Table 2).

Table 2. The effect of Thermolife Ixir use on some biochemical parameters in rats.

	Control	1 gr Thermolife İxir	1,5 gr Thermolife İxir
Glucose (mg/dl)	143,2±28,8 [a]	117,75±13,02 [b]	116,78±12,05 [b]
Total Cholesterol (mg/dl)	55 ± 24 [a]	51±22 [a]	51±22 [a]
Triglyceride (mg/dl)	128,75±48,25 [a]	112,5±23,5 [b]	99,3±22,7 [c]
HDL (mg/dl)	38,3±11,7 [a]	53,1±12,9 [b]	55,2±9,8 [b]
LDL (mg/dl)	16±5,3 [a]	17,25±5,64 [a]	17,01±6,09 [a]
ALT (U/L)	99,2±8,3 [a]	75,75±16,02 [b]	77,52±14,08 [b]
AST (U/L)	198,4± 45,45 [a]	143,80±35,65 [b]	146,60±42,40 [b]

HDL: High density lipoprotein; LDL: Low density lipoprotein; ALT: Alanine aminotransferase; Aspartate aminotransferase. (a, b and c represent similar and different statistical values)

HDL values

The mean HDL level was 38.3 ± 11.7 mg / dl in the control group while the mean HDL level of the group given 1 gram of Thermo ixir per day was 53.1 ± 12.9 mg / dl. The HDL level of the group given 1.5 grams of Thermo İxir per day was found to be 55.2 ± 9.8 mg / dl. Statistically, a difference was found among groups p<0.01 (Table 2). No equipment was used for any exercise enhancement in the cage where the rats were located.

LDL values

While the mean LDL level in the control group was 16 ± 5.3 mg / dl, the average LDL level of the group given 1 gram of Thermo ixir per day was 17.25 ± 5.64 mg / dl. The LDL level of the group whose daily dose was 1.5 grams of Thermo İxir was found to be 17.01 ± 6.09 mg / dl after the study. Statistically, there was no difference among groups (p>0.05) (Table 2).

ALT and AST values

At the end of the study, the mean ALT value of the control group was measured as 99.2 ± 8.3 U / L and the AST value as 198.4 ± 45.45 U / L. The average ALT value of the group receiving 1 g of product per day is 75.75 ± 16.02 U / L, the AST value is 143.80 ± 35.65 U / L, and the average ALT value of the group that takes 1.5 g of product per day is 75.75 ± 16, 02 U / L and AST value measured as 146.60 ± 42.40 mg / dl. Although there was a difference among the groups for both values, but the difference was not significant (p>0.05) (Table 2).

Necropsy Findings

During the study, the rats fed a high-fat special diet were performed USG at the end of the first 30-day period of the study and the increased adipose tissue was visualized (Figure 1). The rats whose fat was confirmed by USG application were randomly grouped and three groups were formed as two different doses of product trials for 30 days and a control. At the end of the study, the necropsies of the rats that were duly terminated were performed. The deposition-distribution of adipose tissue in the abdomen was observed and the results were compared. While intense fat accumulation was observed in all rats in the control group (Figure 2), 2/10 of the rats in the group treated with 1 gram of Thermoixir per day had dense fat mass, while little or no fat accumulation was observed in the rats in group C (Figure 3 and 4).

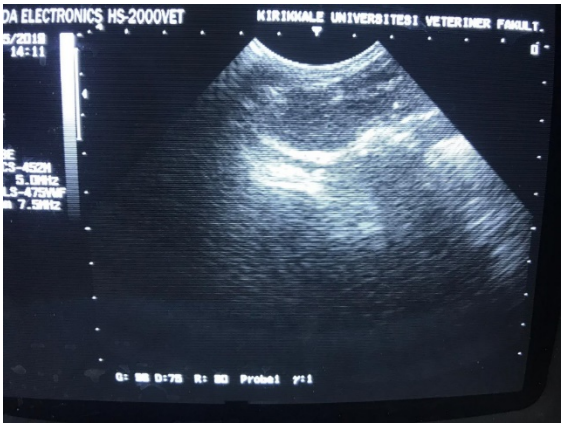

Figure 1. Ultrasonographic view of the abdomen.

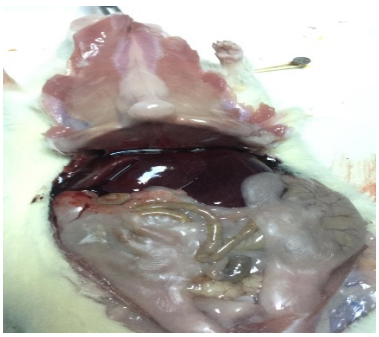

Figure 2. Adipose tissues in the omentum.

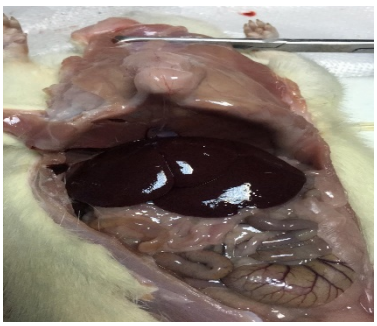

Figure 3. Low fat necropsy appearance.

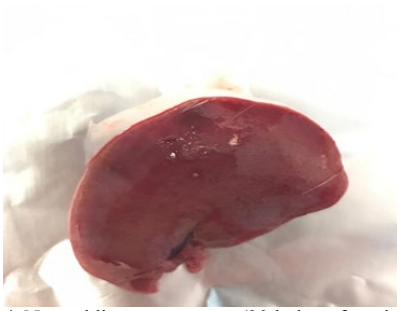

Figure 4. Normal liver appearance (30th day of product use).

Histopathological Findings

From rats fed a special diet for 8 weeks; In the histopathological examination of 10 rats that constitute the control group, an average of 10% steatosis was detected in the liver after the study (Figure 5). Fat cells were not observed in the liver histopathological examination or very mild steatosis was detected at a rate of 1% (Figure 6).

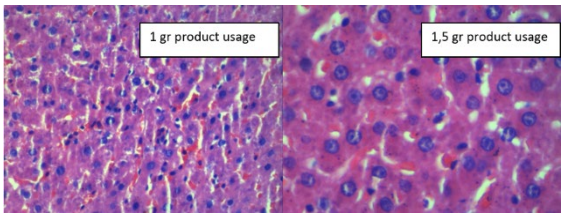

Figure 5. Normal Liver Appearance (seen n Group B and C rats 30 days after the use of the product).

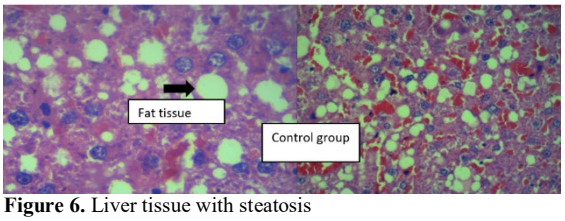

Figure 6. Liver tissue with steatosis

DISCUSSION AND CONCLUSION

Karabekir and Özgörgülü (2020) reported that in their studies where the protective effect of resveratrol in hepotocellular carcinoma was subject, AST and ALT values decreased in rats given resveratrol compared to the control group, but this decrease was not statistically significant. In the same study, although there was no statistical difference in the decrease in AST and ALT, it was interpreted that the decrease in the experimental group could be interpreted as the protective effect of resveratrol on the liver. Similar to Karabekir and Özgörgülü (2020), in our results, AST and ALT values were found lower in the resveratrol groups compared to the control group, although there is no statistical significance.

Sharma et al. (2017), in their study investigating the effect of resveratrol on the change in body weight in rats whose menopause model was created by applying overiorectemia, found the weight loss in resveratrol given groups to be significant compared to the groups not given resveratrol ($p<0.05$). In the study summarized similarly, the difference in body weight was found statistically significant in the groups in which 1 g and 1.5 g of resveratrol were used compared to the control group ($p<0.001$).

Sharma et al. (2017) reported that after the use of resveratrol in healthy rats fed with a high-calorie diet, the blood glucose level decreased, but there was no statistically significant difference ($p>0.05$). Bujanda et al. (2008), in rats with experimental fatty liver, glucose levels were measured differently between the control group and the steatosis groups and the resveratrol group, and the glucose level decreased in the resveratrol group. Similarly, with the use of reveratrol in rats fed with high fat (35%) diet, a decrease in blood glucose level was obtained compared to the control group, and this decrease was found to be statistically significant ($p<0.05$).

Studies have reported that various phytochemicals may be effective in reducing adipose tissue by mechanisms such as suppressing the differentiation of preadipocytes, stimulating lipolysis, and inducing apoptosis of existing adipocytes. In particular, resrevatrol causes a decrease in fat mass by decreasing adipogenesis in preadiocytes, increasing lipolysis in mature adipocytes and modulating mitocontrial function. Resveratrol increased resistance to weight gain, especially in mice fed a high-fat diet (Baile et al., 2011). Alberdi et al. (2011) reported that in rats fed a diet containing 20% sucrose and 22.5% fat, there was no statistically significant difference in body weight and live weight gain between the resveratrol group and the control group. However, it is seen that the weights in the resveratrol group were lower. At the same time, in the necropsies of rats using resveratrol, a serious reduction in adipose tissue in 4 different parts of the body was reported. In our study, weight loss was measured close to each other between the groups fed 1 g and 1.5 g of resveratrol per day, while adipose tissue was observed in 2/10 rats in the group given 1 g of product in the necropsy group, while no rats were observed in the necropsy of the group receiving 1.5 g of product. However, fattening was observed macroscopically in all individuals in the control group. In addition, weight loss in the control group was quite low compared to the study groups, the difference was found to be significant ($p<0.001$).

Chang et al. (2015) examined the changes that high and low doses of resveratrol use in mice caused on various biochemical markers in serum. In the study where there was no significant difference in triglyceride, total cholesterol and HDL levels between groups, it was reported that LDL levels of mice in the high dose resveratrol group decreased significantly. Sharma et al. (2017) reported that the levels of triglyceride in the blood of rats on the diet given with resveratrol decreased significantly compared to the control group. In our study, similar to Chan et al., While the difference between total cholesterol and LDL values was found to be insignificant in the control and study groups, the HDL value was found to be significantly higher in the resveratrol-containing product groups compared to the control group. In triglyceride measurements, it was observed that resveratrol use decreased triglyceride level significantly, as in Sharma et al. (2017).

Bujanda et al. (2008) reported in a study on rats with hepatic steatosis that steatosis decreased after resveratrol administration and that the substance used was related to the decrease in TNF-α production. In this study, it was observed that the study groups using resveratrol decreased fatty liver and it was found to be in accordance with the report of Bujanda et al (2008).

It was observed that the product THERMOLIFE İXİR with PATENT NO 2017- 07930 caused weight loss in rats, decreased glucose and triglyceride values in blood, and increased HDL levels. On the 30th day following the use of the product, macroscopic examination of the necropsy performed on rats; It was determined that there was fat in various parts of body cavities and organs in the control group, fat (adipose tissue) was not observed in most of the rats in the group in which 1 gram of product was used, and the rats in the group using 1.5 grams of product had no trace or no fat tissue. It was determined that the liver tissues of the rats were covered with fat cells (steatosis), and the rats that constitute the study group: Fat cells were normal in the liver and no pathological tissue (steatosis) was observed.

As a result; In a dependent manner, the rats in groups B and C had lower Triglyceride and Glucose levels and

higher HDL levels. In conclusion, the Thermolife Ixir product causes weight loss and fat burning in rats in a dose dependent manner that is also associated with increase in HDL as well decrease in triglyceride and glucose levels.

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This study was carried out by researchers with the contribution of the pharmaceutical industry of GEA and is the summary of the animal trials of the relevant product.

Conflict of Interest
The authors declare that there is no conflict of interest in the content of the article

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