

Araştırma Makalesi / Research Article

The Determination of the Antiobesity Effects of Nicotine and Ginger In the Rats with Obesity Using Fish Oil

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Geliş Tarihi: 01.07.2019;

Kabul Tarihi: 31.08.2019

Abstract

Obesity is a disorder of energy metabolism that can cause mental and physical problems caused by excessive fat storage in the body. In this study; We aimed to determine the role of fish oil in the formation of obesity and the effects of ginger and nicotine as an antiobesity agent within complementary and alternative medicine (CAM). This study, includes 23 male rats and the groups were performed like this; Group 1 as the control (n=4), Group 2 performing experimental obesity with fish oil (n=19), Group 2a the control group (n=3, no treatment), for treatment; Group 2b the ginger applying (n=8), Group 2c the nicotine applying (n=8). In the study, weights were recorded and statistical analyzes were performed to determine the effects of obesity formation and antiobesity nutrients as well as Biochemical parameters, pathological examination and genetic analysis were applied and the results were collected. According to results, weight gain has increased in fish oil application but this gain was not found significantly important. Feeding with fish oil does not produce the expected fat and the accumulation of glycogen. In the treatment; ginger has been observed to be pathologically more effective than nicotine by removing glycogen accumulation and acting antiobesitic. Experimentally, the administration of fish oil in the obesity rat model didn't give expected weight gain. Fish oil application seems to be beneficial in terms of fatty acids consuming for health. On the contrary; the statistically significant effect of ginger, leading to more weight loss, in the anti-obesity treatment was observed.

Keywords

Antiobezite; Obesity;
Fish Oil; Ginger;
Nicotine.

Balık Yağı Kullanılarak Obezite Oluşturulan Ratlarda Nikotin ve Zencefilin Antiobezite Etkisinin Belirlenmesi

Öz

Obezite, vücutta aşırı yağ depolanması nedeniyle oluşan zihinsel ve fiziksel sorunlara neden olabilecek bir enerji metabolizması bozukluğudur. Son yıllarda, beslenme alışkanlığındaki yanlışlar sebebi ile şişmanlık insidansı artmıştır. Bu çalışmada; Balık yağının obezite oluşumundaki rolünü ve zencefil ve nikotinin bir antiobezite ajanı olarak tamamlayıcı ve alternatif tıpta (CAM) işlev ve etkilerini belirlemeyi amaçladık. Bu çalışmada 23 erkek rat kullanılmış ve gruplar şu şekildedir; Kontrol grubu olarak Grup 1 (n = 4), balık yağı ile deneysel obezite yapan Grup 2 (n = 19), grup 2a kontrol grubu (n = 3, tedavi yok), zencefil uygulayan tedavide Grup 2b (n = 8), Grup 2c nikotin uygulayarak (n = 8). Çalışmada besleme süresince tartımlar yapılarak kaydedilmiş ve obezite oluşumu ile antiobezite amaçlı verilen besinlerin etkisini belirlemek üzere istatistiksel analizler ile biyokimyasal parametreler (The total kolesterol, triglycerides, LDL ve HDL kolesterol), patolojik inceleme (karaciğer ve böbrekte) ve genetik analiz (leptin sentezi) uygulanarak sonuçlar toplanmıştır. Elde edilen sonuçlara göre balık yağı uygulamasında kilo alımının kontrole kıyasla

Anahtar kelimeler

Antiobezite;
Obezite; Balık yağı;
Zencefil; Nikotin.

arttığı ancak bu kazancın anlamlı derecede önemli olmadığı bulunmuştur. Balık yağı ile besleme beklenen yağlanmayı oluşturmadığı gibi obezitenin öncü göstergesi kabul edilen glikojen birikimi de dokularda yeterince görülmemiştir. Tedavide; Zencefilin, glikojen birikimini kaldırarak ve antiobesitik olarak etki göstererek, nikotinden patolojik olarak daha etkili olduğu gözlenmiştir. Deneysel olarak, obezite sıçan modelinde balık yağı uygulaması beklenen kilo alımını vermedi. Balık yağı uygulamasının sağlık için tüketilen yağ asitleri açısından yararlı olduğu görülmektedir. Tam aksine; Zencefilin istatistiksel olarak anlamlı etkisinin, obezite tedavisinde daha fazla kilo kaybına neden olduğu görülmüştür.

1. Introduction

Obesity is a disorder of energy metabolism that can cause mental and physical problems caused by excessive fat storage in the body. It can be seen not only in advanced ages, but also in very young ages. The onset of obesity in the majority of adults is known to extend to childhood (Zitsma *et al.* 2014).

In our country, according to the preliminary study conducted by the Ministry of Health 'Turkey Nutrition and Health Survey' in 2010; it was reported that the incidence of obesity in men 20.5%, women 41.0%, while the total rate was found to be 30.3%. In addition, the incidence of morbid obesity was 2.9% (Web 1).

Obesity causes disruptions in the functioning of both the physical appearance and the internal structure of the body and causes various chronic diseases. These chronic diseases have been reported by the World Health Organization (WHO) as hypertension, diabetes, cardiovascular diseases (Web 2).

Although obesity occurs as a result of imbalance between calorie intake and usage, various factors are effective in its etiology (Günöz 2002). Some of these factors; genetic factors, age, eating habits, physical activity, psychological factors and socioeconomic cultural level. According to the researches conducted in recent years, the decrease in physical activity level in the world and in our country, saturated fatty acids with high nutritional energy and high salt content, vitamins A and C, pulp content and calcium inadequate nutrition preference, increased time spent on television and computer shows that the prevalence of obesity has reached alarm levels among adult men and women as well as children and adolescents (Web 2).

Obesity, which is characterized by the increase in body fat mass compared to lean body mass, is defined as a chronic disease caused by the fact that the energy taken by the body is higher than the energy consumed (Web 2).

Body Mass Index (BMI) is generally used to determine obesity based on obesity classification by WHO (Web 2). BMI as a value determined by dividing an individual's body weight (kg) by the square meter (BKI = kg / m²) of height.

Table 1.: Weakness, overweight, and obesity in adults compared to BMI Classification (Web 2).

Classification	BMI(kg/m ²)	
	Principal cut-off points	Additional cut-off points
Underweight	<18.50	<18.50
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	18.50 - 24.99	18.50 - 22.99
		23.00 - 24.99
Overweight	> 25.00	> 25.00
Pre-obese	25.00 - 29.99	25.00 - 27.49
		27.50 - 29.99
Obese	> 30.00	> 30.00
Obese class I	30.00 - 34.99	30.00 - 32.49
		32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49
		37.50 - 39.99
Obese class III	> 40.00	> 40.00

Source: Adapted from WHO, 1995, WHO, 2000 and WHO 2004.

To achieve optimal health by the WHO, the median BMI for the adult population should be between 21 and 23 kg / m². However, for individuals, the target BMI should be maintained at 18.5-24.9 kg / m². 25,0-29,9 kg / m² distribution of BMI increases the risk of disease. In the case of BMI of more than 30 kg / m², the associated disease risk increases from moderate to severe. In recent years, researchers have focused on the region and distribution of fat in the body rather than the total amount of fat in the body. The region of fat in the body and its distribution are associated with morbidity and mortality by WHO (Web 2). Regional fat distribution in men and women

is genetically different. In male pattern obesity, fat is collected in the upper part of the body, waist, upper abdomen and chest (apple type). In female type obesity, fat is collected in the lower part of the body in the hips, thighs and legs (pear type).

Obesity has been classified into different forms due to differences in the way of occurrence, and the findings in each disease are not the same (Kandemir 2000).

1.1 According to Fat Distribution

- Central (Male Type) Obesity: This type of obesity is known as apple type, abdominal, belt or over the belt and central obesity. In central obesity, the amount of fat cells per unit is higher. fats collect generally in the trunk and abdomen, more than arms and legs. This type of obesity causes more metabolic diseases (Kandemir 2000).

- Subcutaneous (female type) Obesity: Other names of this type of obesity include; there are gluteofemoral, subcutaneous, subcutaneous, female type (gynecoid), pear type. The accumulation of fat is seen under the skin and on the hip in this type of obesity. Risks and hazards are less than male-type obesity (Kandemir 2000).

1.2 According to the age of onset of obesity

- Hypercellular Obesity: Obesity type is seen in childhood. The reason for this obesity is the increase in the number of fat-containing cells in the body.

- Hyperplastic Obesity: Obesity type is seen in adults. The reason for this is the increase in the volume of cells that store fat in the body. Although there is no change in the number of cells, it causes the increase in the volume of the cells (Web 2).

The main factor causing obesity is that the amount of energy entering the body, exceeds the amount of energy spent. Much of this extra energy surplus is due to increased carbohydrate and fat consumption. In recent years, the incidence of obesity has increased due to the increase in consumption of carbohydrate, fat-rich foods and carbonated beverages. Fish oil and corn syrup, which are among the factors that may cause obesity as a result of

nutrition, are frequently used in similar study to ours in recent years.

1.3 Fish Oil

Fish oil is very rich in omega-3 fatty acids. Omega-3 fatty acid decreased total cholesterol and LDL-cholesterol levels, especially triglyceride, and increased HDL levels. Cold water (dip) fishes are rich in omega-3 (Çakmakçı and Kahyaoğlu 2012).

In a study, obesity was seen in rats fed on a high fat diet. C57BL / 6J rats were fed with different rations for 19 weeks and obesity was observed at different levels in the feeding result including fish oil (Ikemoto *et al.* 1996).

1.4. Methods Used in Obesity Treatment

The goal of obesity treatment is to lower the energy intake below energy consumption in the body. Therefore, most diets are composed of cellulosic substances. These substances are not high in nutrients and causes to swelling in the stomach creates a feeling of satiety (Grenway and Smith 2000). Therefore, it should be paid attention to the intake of these substances in dietary treatment. For these purposes, it has made use of certain substances in dietary treatment as an alternative to known obesity treatments. These substances are included in supplementary foods that can be listed under complementary alternative medicine (CAM). One of the ingredients in dietary therapy is the use of ginger. The biggest and most important feature of the ginger is saturation. It promotes metabolism by evoking a sense of satiety. It is used extensively in China especially as an CAM technique (Frank *et al.* 2010).

1.5 Ginger

Ginger is one of the most widely used spices in diet studies in the world.

In our study, the ginger substance used in dietary treatment is also used with the effects of being appetite suppressant and facilitating digestion. Behavioral therapy and exercise are used as alternative treatment methods in cases where diet treatment of obesity is not sufficient.

1.6 Nicotine

Nicotine, one of the main ingredients of cigarette, promotes weight loss in humans and rats. Nicotine has been shown to play a role as an energy balance provider in the central nervous system. Especially, nicotine stimulates hypothalamic AMPK (activated protein kinase) and reduces nutrition and promotes adipose tissue accumulation leading to weight loss. According to these results, it is stated that nicotine is good for metabolic disorders and causes a general weight loss and thus can be used as an alternative treatment against obesity (Collazo *et al.* 2014).

1.7 Leptine

Leptine is also called 'obesity hormone' and is secreted from the fat cells. The levels are positively related with the body fat ratio and body mass index (Lönqvist *et al.* 1997). The most important function of leptin is to prevent obesity with a negative feedback effect on the hypothalamus creating prevention on too much weight gain (Pelleymounter *et al.* 1995, Jequier and Taaop 1999).

In this study; We aimed to determine the role of fish oil in the formation of obesity and the effects of ginger and nicotine as an antiobesity agent. We aimed to determine the importance and results of more natural nutrition by determining what should be included in our nutrition and what might be beneficial for us to consume more, especially the effectiveness of ginger and nicotine within CAM. It is thought that our findings may help to establish a daily diet program.

2. Material and Method

This study was carried out with etics rapor no: AKUHADYEK-388-14; obtained from Afyon Kocatepe University, Animal experiments local ethics committee (AKUHADYEK).

In this study; 23 Sprague-Dawley male rat with each 1-1,5 months old and 110 g weight were used. The rats were fed with standard diet and did not receive any limitation in drinking water. The environmental conditions were kept under control for all

experimental groups (12 h / 12 h light / dark cycle, 25-28 ° C ambient temperature).

The groups were performed like this; Group 1 as the control group (n=4), Group 2 performing experimental obesity with fish oil (n=19), Group 2a the control Group (only fish oil n=3, no treatment), Group 2b for treatment the ginger applying (n=8), Group 2c for treatment the nicotine applying (n=8).

Group 1 as the control (n=4) no any application;

Group 2 Fish Oil Application (n = 19): With giving orally 0,4 cc doses fish oil daily to each rat; obesity was started.

Obesity procedure was continued for 30 days. At the end of 30 days, the group was divided into two groups as 8 for the treatment of antiobesity.

Group 2a: 3 rats in the group were divided as control and no antiobesity treatment was applied.

Group 2b Therapeutic Ginger Application (n = 8): In this group, the antiobezite treatment was applied for three weeks, as daily 0.1g / 200 g ginger was given with 1cc gavage method. Weighed every week on Sunday and weekly weight tracking was done.

Group 2c Therapeutic Nicotine Treatment (n = 8): In this group, nicotine was given as an inhaler for antiobesity treatment. 8 rats were placed in the cages with the dimensions of 70x50x50cm. After the end of one cigarette was burned with the match, all the smoke was sprayed into the enclosed cage with the help of a special arrangement until it was completely finished. The rats were exposed to cigarette smoke for 20 min at this time, after which the cage was ventilated. This procedure was repeated twice a day (Waldum *et al.* 1996).

The active ingredients (fish oil, corn syrup, ginger and nicotine) were applied for 7 weeks every day at determined times according to the rats' kilograms. The fish oil was used as Zincomega fish oil for 100 ml; including every 5 ml (1 Scale) value was refined fish oil 750 mg, Vitamin C 7.5 mg, Vitamin E 1.5 mg, Vitamin A 600 mcg, Vitamin D 5 mcg. The animal feed is in the form of a standard commercial pellet (12-16 mm in diameter), containing 20-22% crude

protein, 4-5% crude oil and 5-7% crude cellulose and provides 2600-2650 kcal / kg energy. Rats consumed an average of 15-25 grams of feed per day (National Research Council 1995).

2.1 Biochemical Analyses:

The total cholesterol, triglycerides, LDL and HDL cholesterol measurements were carried out with using Roche commercial kits in Roche Cobas C501 otoanalyzer from rat serum (Roche Diagnostics International Ltd., Rotkreuz, Switzerland). The results is evaluated as mg/dl.

The Leptine level measurement in rat serum was carried out with using Rat Leptine Elisa Kits (Sunred Biological Technology, Jufengyuan Road, Baoshan District, Shanghai) in a Elisa Reader machine ChemWell 2910 (Awareness Technology, Inc. Morton Hwy. Palm City, USA). The results is evaluated as pg/ml.

2.2 Pathologic examination:

Extracted liver and kidney tissue samples were used. The results were evaluated on light microscopy, using 5 ICC Zeiss camera and ZEN software imaging (Zeiss axiolab.a1) programme.

2.3 Genetic Analysis:

After RNA isolation and cDNA Synthesis; the Real-time PCR analysis was carried out with using the Maxima sybr green/ROX qPCR Master Mix (thermo scientific, K0223) in Stratagene MxPro Mx3005P Real Time PCR machine and the data analysis is performed using the LightCycler 480 instrument channel 465-510.

M_053842,1 Rattus norvegicus leptin mRNA
 F5': CCTGTGGCTTTGGTCCTATCTG 3'
 R 5': AGGCAAGCTGGTGAGGATCTG 3'

NC-- 005111.4 Rattus norvegicus β -actin
 F 5': GAGGGAAATCGTGCCTGACAT 3'
 R 5': ACATCTGCTGGAAGGTGGACA 3' primers

were used in genetic analysis. The graph is formed by calculating the changing rates of the target gene mRNA expression levels using 2- $\Delta\Delta$ Ct methods and using the values, obtained by relative quantitation analysis (Target gene / reference gene) (Pfaffl 2001). The $\Delta\Delta$ Ct= (Ct target gene-Ct actb) subject group - (Ct target gene-Ct actb) control group formula was used in the calculations.

The Statistical Package for the Social Sciences (SPSS) 18.0 were used for the statistical analysis. ANOVA analysis was used for comparing the difference between the groups. To compare the all groups averages, the one-way variance analysis (one way anova) was used. The Kolmogorov-Smirnov test are applied to test whether normally distributed continuous variables, and p <0.05 value was set for significance level.

3. The Results:

3.1 The statistical Analysis Result:

Table 2. Weekly Weight Monitoring Table of Groups.

Groups	Cages	Beginning weight	1.week weight	2.week weight	3.week weight	4.week weight	Treatment	5.week weight	6.week weight	7.week weight
Control	5	110	130	140	165	182	-	200	220	242
Fish Oil Control	3	110	125	165	185	210	-	238	253	265
Fish Oil	9	110	135	145	167	197	Zencefil	197	195	195
Fish Oil	11	110	130	145	164	199	Zencefil	212	200	195
Fish Oil	12	110	130	165	185	217	Zencefil	217	210	203
Fish Oil	13	110	130	150	180	210	Nikotin	201	200	198
Fish Oil	14	110	145	163	184	214	Nikotin	216	216	210
Fish Oil	14	110	140	160	182	212	Nikotin	210	210	204

Table 3. Comparison of averages according to weight gain.

	\bar{x}	Std. Deviation	F	P
Fish oil	168,36	29,035		
Control	154,25	23,641	1,0000	0,374
p>0,05				

According to table 3 results; Compare to control, weight gain has increased in fish oil application compare to control but this gain was not found significantly important (p>0,05). Fish oil application seems to be beneficial in terms of fatty acids consuming for health.

Table 4: Comparison of averages according to weight gain.

	\bar{x}	Std. Deviation	F	P
Fish oil+Nicotine	207,22 ^b	6,741		
Fish oil+Ginger	202,89 ^b	8,418	22,005	0,000
Fish oil+Control	252,00 ^a	13,528		
p<0,05				

a,b,c: The difference between groups of different letters is significant.

According to the Table 4 results; There was a statistically significant difference between groups a, b, c for weight loss (p <0,05). Both weight loss effective materials (nicotine and ginger) had the same level of anti-obesity effect within fish oil application and both resulted with serious weight loss in fish oil weight gain application group.

Table 5. Comparison of fish oil with nicotine and fish oil with ginger according to weight loss.

Feeding	N	Rank average	1.quartil	3.quartil	P
Fish Oil+Nicotine	9	11	200,50	213,00	0,229
Fish Oil+Ginger	9	8	195,00	211,00	
p>0,05					

According to the results of the study conducted in Table 5, it was found that there was no statistically significant difference between the groups in terms of attenuation of nicotine and ginger (p> 0.05). Both weight loss factors showed the same antiobesity effect in fish oil application.

3.2 Biochemical Analysis Result:

Biochemical analysis showed that HDL-C cholesterol level (normal range 40-60 mg / dl) was low in fish oil + nicotine (32,56 mg / dl) group. This is support the reality of smoking is an important factor in increasing HDL cholesterol levels. There was no significant difference between groups on the basis of LDL-C, triglyceride and leptin levels.

3.3 The pathological Results:

PAS-diastase: According to these results, fish oil feeding does not constitute the expected fatigue, nor is glycogen accumulation, a leading indicator of obesity. The treating role of fish oil has been demonstrated. The ginger has been observed to be pathologically more effective than nicotine in that it prevents the formation of precursor obesity by removing glycogen accumulation almost immediately and can be accepted more effective as anti-obesity factor.

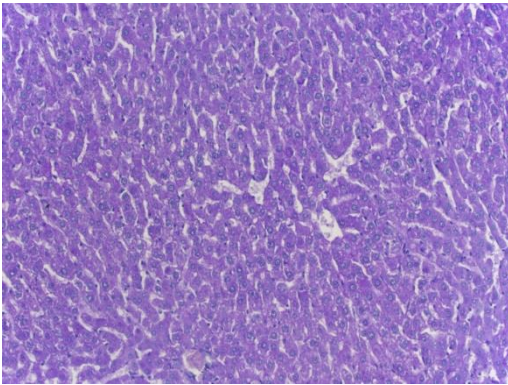


Figure 1. Fish oil feeding control group.

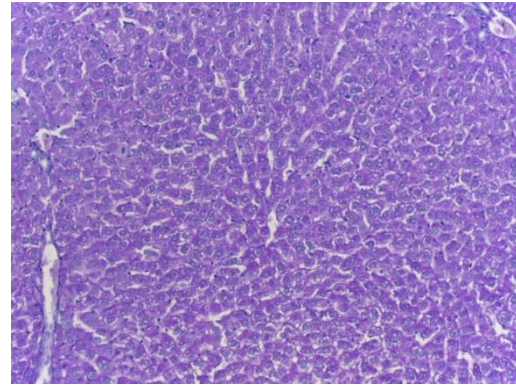


Figure 2. Control group.

PAS-diastase staining technique. Decreased glycogen staining in the portal (Fig. 1-2) and midzonal regions (Fig. 2). 20x

3.4. The genetical analysis Results:

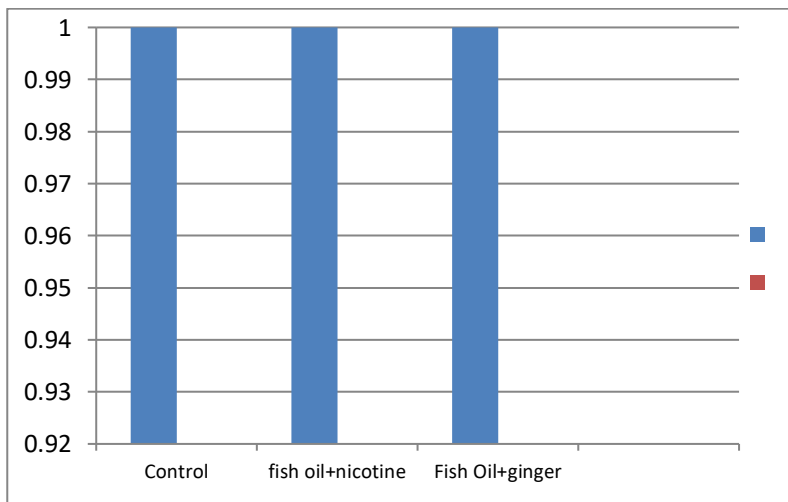


Figure 3: Leptin liver tissue sample mRNA results.

The administration of ginger and nicotine for treatment does not make a significant difference in the level of leptin secretion (column 2 and 3 compare to control column 1). This result can be interpreted like that; because using of fish oil doesn't make a significant weight increase compare to control also using of nicotine and ginger as an treatment does not make a significant difference between control and applied groups on the basis of leptin synthesis. This finding was also supported with biochemical leptin analysis result which was obtained as similar for all groups as well. It was concluded that feeding with fish oil does not make a big difference in terms of weight and even more beneficial in terms of health.

4. Discussion

El Gendy investigated the effects of omega-3 (fish oil) fatty acids on hemostatic functions in rats with obesity. They concluded that omega-3 improves insulin resistance to coagulation in rats and leads to a reduction in platelet aggregation. In our study, no statistically significant difference was observed between the weight gain of control and fish oil subjects ($p > 0.05$) (El Gendy *et al.* 2014).

In other research, high-energy content (HFD; 45 kcal) diet-fed rats leptin or green fluorescent protein (rAAV-GFP, control) responsible for the production of recombinant adeno-virus (rAAV) was injected intraventricularly for therapeutic purposes. Calorie consumption and body weight were recorded weekly until rats were 9 weeks. At the end of 9 weeks, serum leptin content, triglyceride level and insulin levels were increased in control rats fed with high energy food. It was determined that energy intake decreased in leptin treatment. According to this result, it was stated that leptin treatment prevents weight gain (Dube *et al.* 2002).

Another study; was carried out to evaluate the anti-obesity activity of barley grass juice (*Hordeum vulgare L.*) in high fat diet induced model. For in vivo studies, obesity was induced by high fat diet model in adult male Wistar rats.

Atorvastatin (10 mg/kg) was used as the standard and barley grass juice was administered at two dose levels (200 and 400 mg/kg) for a period of 60 days. Results indicated that barley grass juice (*Hordeum vulgare L.*) exhibited potent in vitro antioxidant activity. Rats administered with high fat diet for 60 days showed a significant increase in body weight, BMI, altered lipid profile and liver function markers. However, administration of barley grass juice for 60 days, profoundly decreased the bodyweight, BMI, improved lipid profile and liver function markers. Histopathological variations observed in liver of high fat diet group, and in barley grass juice treated group. All these findings indicated the antiobesity activity of barley grass juice and it can be an effective nutraceutical in the management of obesity (Thatiparthi *et al.* 2019). Another study based on the antiobesity benefits found in stingless bee honey (SBH) from *H. itama*. The research was conducted by using rats that were given a high-fat diet (HFD). In total 48 male Sprague Dawley (SD) rats were given a formulated HFD to increase the levels of obesity, the HFD was administered with a value of 0.68 g/cm². The duration of the treatment was six weeks, and the results show that the induction obesity using the HFD was successful. Following this, the rats were then treated with SBH (at dosages of 1000 mg/kg, 750 mg/kg or 500 mg/kg), with orlistat or with a placebo. Compared with typical obesity treatment methods, the one that used the three dosages of SBH showed a higher reduction in body mass index (BMI), percentage of body weight gain, adiposity index, and relative organ weight (ROW). The levels of liver enzymes (ALT, AST, and ALP) were also significantly lower in SBH-treated groups. The levels of triglycerides and LDL-cholesterol were significantly lower, while the level of HDL-cholesterol was significantly higher in comparison with the control obese group. In terms of morphological structures, the number of adipocyte cells was reduced, and the hepatocytes found in the liver were less prone to

rupturing when treated with SBH. In conclusion, the administration of SBH led to an improvement in indicators associated with obesity reduction. SBH also possesses a hepatoprotective potential which can reduce the health risks related to obesity; supporting our findings with fish oil (Mohd Rafie *et al.* 2018).

Different study based on Anti-Obesity Effect of Arq Zeera and Its main components Thymol and Cuminaldehyde in High Fat Diet Induced Obese Rats. Male Wistar rats were fed with HFD for 42 days to induce obesity. HFD-fed rats were administered with arq zeera, thymol, cumic aldehyde, thymol + cuminaldehyde and orlistat for 28 days. During the course of treatment, body weight and food intake frequently observed and after end of treatments, liver weight, insulin, leptin levels and pancreatic lipase activity were studied on all treated obese rats. The histopathology of liver was also studied. After the treatments of arq zeera and its main components, body weight, food intake, liver weight, visceral fat pad weight and the level of lipid profile, insulin, and leptin were found to be decreased and pancreatic lipase inhibition were increased. Arq zeera showed more potential antiobesity effect than orlistat. According to findings, arq zeera and its main components possessed potent antiobesity effect on high fat diet -induced obese rats supporting our findings (Haque and Ansari 2018).

In another study, the antiobesity effects between gochujangs prepared using different koji products and Tabasco hot sauce in rats fed a high-fat diet (HFD) were determined. Male Sprague-Dawley rats were fed HFD containing four different types of 10% gochujang powder or 0.25% commercial Tabasco sauce powder for 8 weeks. The body weight gain, liver and epididymal and mesenteric fat pad weights, serum leptin levels, and lipogenesis-related mRNA levels of HFD-gochujang supplementation groups were significantly decreased compared with those of the HFD group. In addition, gochujang supplement significantly reduced adipocyte size; hepatic triglyceride and total

cholesterol levels. These effects were greater in the gochujang-supplemented groups than the Tabasco hot sauce-supplemented group. The current results indicated that the gochujang products have the potential to reduce fat accumulation and obesity (Son *et al.* 2018).

In different study, the antiobesity effects of quercetin-rich supplement (QRS), which contain quercetin, lycopene, taurine, and litchi flower extract, on a high-fat diet (HFD)-induced obese rats were investigated. The rats that consume HFD with QRS (185 mg/kg rat) have significantly modulated the final body weights [490 ± 11 (HFD) \rightarrow 441 ± 11 (HFD+QRS) g], total body fat [112.9 ± 4.5 (HFD) \rightarrow 86.6 ± 5.7 (HFD+QRS) g], liver weights [14.8 ± 0.4 (HFD) \rightarrow 12.6 ± 0.4 (HFD+QRS) g/rat], and the serum TG [102.5 ± 7.3 (HFD) \rightarrow 90.7 ± 6.5 (HFD+QRS) mg/dL] to a level that resembled the regular diet-consumed rats ($p < 0.05$). In the histological analysis, quercetin-rich formulation supplemented groups presented a much less lipid accumulation and smaller size of adipocytes supporting our study findings (Ting *et al.* 2018).

Another study based on determination of *Vernonia amygdalina* (VA) leaves into high-fat diets on some biological markers of adiposity. Experimental diets consisted of CD (control diet); HFD (high-fat diet); and HFD- VA (HFD containing 10% *Vernonia amygdalina* leaves) supplementation. Fifteen male Wistar rats were randomly divided into three groups of five animals each. After twelve weeks of feeding, serum lipid profile, blood glucose concentrations, body weight, adiposity index, feed intake, fecal loss and relative organ weight were investigated. As a result; *Vernonia amygdalina* (VA) inhibited HFD-induced weight gain and adiposity in rats. HFD-induced obese rats showed a significant increase in the levels of serum TG and TC compared to rats on a normal diet. However, the levels of serum TG, TC, LDL-C in HFDVA rats reduced significantly relative to the levels in HFD rats. These results suggested that incorporation of *Vernonia amygdalina* into high-fat diets may have therapeutic potentials

for obesity and related metabolic disorders; supporting our findings of obesity effect of fish oil and antiobesity effect of ginger (Ekeleme-Egedigwe *et al.* 2017).

5. Conclusion

Experimentally, the administration of fish oil in the obesity rat model didn't give expected weight gain. Fish oil application seems to be beneficial in terms of fatty acids consuming for health. In addition, it was observed that statistically significant effect of ginger, leading to more weight loss, in the anti-obesity treatment. It can be said that our experimental model provides the desired aim and success in this aspect.

The rats used in this study were used as a human model in a sense. After the formation of obesity with fish oil, in the treatment we used ginger and nicotine. Our results showed weight gain has increased in fish oil application compare to control but this gain was not found significantly important in the formation of obesity, and ginger as an antiobesity treatment come to forward. These findings give a chance to use alternative medicine with a more relieble results especially for obez people who have not found a cure with scientific methods. On the other hand, it is thought that advanced studies with wide participation are needed with effective treatment options in order to prevent pathology of obesity disease at the molecular level and to prevent the disease from occurring before.

Fundings

This study was supported by AKU-BAP Project No: 14.SAĞ.BİL.05.

6. References

Collazo, P., Pablo, B., Martínez, D.M., Johan, F., Carlos, D., Ruben, N. and Miguel, L., 2014. Nicotine Improves Obesity and Hepatic Steatosis and ER Stress in Diet-Induced Obese Male Rats. *Endocrinology*, **155**(5), 1679.

Çakmakçı, S. and Kahyaoğlu, D.T., 2012. Yağ Asitlerinin Sağlık ve Beslenme Üzerine Etkileri. *Türk Bilimsel Derlemeler Dergisi*, **5**(2), 133-137.

Dube, M.G., Beretta, E., Dhillon, H., Ueno, N., Kalra, P.S. and Kalrasatya, P., 2002. Central Leptin Gene Therapy Blocks High-Fat Diet-Induced Weight Gain, Hyperleptinemia, and Hyperinsulinemia Increase in Serum Ghrelin Levels. *Diabetes*, **51**,1729-36.

Ekeleme-Egedigwe, C.A., Ijeh, I.I. and Okafor, P.N., 2017. Modulatory effects of dietary supplementation by *Vernonia amygdalina* on high-fat-diet-induced obesity in Wistar rats. *Acta Scientiarum Polonorum, Technologia Alimentaria*, **16**(4), 431-442.

El Gendy, A.A. and Abbas, A.M., 2014. Effect of omega-3 fatty acids on haemostatic functions in urocortin-treated obese rats. *Journal of Physiology and Biochemistry*, **70**(3), 809-20, 2014.

Frank, C., Eteng, M.U. and Umoh, I.B., 2010. Protective Effects of Ginger Towards Cadmium-Induced Testes and Kidney Lipid Peroxidation and Hematological Impairment in Albino Rats. *Journal of Medicinal Food*, **12**(3), 47-53.

Grenway, F.L. and Smith, S.R., 2000. The future of obesity research. *Nutrition*, **16**, 976-982.

Günöz, H., 2002. Obezite, 202, *Pediatric 1. Nobel Tıp Kitapevi*, 221-226.

Haque, M.R. and Ansari, H.S., 2018. Anti-Obesity Effect of Arq Zeera and Its Main Components Thymol and Cuminaldehyde in High Fat Diet Induced Obese Rats. *Drug Research (Stuttg)*, **68**(11), 637-647.

Ikemoto, S., Mayumi, T., Nobuyo, T., Kayo, M., Hiroshige, I. and Osamu, E., 1996. High-fat diet-induced hyperglycemia and obesity in mice: Differential effects of dietary oils. *Metabolism*, **45** (12), 1539-1546.

Jequier, E. and Taaop, L., 1999. Regulation of Body Weight in Humans. *Physiological Reviews*, **79**(2), 451-480.

- Kandemir, D., 2000. Obezitenin Sınıflandırması ve Klinik Özellikleri. *Katkı Pediatri Dergisi*, **21 (4)**, 500-506.
- Lönnqvist, F., Nordfors, L., Jansson, M., Thörne, A., Schalling, M. and Arner, P., 1997. Leptin Secretion from Adipose Tissue in Women. *The Journal of Clinical Investigation*, **99(10)**, 2398-2404.
- Mohd Rafie, A.Z., Syahir, A., Wan Ahmad, WAN., Mustafa, M.Z. and Mariatulqabiah, A.R., 2018. Supplementation of Stingless Bee Honey from *Heterotrigna itama* Improves Antiobesity Parameters in High-Fat Diet Induced Obese Rat Model. *Evidence Based Complement ary and Alternative Medicine*, **2018**, 6371582.
- National Research Council., 1995. Nutrient Requirements of Laboratory Animals Fourth Revised Edition, National Academy of Sciences, Washington, DC.
- Pelleymounter, M.A., Cullen, M.J., Baker, M.B., Hecht, R., Winters, D., Boone, T. and Collins, F., 1995. Effects of the obese gene product on body weight regulation in ob/ob mice. *Science*, **269**, 540-543.
- Pfaffl, M.W., 2001. A new mathematical model for relative quantification in real time RT-PCR. *Nucleic Acids Research*, **29(9)**, e45.
- Son, H.K., Shin, H.W., Jang, E.S., Moon, B.S., Lee, C.H. and Lee, J.J., 2018. Comparison of Antiobesity Effects Between Gochujangs Produced Using Different Koji Products and Tabasco Hot Sauce in Rats Fed a High-Fat Diet. *Journal of Medicinal Food*, **21(3)**, 233-243.
- Thatiparthi, J., Dodoala, S., Koganti, B. and Kvsrg, P., 2019. Barley grass juice (*Hordeum vulgare L.*) inhibits obesity and improves lipid profile in high fat diet-induced rat model. *Journal of Ethnopharmacology*, **238**, 111843.
- Ting, Y., Chang, W.T., Shiau, D.K., Chou, P.H., Wu, M.F. and Hsu, C.L., 2018. Antiobesity Efficacy of Quercetin-Rich Supplement on Diet-Induced Obese Rats: Effects on Body Composition, Serum Lipid Profile, and Gene Expression. *Journal of Agricultural and Food Chemistry*, **66(1)**, 70-80.
- Zitsman, J.L., Inge, T.H. and Reichard, K.W., 2014. Pediatric and adolescent obesity: Management, options for surgery, and outcomes. *Journal of Pediatric Surgery*, **49(3)**, 491-4.
- Waldum, H.L., Nilsen, O.G., Nilsen, T., Rervik, H., Syversen, U., Sandvik, A.K., Haugen, O. A., Tarp, S.H. and Brenna, E., 1996. Long-term effects of Inhaled Nicotine. *Life Sciences*, **58(16)**, 1339-1346.

Internet resources

- 1-<https://hsgm.saglik.gov.tr/tr/obezite/turkiyede-obezitenin-gorulme-sikligi.htm> (26.11.16)
- 2- <http://www.who.int/media-centre/factsheets/fs311/en/> (26.11.2016).