ANTI-HYPERLIPIDEMIC AND WEIGHT REDUCTION EFFECT OF DIFFERENT DOSES OF FERULAGO ABBREVIATA C.C. (TOWNS (APIACEAE)) IN MALE ALBINO RATS

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ABSTRACT

Background

A large number of studies on the active compound of herbal medicine proved that plant extract is very effective and safe in patients especially in hyperlipidemia, regarding the International Lipid Expert Panel (ILEP), pharmaceutical compounds containing herbal monomers and derivatives are very effective and safe in the treatment of hyperlipidemia and reducing body weight, for example, onion, garlic, flaxseed oil, celery and Ferulago angulate (Schltdl.) Boiss Ferulago abbreviata C.C. Towns. (Apiaceae; Kurdish: Chnor) are another species of the family of Apiaceae used in this study to investigate their effect on the serum lipid profile and body weight.

Objectives

Evaluation and comparing effect of different doses of Ferulago Abbreviata as anti-hyperlipidemia, and weight reduction.

Materials and Methods

We divided fifteen male albino rats into 3 equal groups(n=5) as follows: (group HFD, FA500, and FA700), collected blood from them and weighted each of them as a baseline, then after six weeks fed a high-fat diet (HFD) to all the groups collected blood and weighted again, and started different regimens of treatment until week ten as follows: HFD group: received a fat-rich diet only; FA500 group: received a fat-rich diet, plus extracts of Ferulago abbreviata at a dose of 500mg/kg; FA700 group: received a fat-rich diet, plus extracts of Ferulago abbreviata at a dose of 700mg/kg. At the end of the study, we collected the blood for investigation of the level of lipid profile and weighted them.

Results

By added extract of Ferulago abbreviate to hyperlipidemic rats the level of cholesterol, TG, LDL, VLD, Atherogenic index and body weight were significantly reduced and HDL level elevated, this finding was significant, also the high dose of the plant considerably very effective in lowering the lipid profile but in reducing the weight of the rats has the same result of a lower dose.

Conclusion

Using hydro-alcoholic extracts of Ferulago abbreviata can decrease the lipid profile and weight significantly.

Keywords: *Natural product, Ferulago abbreviata, Anti-hyperlipidemia, weight gain.*

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INTRODUCTION

Hyperlipidemia is an abnormal process of lipid metabolism, which increased the risk of Coronary Artery Disease, Ischemic stroke, cardiovascular disease, Myocardial Infarction (MI), Cerebrovascular Accident (CVA) [1]. It is divided into primary and secondary, fortunately, most of the time secondary dyslipidemia which accounted for 40% of all the cases, can be turned into the normal situation if the causative factors are withdrawing or treating [2]. The American Heart Association had identified different treatments for decreasing hyperlipidemia[3], for example, Statins, Niacin, Fibrates, Bile acid-binding resins, cholesterol absorption inhibitor, Omega-3 fatty acids, Inhibition of microsomal triglyceride transfer protein (MTTP), proprotein convertase subtilisin/Kexin type 9 (PCSK9) inhibition, unfortunately, the long-term using of these medications can cause adverse effects, therefore continue researching for new hypolipidemic drugs especially natural product is important for preventing and treatment dyslipidemia and it is a hard process [4, 5].

Weight gain and obesity is another global health problem, the prevalence of overweight according to the world health organization (WHO) in 2014, about 39% of the population are overweight and 13% of them are obese, besides the physical disability overweight consider as a risk factor for various chronic diseases such as; cardiovascular disease, hypertension, a certain type of cancer and type two diabetes [6, 7],. the strategy for reducing weight include; decrease dietary fat and sugar consumption and changing it to normal food or low fatty food, consumption of natural fruit and vegetables, increase physical activity [8,9].

In most developing country herbal medicine and traditional medicine have an important role in the management of different types of disease in humans, because of; a) efficacy and safety of herbal medicine, b) acceptable and interest by the community, c) lower cost of and d)movement toward self-medication [10]. different parts of plants used such as seeds, flowers, berries, leaves, barks, stems, and roots for the treatment of a variable medical condition, using of the plant as therapeutic had a long history from the ancient day but in the century of 19th, the scientist considered it as important part from medicine especially after identified chemical component of plant and extraction of active ingredients, according to the (WHO) reported about 80% of human globally have faith to botanical medicine [11]. Worldwide a lot of plants are used for the treatment of hyperlipidemia such as flaxseed, celery eta. Ferulago abbreviata C.C. Towns. (APIACEAE; K: Chnur) is another example which under the concern of scientists beuseca the family of this plant have therapeutic properties and act as anti-hyperlipidemic medicine[12], antioxidant [13], antibacterial [14], anticancer [15], and anti-inflammatory [16] agents.

Aims of the study

To evaluate and compare the effectiveness of different doses of Ferulago abbreviata C.C. Towns extract on lipid profile and body weight in hyperlipidemic rats after 4 weeks of administration.

MATERIALS AND METHODS

Ethical and scientific Consideration: approval from the Ethical Committee of the college of the Medicine/ University of Sulaimani was taken officially.

Animal Selection: Fifteen male albino rats were purchased from the college of the education biology/ university of Sulaimani, initially their weight ranged between 180 gm to 300 gm and housed in standard and clean cages (five rats per cage) under controlled environmental conditions and acclimated for one-week prior starting the study.

Experimental design: the experimental study started on the 20th of September 2019 until the first of December 2019. Fifteen male albino rats were divided into 3 equal groups(n=5) as follows: (group HFD, FA500, and FA700), collected blood from them and weighted each of them as a baseline, then after six weeks fed a high-fat diet (HFD) to all the groups collected blood and weighted again, and started different regimens of treatment until week ten as follows: HFD group: received a fat-rich diet only; FA500 group: received a fat-rich diet, plus extracts of Ferulago abbreviata at a dose of 500mg/kg; FA700 group: received a fat-rich diet, plus extracts of Ferulago abbreviata at a dose of 700mg/kg. At the end of the study, we collected the blood for investigation of the level of lipid profile and weighted them.

Hyperlipidemia development: hyperlipidemia was developed in the rats by daily fed a preparation which was composited of 79% standard diet and 21% saturated fat for more than six weeks [17].

Preparation of Plant Extract: Ferulago abbreviata C.C. Towns grows on rocky place, cliffside, and eroded sandy soil. Which was collected in June from

Piramagrooun(Zewe) mountain north East of Kurdistan Iraq, which was identified by Kurdistan Botanical Foundation (KBF.) (Identified by Haines, R.W. (14-7-1961) in the herbarium of Royal Botanic gardens), the areal part of the plant dried under the shade and then crushed in to powder with a blender. 100gm of the powdered was solved in 100 ml of 75% ethanol then put in shaking incubator at room temperature(25°C) for 72 hours, then the extract was filtered used Whatman filter paper No. 1, then for evaporating ethanol from the extracted material used vacuumed rotary evaporator at a temperature of 37 °C and rotate at 180 rpm, then put in lyophilizing for 48 hours to evaporate water finally put the dried powder in -20 °C until use.

Study Measurements

The blood samples after collected directly from the rat's retro-orbital vein at the week (0 to six) and directly from the rat's heart at week 10 were centrifuged at 3500 gm for 20 min, lipid profile (except cholesterol) was measured using commercially available kits, Serum samples were analyzed with a Cobas C 3011, To investigate the possible effects of the plant, also the cholesterol was measured using rat cholesterol ELISA kit.

Statistical Analysis

To compare the measured biomarkers among the animal groups, a one-way analysis of variance (ANOVA) test followed by a Tukey test was used. P-values of 0.05 or less were considered statistically significant, the data expressed as mean ± standard error, the statistical analyses were performed by using SPSS (version 26).

RESULTS

At the end of week six the level of the cholesterol, triglyceride, low-density lipoproteins (LDL), very-low-density lipoproteins (VLDL) and atherogenic index of all the groups were rose significantly as a result of high-fat diet (Table 1), but after four weeks treated with the different regimen, the level of all parameters was significantly reduced in both groups which taken the plant but the stronger dose more effective also in high dose the level of high-density lipoproteins (HDL) more significantly rose and it is indicated that high dose more effective (Table 1).

Regarding the weight of the animals: the weight of all rats rose in week six, but in week 10 only the weight of the HFD group continue on elevation, but the weight of two other groups is declining the percentages of variation can be shown in the (Table 2), and the weight change of each group separately clarified in the (Figure 1).

Table 1. Lipid profile of different groups of rats at a different time (week 0, 6, and 10) for comparing the effect of the Ferulago abbreviata (n=15) (mean ±SEM)

Name	week 0	week 6	week 10
Cholesterol			
HFD			350.4±32 [b]
FA500mg	74.9± 0.9[a]	389.5 ± 28.9[b]	121± 2.9 [a]
FA700mg			99.1 ± 5.5 [a]
Triglyceride			
HFD			332±36 [b]
FA500mg	43.5±1.2 [a]	373.2±22 [b]	103.6±15.8 [a]
FA700mg			90.6±12 [a]
LDL			
HFD			25.2±1.4 [b]
FA500mg	17.9±0.6 [a]	28.36±0.9 [b]	17.4±3.3 [a]
FA700mg			16.7±1.2 [a]
VLDL			
HFD			44.8±4.2 [b]
FA500mg	8.6±0.3 [a]	74.6±4.5 [c]	20.7±3.2 [a]
FA700mg			18.1±2.4 [a]
HDL			
HFD			20.4±2 [b]
FA500mg	15.1±0.4 [a]	22.9±0.48 [b]	21±1 [b]
FA700mg			32.3±1.5 [c]
Atherogenic Index			
HFD			1.21±0.02 [c]
FA500mg	0.46±0.2 [a]	1.2±0.03 [c]	0.68±0.075 [b]
FA700mg			0.43±0.05 [a]

*** a, b, c: Different superscript letters denote significant difference within a row at p < 0.05**

Table 2. The percent of weight gain and reduction of the rats (n=15) at week 6 and week 10 (mean ±SEM).

Duration	HFD only	HFD+FA500mg	HFD+FA700mg
At week 6	↑ 1.2±0.33[a]	↑ 1.4±0.035 [b]	↑ 1.3±0.05 [a, b]
At week 10	↑ 1.02±0.023 [b]	↓ 0.87±0.016 [a]	↓ 0.88±0.19 [a]

*** a, b, c: Different superscript letters denote significant differences within a row at p < 0.05 between the groups.**

***↑:Increase, ↓: Decrease.**

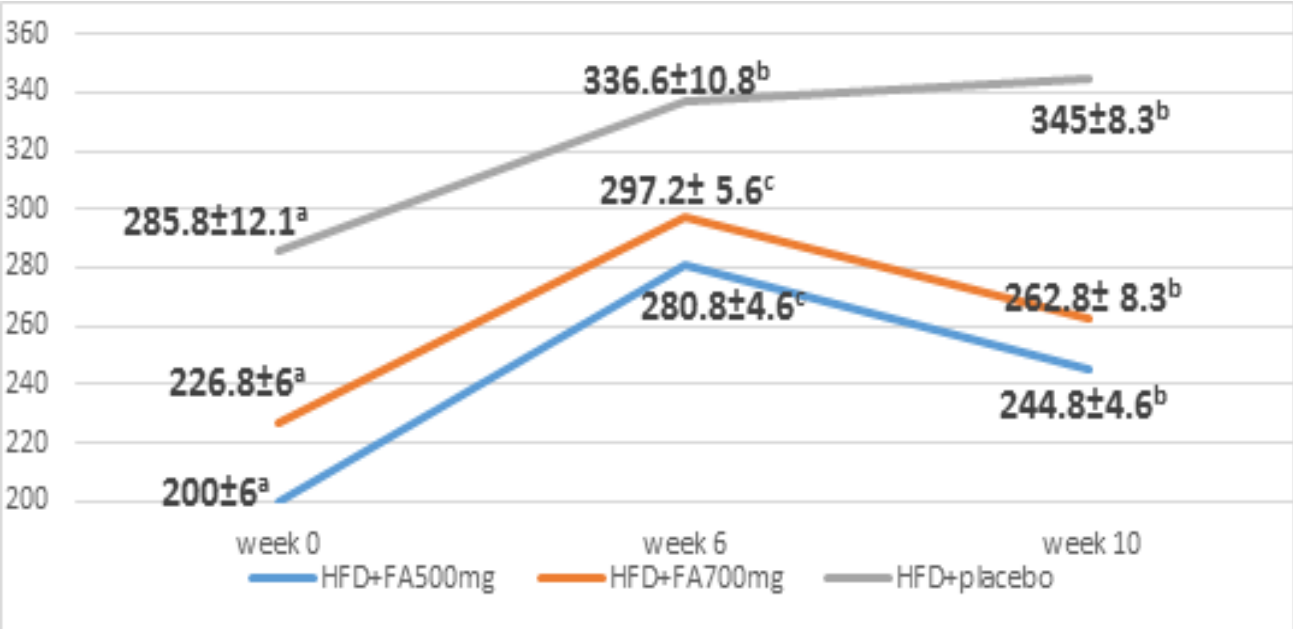

Figure 1. The weight of the rats at different weeks (weeks 0, 6, and 10) (n=15) (mean ±SEM).
*** a, b, c: Different superscript letters denote significant differences within a row at p < 0.05.**

DISCUSSION

European Society of Cardiology (ESC) and its partners such as European Atherosclerosis Society (EAS) and some other organizations suggested a large number of guidelines for the management of dyslipidemia, one of the newest pieces of evidence suggested that starting treatment even hyperlipidemia by retention the cholesterol, LDL and other forms of cholesterol to normal [18].

In the present study after six weeks of fed HFD to rats, the level of cholesterol, TG, LDL, and VLDL elevated and HDL reduced significantly, so hyperlipidemia induced in the rats by atherogenic diet. These results were following the findings of Munshi & *et al*. 2014 [19] then after 28 days of treatment with different dose of the plant we found that both doses of hydro-alcoholic extraction of *Ferulago abbreviata* (500 mg/kg-700 mg/kg) showed a beneficial effect in the reducing level of lipid profile and rose in level HDL of hyperlipidemic rats, and if we concerning the stronger dose of *Ferulago abbreviata* (700 mg/kg) more powerful than the lower dose, this results of hypolipidemic effect agree with the finding of Mahmoud R. et al 2014 [12] who confirmed the hypolipidemic effect of other species of the same family at a dose of (400mg/kg and 600 mg/kg).

The mechanism behind the hypolipidemic effect of *Ferulago abbreviata* not clear but may be due to several constituted in their structure such as the phenolic group which may inhibition the enzyme HMG-CoA reductase as can be seen in the finding of Espindola et al, 2016 [20], in despite the reducing in the level of TG can entail elevating the lipolysis as a result of increasing the catabolism of VLDL and chylomicrons, or maybe as a result of lipoprotein lipase activity or elevate excretion of cholesterol and bile acid through the fecal route, also reduced the VLDL concentration by inhibiting denovo TG synthesis [21], or may by prevent the absorption of cholesterol through formation insoluble deposition of dietary cholesterol, and stimulation synthesized of cholesterol that excretion into the intestinal duct and inhibit there absorption Kajimoto, O. & *et al*. 2003 [22].

Also, this plant may have alkaloid in their composition which affect the lipid profile as showing in the finding He, Kai, et al. 2016 [23] who identified the effect of alkaloid, suggest that anti-hyperlipidemic effect of alkaloid occur as a result of various mechanism such as inhibition of HMG COA reductase, elevated the level of LDL-receptor and raising the level of CYP7A1 level may have a role in reducing cholesterol level in the plasma, also it inhibits reabsorption of bile acid and cholesterol after excretion into the intestine.

Regarding body weight: weight gain is phenomena characterized by the accumulation high amount of fat in the adipose tissue, in the last few decades classified as a

health disorder and consider as a risk factor of several various diseases, that is why weight loss considerably important and many methods are developed to reduce body weight among them deity therapy, physical activity and medication [24].

After six-week fed high fatty diet to all the groups, there was a percentage rose in the body weight can be noted in all rats, it was not agreed with the finding of Buettner, R., & et al [25], while it was agreed with the finding of Buyukdere Y, & et al 2019 [26].

At the week 10 the percentage of weight increase continued in HFD groups, while those group which used *Ferulago abbreviata* at both doses (500 mg/kg and 700 mg/kg) were significantly reduced weight of rats, the exact mechanism of action is unclear but may be due to the effect of polyphenol which inhibits the action of leptin or maybe as a result of inhibiting food absorption from the intestine, but both doses of the plant have a similar result in weight reduction.

Concluion

Ferulago abbreviata extract has an anti-hyperlipidemic activity which reduces the serum level of cholesterol, TG, LDL, VLD and raises HDL, also it can result in reducing body weight, that is why consider as an important agent for cardioprotective, for optimal dosage, more safety, and the best time of administration of this plant further studies are needed.

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Conflict of Interests

Regarding this paper, the authors declare there is no considering conflict

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