Lipid profile of Hyperlipidemic mice induced by dexamethasone treated with 105 herbals oil mixture

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Abstract

Background: Lipid profile is a panel of blood tests that serves as an initial broad medical screening tool for abnormalities in lipids, such as cholesterol and triglycerides.

Objective: This study estimates the activity of mixture of three herbal seed oil on the lipid profile of hyperlipidemic mice induced by glucocorticoid drug.This mixture 105 composed of: 30% Petroselinumcrispum, 35% Lepidiumsativumand 35% Eruca sativa seed oil.

Patients and Methods: The study was conductedusing 30 Swiss albino mice of 4 weeks age, which were divided into three equal groups. First group treated with dexamethasone drug, the second group treated with dexamethasone plus oil mixture,while the third group served as control.

Results: It showed that the mixture [105] had the activity to decrease the lipid profile of hyperlipidemic mice induced by dexamethasone after treatment with 7, 14, 21 days.

Conclusion: Petroselinumcrispum, Lepidiumsativumand Eruca sativa seed oil have activity to decrease the levels of lipid profile in dexamethasone –induced hyperlipidemia mice.

Key words: Petroselinumcrispum, lepidiumsativum, eruca sativa, seed oil, dexamethasone herbal oil.

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Introduction

Glucocorticoids are used for years in the treatment of autoimmune and allergic diseases as through exogenous administration of excesses glucocorticoids acts as potent anti- inflammatory agents. They have several inverse effects including cardiovascular disorders such as hypertension and athero- sclerosis, obesity, and osteoporosis [1]. Dexamethasone is a drugis potent 25 times more than cortisol in its glucocorticoid effect while having minimal mineralo corticoid effect [2].

Cholesterol [CH] is waxy water-insoluble material, it plays a critical role in certain hormone production, build up cell membranes, and also it is needed to insulate nerves. Their transports inside lipoproteins low density lipoprotein [LDL] and high density lipoprotein [HDL], Triglycerides are the most common type of fat in the body. LDL, HDL and VLDL compose the total cholesterol count in the body [3]. About one forth to one third of blood cholesterol is carried by HDL which transports cholesterol from the blood vessel

to liver to be excreted from the body [HDL is called the good cholesterol] [4], while LDL is called bad cholesterol because of its ability to build up fatty deposits in artery walls and increase the risk of heart attack and stroke [3].

Petroselinumcrispum [Parsley] is a species under Apiaceae family cultivated in the Mediterranean region [5]. It is a bright, green, biennial herb, fern-like leaves. Typical height of parsley is 12 to 15 inches. When it produces bloom and seed-producing stems it can reach a height of 27 to 30 inches. It has highly nutrients value contain vitamins A, B, and C and the minerals iron, calcium, and magnesium, with antiseptic effect because of presence of high amounts of chlorophyll [5].

Parsley contain Phenolic compounds include various phenolic acids, notably caffeic acid [6] also contains poly acetylenes, which are toxic to fungi, bacteria and some cancer cells, as well as having anti-inflammatory and anti-platelet aggregating activity. Also, it has neurotoxic effects that induce allergic responses in the skin. Parsley compounds have ability to reduce tumor formation in animals [7]. The antioxidant properties of parsley essential oil [probably extracted from seeds, which are likely to differ in composition from the leaves], [7] found relatively strong antioxidant activity according to the β-carotene bleaching assay. The major compounds identified in parsley essential oil in that study were myristicin [32.75%] and apiol [17.54%].

Lepidiumsativum [Garden cress] is a polymorphous species. Garden cress is fast growing edible plant. The crop is mainly cultivated for seeds because of its medicinal effects. Which are good source of protein, fat, calcium, iron and phosphorous. The properties of the seeds are described as diuretic, laxative, tonic, aphrodisiac, and galactogogue, The seeds are also used in the treatment of diarrhea, diabetes, high blood pressure, respiratory disturbances, rapid fracture healing, hyper -cholesterolemia and anemia [8]. The seeds on steam distillation yield a volatile oil which showed pronounced estrogenic activity in immature rats when it was given in the diet [9].

Erucastiva is a species from Brassicacae family, known as 'jarjeer' in Arabic area. it's a tulip vegetable and spice rocket especially among Middle Eastern populations and Europeans. The plant has therapeutic activities include gastric anti-ulcer potential [10] inhibition of tumorigenesis, and hepato protective activities [11]. It's used as a diuretic stimulant, and in the treatment of stomach disorders and scurvy Tender leaves and seed known as aphrodisiac plant also used as a carminative and improve digestion [12].It has been reported that the rocket seed ethanolic extract possesses potent antioxidant and renal protective and diuretic activities Phytochemical studies of rocket leaves and seeds have revealed the presence of glucosinolates [13].

This study aims to estimates the activity of mixture of three herbal seed oil on the lipid profile of hyperlipidemic mice induced by glucocorticoid drug.This mixture 105 composed of: 30% Petroselinumcrispum, 35% Lepidiumsativumand 35% Eruca sativa seed oil.

Patients and Methods

Material

The mixture 105 composed of: 30% Petroselinumcrispum, 35% Lepidiumsativum and 35% Eruca sativa seed oil, which was purchased from local market of Baghdad city, Iraq, stored in a dark bottle in the refrigerator until use.

Hyperlipidemia induction

Dexamethasone sodium phosphate ampoules of 8 mg/2 ml [H-tech international enterprises Co. ltd] were used for inducing hyperlipidemia at a dose [1mg/kg of body weight intramuscularly daily for 22 days [3].

Animals

Thirty Swiss albino mice 4 weeks age weighing 24- 27 g were obtained from animal house of medical College of Baghdad University placed under standard diet and water belonged the period of experiment in the metal cages. These animals were divided into three equal groups:

1-First group were administrated 1mg\ kg weight. of dexamethasone once daily intramuscular injection for 22 days.

2-Second group were administrated the same dose of dexamethasone and same route of administration back traced with 0.1 ml of 105 oil mixture after one hour orally by gavages needle for 22 days.

3-Third group was served as control group.

Sample collection

Blood samples were collected at zero, 7, 14 and 21 days after overnight fasting from the orbital venous into clean dry anticoagulant free centrifuge tube allowed to clot. Serum was separated after centrifugation at 1500 rpm for 15 minutes [12]. Lipid profile was estimated calorimetrically. All animals were weight at the same days of sample collection.

Statistical analysis

Collected data were tabulated and needed statistical analyses were done using the computer data processing [SPSS, version 18]. Data are expressed as means ± standard deviation (M±SD). Comparisons were done using t- test. A probability value [P] of ≤ 0.05 was considered to be statistically significant.

Results

Hyperlipidemia defined as an increase in blood plasma lipid and or lipoprotein lipoprotein fractions such as increase of serum total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG) concentrations, and a decrease in the high-density lipoprotein (HDL) concentration. There are some causes either genetic defects its familial or called primary hyperlipidemia or acquired or called secondary which caused from some disorder or disease like hypothyroidism, diabetes, and nephrotic syndrome, as well as the dietary intake and alcohole. Or it may occur without any specific cause (idiopathic) [14].

Table (1): Effect of dexamethasone on lipid profile of mice.

Groups		Cases [n=10] Mean ± SD	t	P-value	C.S
CH mg/dl cholesterol	Control	146.6 ± 4.766	6.900	0.000	P< 0.01 [HS]
	Dexamethasone	163.4 ± 4.575			
TG mg/dl triglyceride	Control	125 ± 3.972	7.861	0.000	P< 0.01 [HS]
	Dexamethasone	140.8 ± 6.512			
LDL mg/dl low density lipoprotein	Control	108.3 ± 4.668	10.136	0.000	P< 0.01 [HS]
	Dexamethasone	128.2 ± 5.095			
VLDL mg/dl Very low density lipoprotein	Control	24.7 ± 3.917	2.661	0.026	P< 0.05 [S]
	Dexamethasone	28.5 ± 1.958			

The results in Table 1 appear high significant [HS] increase P<0.01 influence of dexamethasone in lipid profile in all groups under study with the exception of the latter very low density lipoprotein [VLDL] was a significant increase in the level at P< 0.05 in contrast with control group.

Table (2): Effect of 105 mixture oil treatment on hyperlipidemic mice induced by dexamethasone after 7 days

Groups		Cases [n=10] Mean ± SD	t	P-value	C.S
CH mg/dl Cholesterol	Dexamethasone	163.4 ± 4.575	12.720	0.000	P< 0.01 [HS]
	After 7 days	138.5 ± 4.089			
TG mg/dl Triglyceride	Dexamethasone	140.8 ± 6.512	20.755	0.000	P< 0.01 [HS]
	After 7 days	100.1 ± 4.533			
LDL mg/dl low density lipoprotein	Dexamethasone	128.2 ± 5.095	31.953	0.000	P< 0.01 [HS]
	After 7 days	71.8 ± 4.872			
VLDL mg/dl Very low density lipoprotein	Dexamethasone	28.5 ± 1.958	6.926	0.000	P< 0.01 [HS]
	After 7 days	20.1 ± 2.846			

Statistical results showed, as shown in Table 2 High significant decreases [HS] in lipid profile of all group subjected to experiment after 7 days of treatment with the oil mixture compared to the dexamethasone group.

Table (3): Effect of 105 mixture oil treatment on hyperlipidemic mice induced by dexamethasone after 14 days

Groups		Cases (n=10) Mean ± Std. Deviation	t	P-value	C.S
CH mg/dl cholesterol	Dexamethasone	163.4 ± 4.575	21.853	0.000	P< 0.01 (HS)
	After 21 days	105.6 ± 6.114			
TG mg/dl triglyceride	Dexamethasone	140.8 ± 6.512	22.425	0.000	P< 0.01 (HS)
	After 21 days	95.3 ± 3.466			
LDL mg/dl low density lipoprotein	Dexamethasone	128.2 ± 5.095	60.532	0.000	P< 0.01 (HS)
	After 21 days	35.1 ± 3.035			
VLDL mg/dl Very low density lipoprotein	Dexamethasone	28.5 ± 1.958	10.002	0.000	P< 0.01 (HS)
	After 21 days	19.8 ± 3.458			

The statistical analysis shown in Table 4 high moral decline of the image of the blood significant decline in lipid profile in all experimented groups after 21 days from treatment.

Discussion

The results of dexamethasone treatment have shown a significant increase in cholesterol may be due to that dexamethasone inhibit nitric oxide synthesis which have a role in regulation of lipid levels in blood [3]. The study agrees with Severino *et al*, 2002 and Bruder, *et al* 2004 and Azeez. And Kheder, 2012 they find significant increases in the level of serum CH and TG after treatments by dexamethasone of rats and mice respectively. [3][15][16] The highly significant effect on Triglyceride levels could be due to stimulatory effect of

dexamethasone to produce and secretion of lipoproteins mainly very low density lipoprotein from liver that rich in triglyceride [17], or may be through stimulate VLDL formation from intestine, the low level of liver lipoprotein lipase activity could have been responsible for the high VLDL–Triglyceride level and VLDL also causes imbalance in lipid metabolism [17][18] or may be because of insulin resistance accomplished by dexamethasone which decrease impact of insulin on adipose tissue and liver officiating to secret triglyceride from liver and debars ability of tissue to riddance lipoproteins from blood [19]. Results of TG in the study agree with Amin *et al* 1999, and Nathalie *et al* 2003 and Erik *et al* 2004 in human[20][21][22].

The results also showed that, after treatment with herbal mixture shown significant and highly significant decreases in all types of serum lipid. These results come from active ingredients of mixture that consist from poly and monounsaturated fatty acid, vitamins, carotenoid, flavonoid, phenols, minerals, etc..., Some of these chemicals have certain mechanisms to produce hypolipidemic effect on blood. Poly unsaturated essential fatty acids mainly Lienolinic and Lienoic acid which consist 85% of components of Eruca sativa seed oil and 34% of components of Lepidiumsativum [23] have reductive effect ofcholesterol [23]. Through several suggested mechanesim:1-decreased cholesterol absorption 2- increased excretion of neutral and acidic steroids 3-decrease cholesterol synthesis 4-transfer cholesterol from plasma to tissues. 5- Change in cholesterol to protein ratio in LDL and 6-change in the rate of synthesis or catabolism of individual lipoprotein. The results of lipid profile agree with El- Missiry and El-Gindy, 2000 who find decrease of cholesterol and triglyceride level in the blood plasma of Alloxan induced diabetes rats after two weeks of treatment [24]. As well as its agree with El-Gengaihi *et al* 2004 and Ibrahim and Sh, 2005 in their study on mice and rabbit respectively [25][26].

The results of cholesterol and triglyceride also agree with Badee *et al*,2003, and Hanan *et al* 2015 they concluded the reductive effect of cholesterol triglycerides and LDL-C levels because of flavonoids component of E.S., Petroslinium and Lepidiumsativum oil, which reduce cholesterol synthesis from hepatic cells due to its inhibitory effects on Hydroxy-3-methylglutaryl coenzyme A reductase[HMG CoA reductase] which is the rate-limiting step in the biosynthesis of cholesterol in humans; inhibition of this enzyme would be an effective means of lowering plasma cholesterol,orbecause the role of flavonoids in abatementing the activity of both hepatic enzyme 3-hydroxy-3-methylglutarylconenzyme A [HMG-CoA] reductase and Acyl Conzyme A: Cholestrole O-acyltransferase(ACAT) [27][28].

Whereas beholds hypocholestrolemia in their results could be attributed to B-Sitosterol content of E.S its plant sterol which is similar in there chemical structure to cholesterol plus ethyl group. This sterol reduces cholesterol absorbent from intestine [22].

Vitamin C in the Erucasativa andPetrosliniumsativumplays a good role in our results due to potency to energize 7α-hydroxylase enzyme in the first step of bile acid synthesis; the activation of this enzyme will promote the disversion of cholesterol into bile acid, thereby resulting in decrease serum levels of cholesterol, so vitamin C might have an inhibitory effect on HMG CoA reductase activity, thus inhibiting cholesterol biosynthesis [29].

Vitamin C also affects fatty acid metabolism by participating in the synthesis of carnitine. Carnitine plays a crucial role in the transport of long-chain fatty acids into mitochondria [30] Carnitine deficiency has

been suspected to play a role in some diseases including hyperlipidemia [30].

Furthermore, it has been reported that people with low vitamin C levels have higher amounts of lipid peroxides in plasma than the people with high vitamin levels. Accordingly, vitamin C could also affect cholesterol metabolism through the antioxidant effect [31].

As well as The presence of tannin and flavonoids as a constituents of Lipidiumsativum may have antioxidant activity whenever the existence of amino acid like glutamate, cysteine, glycine in the Lipidiumsativumare intermediates for synthesis of the endogenous antioxidant glutathione [32].

Very-low-density lipoprotein [VLDL] is synthesized in the liver that enables fats and cholesterol to move within the water-based solution of the bloodstream. VLDL is assembled in the liver from triglycerides, cholesterol, and apolipoproteins. VLDL is converted in the blood stream to low-density lipoprotein [LDL] [33].The results of LDL and VLDL agree with Ghada *et al* 2014 who find low level of these parameters that's could be due to antioxidant effect of vitamin c one of E.S.seed oil and Lepidiumsativum seed oil constituents which may reduce lipid oxidation, either directly or indirectly, by regenerating vitamin E. [23]. It has been reported recently that vitamin C may protect LDL and plasma lipids against free radical-mediated oxidation [35].

It could be conclude that because of the synergistic effect of the chemical ingredients of 105 herbal oil mixture, the present study demonstratedthe significantly contribution to improving hyperlipidemia status induced by dexamethasone , one of important drug which is used for years in the treatment of allergic and autoimmune diseases.

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