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A Novel Herbal Remedy to Alleviate Drawbacks of Heat Stress in Rats with Special References to Some Reproductive and Molecular Alterations

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Abstract: In most mammalian species, the temperature of the testes is tightly regulated, to assure optimal reproductive function. *Ferula hermonis* has been prescribed as a tonic, stimulant and aphrodisiac for both male and female suffering from sexual insufficiency .This study was designed to elaborate the possible role of this herb to alleviate the drawbacks of heat stress on the reproductive performance. Forty albino rats were divided into four comparable groups, G1 is left as control,G2 is given the water extract of the plant,G3 was stressed in hot and humid climate, G4 was given the plant extract while subjected to heat stress the same like G3.After 8 weeks ,animals were slaughtered and examined for the changes in serum chemistry, semen picture, cytogenetical alterations in Bone marrow and some molecular changes in testis,liver,kidney and brain. The heat stressed animals in G3 showed Oligozoospermia and Teratozoospermia. Also breaks, deletion and gaps were the most obvious chromosomal aberrations in the same group. analysis of serum chemistry showed elevation in blood glucose, γ glutamyl transferase (γ GT), uric acid, creatinine, cholesterol, low density lipoprotein (LDL), total lipids and malondialdehyde (MDA) while the levels of total antioxidants(TAC), cholinesterase and testosterone , DNA, RNA and total protein were markedly decreased in tissue of testis, liver, kidney and brain in the same group of animals (G3). The chromatographic analysis of the plant extract showed high level of phenolic compounds and the administration of the plant has no side effect for animals as shown in G2 and in the same time it showed protective effect from the hazards of heat stress as shown in G4. The study ascertained that the oxidative stress is the central component of the heat stress. *Ferula hermonis* is a wonderful antioxidant, aphrodisiac herb. It could be a promising formulation which can alleviate the health hazards resulting from heat stress, especially in tropical and subtropical countries.

Key words: *Ferula hermonis* · *Silsh El-zallouh* · Spermatogenesis · Heat stress · Oxidative stress · Apoptosis · Chromosomal aberrations · Sexual insufficiency · Treatment option

INTRODUCTION

Heat stress is an impotent cause of direct and indirect losses in animal production enterprises. The importation of foreign breeds from the temperate zones into tropical and subtropical countries becomes a common practice worldwide. Moreover, exposure of these animals to heat stress, virtually reduce their growth, conformation characteristics and production if compared to these parameter at their home countries. The thermal comfort zone for most animals is between 4 and 25°C. When temperature exceeds 25°C, animals suffer from heat stress. In severe cases, the core temperature rises, cells are affected and production performance is reduced, especially when the relative humidity is greater than 50% [1].

Animals typically react to heat stress conditions by eating less food, thus naturally controlling the rise in deep body temperature caused by digestion, appetite is depressed by 1.5% for each degree rise above 20°C and for every 1°C rise in body temperature, metabolism increases 20-30%, respiratory rate rises and there is a marked increase in insensible heat loss by evaporation of water from the lungs. They also drink at least 5 times

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the amount of water they would under temperate conditions, urine output increases and many mineral ions are lost [2]. For normal spermatogenesis, in most mammals, scrotal temperature is 2-8°C below core temperature [3]. Raised scrotal temperature induced changes in testicular weight, sperm viability, morphology and motility [4]. Also, it was reported that germ cells of heat stressed animals showed altered synthesis of DNA, RNA and proteins, as well as protein denaturation and abnormal chromatin packing [5]. Following heat stress, the epidedymis lose its ability to store and maintain viable spermatozoa, resulting in the gradual and progressive accumulation of dead, decapitated and immotile spermatozoa[6]. A negative correlation was found between high scrotal temperature and sperm output with sperm concentration being decreased 40% per 1°C increment of median day time scrotal temperature [7]. Management programmes to offset these losses should be developed. Manupulation of the ration, such as increasing energy intake, should be done carefully. Vitamins E,C, Biotin, Riboflavin and K should also be increased and an extra antioxidant should be added [8], medicinal plants may offer a therapeutic option.

Ferula hermonis as a tonic, stimulant and aphrodisiac was prescribed as an anti-impotency medication for both sexes As well as increasing the "stamina" of animals. Other traditional uses for *Ferula hermonis* are cauterizing wounds, Curing animal infections and increasing the milk production of cows [9].

Despite the spread of the herb in the market, prescribed to hundreds of patients with amazing curative rate, it is not yet supported by recent research work. So, this study was designed to investigate the possible protective effect of *Ferula hermonis* from the hazards of heat stress as monitored by changes in spermatogenesis, some molecular findings and general health condition in rats as a model.

MATERIALS AND METHODS

Animals: The current experiment was carried out on 40 adult male albino rats (180-185 g live body weight). Animals were housed in polycarbonate cages in an air-conditioned room at the Laboratory of the Animal house of the National Research Center and had free access to water and pelleted diet (mycotoxin free). Animals were fed on basal control diet (Table 1) with mineral and vitamin mixture (AIN-93G-Mx) that supplies the recommended concentration of elements for AIN-93 G and AIN 93 diet [10].

Table 1: Composition of control diet (AOAC,2000)

Ingredients	%
Casein	10
cellulose	10
Corn oil	10
Salt mixture	4
Vitamin mixture	1
L- cystine	0.018
Choline chloride	0.025
Corn starch	64.957

The Herbal Remedy: Roots of *Ferula hermonis* (FH)were obtained from the experimental station of medicinal plants, Ministry of Agriculture, Cairo, Egypt. Phenolic compounds of plant sample were extracted according to the method outlined by Duke *et al* [11]. The identification of the individual phenolic compounds was performed on high liquid chromatography JASCO HPLC,using hypersil C18 reversed place column (250x 4.6mm)with 5 u particle size)

The herb was given to the treated animals orally(using oral tube), twice weekly as prescribed by herbalist (0.025 ml/ 100 g body wt from plant water extract 50%) prepared in the form of water extract (by soaking in boiled water over night) for 8 successive weeks.

Experimental Design: Rats were proven fertile, successfully bred before the start of the experiment. Rats were divided into four comparable groups, 10 rats each. The first two groups G1 and G2 were kept in air conditioned room while the rest of animals were kept apart and subjected to heat stress using small lamp(45 watt 1 meter high from the cages) and a thermometer was kept beside the cages just to keep animals in worm weather (42±1°C) for 4 hours daily (in the early morning) for 8 successive weeks. The humidity was not less than 50% during this period of time.

- The first group (G1) was healthy animals kept on basal diet without any additives.
- The second group (G2) was given FH and kept on the basal diet in an air conditioned room.
- The third group (G3) was kept in worm weather and kept on the basal diet.
- The fourth group (G4) was given FH similar to G2 and subjected to heat stress the same way as G3.

Sampling and Analysis: At the end of the experiment rats were slaughtered, blood samples were collected in tubes, centrifuged and serum is separated, kept on -20°C to perform some relevant analysis such as γ glutamyl

transferase [γGT; 12]. Total protein, glucose, urea creatinine and cholesterol [13], high density lipoprotein [HDL; 14] and law density lipoprotein (LDL; 15], triglyceride, total lipids [16]. Oxidant/ antioxidant markers including malondialdehyde [MDA; 17] , total antioxidant [TAC, 18] were calorimetrically assayed using chemical kits from Bio Diagnostic, Egypt. Also cholinesterase activity was assayed in serum [CHE; 19] and testosterone level was assayed using ELISA microwell method according to Parker [20] .

Semen Qualification: In order to obtain semen specimens for evaluation, the epididymes were excised and minced with small scissors. A fresh smear of semen from each rat was stained by eosin-nigrosin prepared according to Blom [21] to be examined for life/dead and morphological abnormalities under oil-immersion lens by counting 700 sperms/ slide as described by Wyrobeck and Bruce[22].

Cytogenetical Examination: For cytogenetical alterations, rats were intra peritoneal injected with 0.6 mg/ kg colchicine, 2.5 hours prior to sacrificing. Femoral bone marrow cells were extracted and treated with hypotonic solution, fixed in methanol/acetic acid mixture and the slides were prepared for examination [23]. Fifty metaphase spreads per animal were examined for chromosomal aberrations.

Micronucleus Estimation: For micronucleus assay, femoral bone marrow cells were expelled onto clean slide and mixed with few drops of fetal calf serum. Cell homogenate was smeared, left to dry, fixed in methanol and stained with Giemsa. A thousand polychromtic erythrocyte /animal were screened for micronuclei [24].

Nucleic Acid Contents and Total Protein in Tissue: Specimens of liver, kidney brain and testis were collected to be examined for RNA, DNA content. One gram of tissue is homogenized in 4 ml distilled water, out of which 1 ml is added to cold Trichloroacteic acid (TCA), centrifuged, boiled in mixture of absolute ethanol and ethanol/ether mixture 3:1. After centrifugation add TCA 5%. The supernatant is separated to be ready to be quantified using specific reagents for DNA (Diphenylamine reagent) and RNA(Orcinol reagent) according to Pears and Schneider [25,26] respectively. Total protein is estimated in tissue using commercial kits according to Peters [27]

Statistical Analysis: Data were statistically elaborated with Analysis of Variance[28] using Mc Graw Hill software[29].

RESULTS

The HPLC analysis of the methanolic extract of the plant revealed high concentration of phenolic compounds.the qualitative and quantitative determination of the polyphenols is recorded in Table (2)

Semen evaluation (Table,3) revealed that heat stress caused a defective spermatogenesis as the epididimal sperm evaluation showed low sperm count (Oligozoospermia) and abnormal sperm morphology (Teratozoospermia) in G3 The most frequent abnormalities were head without hock, banana head,

Table 2: HPLC of polyphenols in methanol extract of *Ferula hermonis*

Ingredients	Mg/100 g
Phenol	30
Resorcinol	670
Protocatchuic acid	340
Catchines	8380
Parahydroxy benzoic	3260
Caffeic acid	420
Daidzin	26 mg
Ferulic acid	880
Coumarine	440
Paracoumaric acid unhydrate	290
Rutin	380
Myricetin	1100
Eugenol	1700
3,5 Dihydroxyisoflavon	1500
Quercedin	220
caumpherol	3840
Pinostrobin	1810

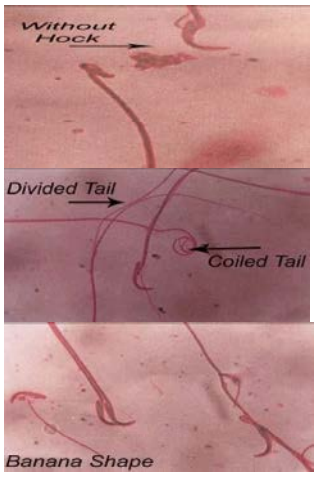


Table 3: Effect of *ferula hermonis* on the incidence of sperm abnormalities in albino rats subjected to heat stress. (mean± SE).

	Groups			
Abnormalities	G1(control)	G2(Plant)	G3 (heat stress)	G4 (heat stress+ plant
Head without hock(%)	1.80± 0.48a^{c}	1.00±0.31^{c}	8.60± 0.67^{b}	3.20±0.37^{a}
Banana shape Head (%)	0.80±0.37^{ac}	0.40±0.24^{c}	6.80±0.37^{b}	1.80±0.37^{a}
Coiled tail (%)	1.20±0.58^{ac}	0.60±0.24^{c}	6.80±0.58^{b}	2.40±0.50^{a}
Divided tail (%)	1.00±0.63 ^{a}	0.40±0.24^{a}	6.80 ± 0.37^{b}	3.00± 0.31 ^{c}
Total abnormalities (%)	4.80±0.66^{a}	2.40±0.50^{d}	29.20±0.58^{b}	11.20±0.80^{c}
Alive sperm (%)	70.40±0.50^{a}	77.80±0.58^{d}	40.40±0.50^{b}	60.40±0.50^{c}
Sperm count (10^{6}/ml)	30.7±0.22^{a}	33.33±0.15^{d}	20.1± 0.01^{b}	28.37± 0.41^{c}

Different letters in superscript means significance (P=0.05)

Table 4: Effect of ferula hermonis on hazarous effect of heat stress on blood chemistry(mean± SE).

	G1(control)	G2 (plant)	G3(heat stress)	G4 (heat stress+ plant
Glucose(mg/dl)	73.40±1.74a	78.16±3.1a	96.78±1.62b	87.46±3.0c
Total protein(g/dl)	8.12±0.20ab	8.46±0.55b	7.08±0.38a	7.41±0.37ab
Uric acid (mg/dl)	5.06±0.11a	5.31±0.18a	6.63±0.31b	6.16±0.30b
Creatinine(mg/dl)	0.71±0.04a	0.71±0.02a	0.95±0.03b	0.80±0.04a
?GT(U/L)	12.20±0.37a	12.67±0.33a	19.37±0.31b	15.91±0.40c
Cholesterol(mg/dl)	93.75±2.17ac	88.61±2.16c	108.50±3.05b	98.41±1.12a
HDL(mg/dl)	44.90±0.78a	49.05±0.34bc	48.52±1.50 bc	51.08±1.22b
LDL(mg/dl)	26.60±0.41a	25.17±0.57c	42.62±0.26b	26.59±0.29a
Triglyceride(mg/dl)	79.53±2.55a	78.49±3.65a	74.98±6.36a	73.09±6.77a
Total lipid(mg/dl)	304.00± 3.08a	253.26±2.50c	339.62±2.58b	250.85±1.56c
MDA(nmol/ml)	2.87±0.27a	2.94±0.16a	5.81±0.17b	4.07±0.18c
TAC(mMol/L)	1.85±0.02a	2.84±0.02b	1.00±0.03c	1.84±0.04a
Cholinestrase(U/L)	6.43±0.24a	6.50±0.25a	3.43±0.25b	5.19±0.23c
Testosterone(ng/uL)	7.36±0.25a	8.44±0.27b	5.65±0.22c	6.25±0.35cd

Different letters in superscript means significance (P≤0.05)

Table 5: Effect of ferula hermonis on the frequency of chromosomal aberrations and micronucleus in bone marrow of rats subjected to heat stress (mean± SE).

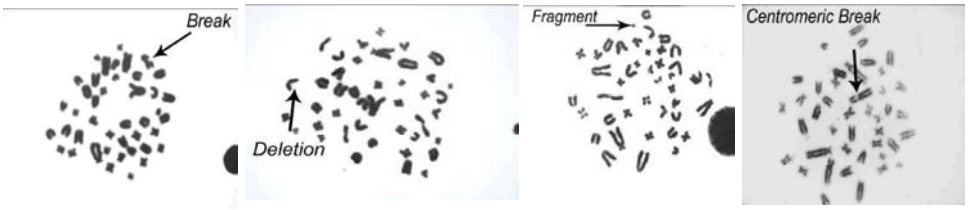
Abnormatiies % per 50 metaphase	G1(control)	G2(Plant)	G3 (heat stress)	G4 (heat stress+plant)
Gaps	1.00±0.63^{a}	0.60±0.40^{a}	3.20±0.58^{b}	1.40±0.50^{a}
Breaks	0.80±0.37^{a}	0.40±0.24^{a}	2.60±0.67^{b}	1.20±0.37^{a}
Cent. attenuation	1.60±0.50^{ab}	0.80±0.37^{a}	2.60±0.40^{b}	1.60±0.50^{ab}
Deletions	0.00±0.00^{a}	0.00±0.00^{a}	1.20±0.37^{b}	0.60±0.24^{abc}
Fragments	0.00±0.00^{a}	0.00±0.00^{a}	1.00±0.31^{a}	0.80±0.50^{a}
End to End	0.00±0.00^{a}	0.20±0.20^{a}	0.60±0.40^{a}	0.40±0.24^{a}
Micronucleus / 1000 cell	22.00±1.41^{a}	14.20±1.85^{b}	107.20±3.61^{c}	33.00±1.64^{d}

Different letters in superscript means significance (P≤0.05)

Table 6: Effect of *ferula hermonis* on tissue protein and nucleic acid remodling in albino rats subjected to heat stress.(mean± SE)

	Organ	G1(control)	G2(Plant)	G3 (heat stress)	G4 (heat stress+plant)
Total protein in tissue (g/g)	liver	7.02±0.08^{a}	7.23±0.12a	5.24±0.18^{b}	6.89±0.14^{a}
	Kidney	6.15±0.10^{a}	6.64±0.28a	4.43±0.11^{b}	6.78±0.11^{a}
	testis	6.86±0.10^{ac}	7.11±0.12a	5.07±0.12^{b}	6.74±0.13c
	brain	7.00±0.06^{a}	7.26±0.17^{a}	4.82±0.21^{b}	6.88±0.13^{a}
RNA in tissue (mg/g)	liver	0.25± 0.01^{a}	0.27±0.007^{a}	0.20±0.002^{b}	0.27±0.008^{a}
	kidney	0.24±0.004^{a}	0.26±0.003^{b}	0.20±0.004^{c}	0.25±0.002^{ab}
	testis	0.27±0.007^{a}	0.28±0.005^{b}	0.21±0.003^{c}	0.30±0.003^{db}
	brain	0.26±0.006^{a}	0.28±0.006^{b}	0.19±0.005^{c}	0.25±0.008^{a}
DNA in tissue (mg/g)	liver	0.42±0.01^{a}	0.42±0.01^{a}	0.31±0.004^{b}	0.37±0.009^{c}
	kidney	0.34±0.005^{a}	0.38±0.005^{b}	0.27±0.007c	0.34±0.008^{a}
	testis	0.43±0.02^{a}	0.44±0.01^{a}	0.30±0.003c	0.39±0.006^{a}
	brain	0.36±0.007^{a}	0.40±0.006^{b}	0.22±0.004^{c}	0.35±0.01^{a}

Different letters in superscript means significance (P≤0.05)



coiled and divided tail. Administration of FH was found to ameliorate the harmful effect of heat stress on semen picture whereas the values came back towards normal as illustrated in G4 if compared to G1.

Analysis of serum chemistry (Table,4) showed elevation in glucose, γ GT, uric acid, creatinine, cholesterol, LDL, total lipids and MDA levels in animals subjected to heat stress(G3). However TAC, cholinesterase and testosterone levels were markedly decreased in the stressed animals.The plant administration did not show any hazards on liver or kidney function as well as glucose level whereas the values in G2 were as normal as control group indicating that the plant is side effect free. Moreover the elevated antioxidant level, lowered LDL and lipids in serum of rats reveals the beneficial use of the plant for health . Also, in G4 FH took all the changed values, due to hazardous effect of heat stress, back towards normal.

Studying the molecular changes took place due to heat stress (Table 5) revealed high percentage of chromosomal aberrations, especially deletions, breaks and gaps. Administration of the plant extract controlled these hazardous alterations to a great extent. Also the prevalence of micronucleus in bone morrow was greatly lowered by FH.

The changes in nucleic acids and total protein in tissues are illustrated in Table (6). Results in G3 showed marked decrease in total protein, RNA and DNA in all tissues indicates high prevalence of apoptotic changes. However the condition was much better in G4 after FH administration.

DISCUSSION

Heat stress affect animal production through reduced feed intake, reduced lactation or laying performance, reduced fertility levels, decreased activity, increased respiratory rate and energy losses ,increased peripheral blood flow and sweating and increased mortality [1]. Oxidative stress (OS) has been identified as the central component of heat shock and the factor that affects fertility status and thus, has been extensively studied in recent years. It mediated damage to sperm in 30 - 80% of cases [30]. Spermatozoa, like any other aerobic cell, a re constantly facing the "oxygen-paradox" [31]. It induces its hazardous effect by two principal mechanisms. First, damage the sperm membrane which in turn reduces the sperm's motility and ability to fuse with the oocyte. Secondly, ROS directly damage sperm DNA, compromising the paternal genomic contribution to the embryo. Despite the common association between compromised sperm quality and oxidative damage, males are rarely screened for oxidative stress nor treated. Direct treatment of oxidative stress may allow for natural conception.

Two factors protect spermatozoa DNA from oxidative stress: the characteristic tight packaging of sperm DNA and the seminal plasma and sperm themselves are well endowed with an array of protective antioxidants [31]. Exposing the sperm to artificially produced ROS causes DNA damage in the form of modification of all bases, production of base-free sites, deletions, frame shifts, DNA cross- links and chromosomal rearrangements [32]. Oxidative stress also is associated with high frequencies of single- and double-strand DNA breaks [32,33] .

The present study revealed high incidence of sperm abnormities associated with elevated oxidative markers that coincide with this theory. In the same time low level of DNA traced in testicular tissue ascertain this explanation. When the extent of DNA damage is small, spermatozoa can undergo self-repair and moreover, the oocyte also is capable of repairing damaged DNA of spermatozoa [34]. However, if the damage is extensive, apoptosis and embryo fragmentation can occur. Decreased fertilization rates and poor embryo cleavage and quality have been reported in infertility cases where sperm samples contain a high frequency of damaged DNA[35] . DNA damage in the Y chromosome also can cause gene deletion in the Y chromosome of the offspring, leading to infertility [36]. In the present study the high amount of total phenolics and the powerful antioxidant effect of Ferula hermonis took part in the regenerative process of the damaged DNA, RNA, Sperm cells and took their value towards normal. The human and animal body have developed several antioxidant strategies to protect itself from ROS damage. This allows for normal oxidative metabolism to occur without damaging the cells, while still allowing for normal ROS-mediated cellular responses such

as destruction of infectious pathogens and in tracellular signaling [37]. Oxidative stress occurs when the production of ROS overwhelms the antioxidant defense mechanisms leading to cellular damage. Superoxide dismutase (SOD) and catalase are enzymatic antioxidants which inactivate the superoxide anion ($O^{\cdot -}$) and peroxide (H_2O_2) radicals by converting them into water and oxygen . SOD is present within both sperm and seminal plasma [38]. While some investigators have reported minor reductions in seminal plasma SOD activity in infertile men [39] many have not [40]. As well as the majority of evidence does support a link between de?cient seminal catalase activity and male infertility [41]. Glutathione peroxidase (GPX) is the Final member of the seminal enzymatic antioxidant triad. It consists of a family of antioxidants (GPX1- 5) that are involved in the reduction of hydroperoxides using glutathione as an electron donor. The GPXs are located within the testis, prostate, seminal vesicles, vasdeferens, epididymis, seminal plasma and spermatozoa themselves [42]. GPX must play an important protective role against oxidative attack since its speci?c inhibition in vitro using mercaptosuccinate leads to a large increase in sperm lipid peroxidation [43]. Male factor infertility has been linked with a reduction in seminal plasma and spermatozoa GPX activity[31].

The non-enzymatic antioxidants present within semen include ascorbic acid (Vitamin C), a -tocopherol (Vitamin E), glutathione, amino acids (taurine, hypotaurine), albumin, carnitine, carotenoids, flavenoids, urate and prostasomes. These agents principally act by directly neutralizing free radical activity chemically. However, they also provide protection against free radical attack by two other mechanisms . Albumin can intercept free radicals by becoming oxidized itself, thereby sparing sperm from attack [41]. Alternatively, extracellular organelles (prostasomes) secreted by the prostate have been shown to fuse with leukocytes within semen and reduce their production of free radicals [44] . A substantial number of researchers have reported a signi?cant reduction in non-enzymatic antioxidant activity in seminal plasma of infertile compared with fertile individuals whereas, Se deficiency causes a marked decrease in GPx activity in an adrenal cell line associated with decreased steroid hormone production [42]. With mild deficiency, Se accumulated in testes; it is preferentially found in the midpiece of spermatozoa, which contains mitochondria. Developmental studies in rats showed changes in the morphology of spermatids and spermatozoa and, finally, complete absence of mature germinal cells associated with Se deficiency [44]. Elinor mentioned that *Ferula hermonis* is rich in selenium and vitamin E [45].

Antioxidants contained within seminal plasma are obviously helpful for preventing sperm oxidative attack following ejaculation. However, during spermatogenesis and epididymal storage, the sperm are not in contact with seminal plasma antioxidants and must rely on epididymal/testicular antioxidants and their own intrinsic antioxidant capacity for protection.

Animal subjected to heat stress (G3) showed marked elevation in all measured metabolic enzyme and serum chemistry .

Hyperglycemia occurs naturally when the body is stressed, endogenous catecholamines are released that - amongst other things - serve to raise the blood glucose levels.

Pancreatic β Cells are sensitive to oxidative stress while showing a low capacity of antioxidative systems. Se-deficient animals have low serum insulin levels and their islet cells show impaired protein secretion that is normalized by Se and vitamin E [46]. Evidence implicated when the production of ROS becomes excessive, oxidative and nitrosative stress will develop, causing functional alterations of biological tissue, However, selenium supplementation played a protective role from hyperglycemic complications [47]. The same findings was recorded by Abu-Zaiton [48] whereas *Ferula asafetida* extract treatment in rats exerted therapeutic protective effect in diabetes by preserving pancreatic beta-cells integrity and activity, which supports traditional usage to prevent diabetic complications. Also lipids are more readily oxidized than glucose. Thus glycoxidation and lipoxidation products appear to be formed together. Plasma level of lipids correlates with level of MDA adducts on LDL [49]. lipoxidation products (MDA and 4-hydroxynonenal)adducts on proteins and protein oxidation products (chloro- and nitro-tyrosine and protein carbonyls) occur together in plaque deposits in atherosclerosis [49,50].

As the plant (*Ferula hermonis*) is rich in antioxidant compounds it took the values of glucose and lipid profile back to normal. The Druze, who live on Mountain, Hermon and its vicinity, have used Zallouh (*F. hermonis*) for generations. They claimed that both men and women can benefit from its aphrodisiac and stimulating properties and that elderly people find it particularly energizing and revitalizing.

Roots of *F. hermonis* contain vitamins A, B1, B2, B6, C, D and E. The minerals magnesium, selenium, zinc and iron have also been identified, as well as a number of sesquiterpenes like ferutinine, teferdin and ferutinol. Ferutinine and tenuferidine have demonstrated estrogenic activity [51].

According to the 1998 CNN piece, Zallouh has been well received among followers of natural remedies. It is offered to the public on the Internet and in Middle Eastern spice and herb shops as an effective, side effect-free, alternative to Viagra.

The study proved that the plant is safe and have no side effect for diabetic or hypercholesterolemia patients whereas it did not cause alteration in blood sugar while it lowered the lipid profile specially LDL also it is safe for liver and kidney functions

In conclusion, the use of *Ferula hermonis* is a new management strategy that can minimize the effects of heat stress, in combination with physical modification of the environment (shading, cooling), genetic development of heat-tolerant breeds and improved nutritional management practices to optimize the animal production in hot, humid climates.

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