Original Article

Attenuation of high-fat diet induced metabolic syndrome in rodents treated with Crocus sativus

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Abstract

Background: Metabolic syndrome is associated with increased risk for morbidity and mortality. Crocus sativus (saffron) is a natural compound known for its anti-inflammatory, anti-oxidant and its potent lipid- and glucose-lowering effects. We sought to examine the hypothesis that saffron exerts a protective role against metabolic syndrome in high-fat diet fed rodents.

Material and Methods: Thirty adult male C57BL6/J mice were randomly divided into three groups; Control group (*n*=10), which received normal diet; High-fat (HF) group (*n*=10), which received a commercial high-fat diet (45% fat); Saffron group (*n*=10), which followed the same dietary as HF group and was additionally supplemented with saffron (100 mg/kg/day). Metabolic profile as well as arterial blood pressure, serum leptin and IL-1α were measured throughout the study.

Results: 12-week administration of Saffron led to decreased levels of glucose, total and LDL cholesterol when compared with the HF group (186 ± 31 mg/dL *vs.* 231±25 mg/dL, *p*=0.01; 131 ± 14 mg/dL *vs.* 150 ± 5 mg/dL, *p*=0.03; and 64 ± 16 mg/dL *vs.* 85 ± 6 mg/dL, *p*<0.001, respectively). Moreover, at the end of the study, all blood pressure indices –except for HR- were significantly lower in the saffron treated group compared with the HF group (*p*<0.01 in all cases). Significant differences were noted in the case of leptin

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and IL-1a during the 8th week (MFIs (Mean Fluorescence Intensity): 1452 ± 205 *vs.* 2164 ± 318, *p*<0.001 and 803 ± 65 *vs.* 1140 ± 114, *p*<0.001, for leptin and IL-1a in HF and Saffron groups, respectively).
Conclusion: Saffron exhibits hypoglycemic, hypolipidemic and pressure lowering actions. Yet, further studies unveiling the exact mechanisms of saffron's mode of actions are required.

Key words: metabolic syndrome; Crocus Sativus; high fat diet; rodent

1. Introduction

Metabolic syndrome is a cluster of metabolic features including excess adipose tissue storage, insulin resistance, dyslipidemia and increased arterial blood pressure [1]. It is often the result of the disequilibrium of the energy homeostasis and it is associated with high risk for morbidity and mortality. Nowadays, it is rapidly expanding worldwide and the need for action is alarming [2]. Treatment strategies for either the metabolic syndrome *per se* or for each of its clinical manifestations separately have been approached. Lifestyle changes are considered as the first-line choice followed by drug treatment in certain cases. Albeit their effectiveness, drug regimens are accompanied by the risk for side-effects [3]. Thus said, the scientific interest is focused on more "crude" ways including plant resins and natural regimens in order to face this pandemic [4,5].

Saffron, the dry stigmas of the plant Crocus sativus has been traditionally studied for its anti-inflammatory and anti-oxidant activities in liver disease, menstrual dysregulations and asthma [6]. Current data suggest saffron's potent protective role against obesity associated diseases, diabetes, insulin resistance and serum lipid disturbances [7]. Human and animal studies have revealed the implication of saffron's components in several metabolic pathways on local and systemic level [6–8]. Nonetheless, the whole range of the exact mechanisms of its action has not yet been fully unveiled.

Aim of our study was to investigate the role of saffron administration in rodents fed a high-fat diet, focusing on saffron's effect on the distinct compartments of metabolic syndrome, namely weight, lipid profile, serum glucose levels and blood pressure. Moreover, per our previous data suggesting a weight-lowering effect of saffron and a protective action against fatty liver disease, the hypothesis that leptin and inflammation are implicated in the protective action of saffron was also examined [6].

2. Material and methods

2.1 Animal housing and welfare

Eight-to-ten week old male C57BL/6J mice were obtained from the Hellenic Pasteur Institute, Athens, Greece. The animals were housed in groups of three or four in cages with European standards (Tecniplast) in the Laboratory for Experimental Surgery and Surgical Research "N.S Christeas", School of Medicine, National and Kapodistrian University of Athens, Greece. A control environment at 20°C ± 2°C, 55% relative humidity, central ventilation (15 air changes/hour) and an artificial 12-hour light-dark cycle were maintained throughout the experimental protocol. Access to food and water was ad libitum for all groups. Animals received humane care in compliance with the "Guide for the Care and Use of Laboratory Animals". Our experimental protocol was approved by the Institutional Animal Care and Use Committee of Athens University Medical School and the Veterinary Directorate of the Athens Prefecture. Animals were marked using auricular badges and they were inspected and weighted once a week.

2.2 Study design

Following two weeks of acclimatization, 30 C57BL/6J mice were allocated into 3 groups: Control group, (n=10): Animals received standard chow diet consisted of ELVIZ 510 food pellets which contain a full nutrient supplementation and normal drinking water. High-fat diet (HF) group, (n=10): Animals were fed a high-fat commercial diet (45% fat, Dieta Speciali, Mucedola SRL, Milan, Italy) and normal drinking water; Saffron group, (n=10): Animals received 100 mg/kg/d saffron in their drinking water and high fat diet. Total duration of the experiment was 12 weeks in addition to the two-week acclimatization period. The dosage of Crocus Sativus was determined according to previous reports of our team6. Dried stigmas of Crocus sativus L have been used. The amounts of crocin, picrocrocin and safranal in dried stigmas have been reported by Hyouta Himeno & Konosuke Sano (1987). (Crocin concentration measured in 2.0 mg of saffron was 5.14 µg (0.26%), Picrocrocin concentration was 1.13µg (0.057%) and Safranal concentration was 0.00µg (0.00%)). To ensure that the mice received the above-stated saffron dosages, the daily water consumption for each cage was measured daily for five consecutive days. The amount of consumed water per animal was then calculated by dividing this number by the number of animals in each cage. Water consumption was re-evaluated every four weeks in order to adjust the quantity of saffron diluted in the water in case of alternations in water consumption. The average dose of Saffron received by the treatment group throughout the study was cumulatively estimated at 104.0 ± 5.1 mg/kg/d.

The number of the animals used per group was defined after performing power analysis for detecting differences in total cholesterol >10% with a type II error <20%.

2.3 Blood sampling and euthanasia

1-1.5 mL of blood was drawn after 12-hour fasting by puncture with capillary tubes into the medial retro-orbital venous plexus under light ether anesthesia. Four pre-specified time points were chosen; baseline (t0), 4 weeks (t1), 8 weeks (t2) and 12 weeks (t3) after the initiation of the study. Blood samples were collected at the same time (10 am) for every measurement. Euthanasia was induced by deep ether anesthesia and cervical dislocation.

2.4 Serum lipid and glycemic profile measurement

Serum levels of total cholesterol (TC), high density lipoprotein cholesterol (HDL-c) and triglycerides (TG) were measured with the use of biochemical analyzer ("Medilyzer BT"- Medicon Hellas, Athens, GR). LDL-cholesterol (LDL-c) was calculated by the Friedewald formula [9]. Serum glucose levels were determined using the Glycerol Phosphate Oxidase-Peroxidase GPO-POD method. ("Medilyzer BT"-Medicon Hellas, Athens, GR).

2.5 Arterial blood pressure measurement

Blood pressure was determined via a non-invasive tail-cuff occlusion instrument and recording system (CODA Noninvasive Blood Pressure Monitor, Kent Scientific Corporation, USA). Unanesthetized mice were warmed to an ambient temperature of 30°C on a thermostatically controlled warming plate. The animals were allowed to habituate to this procedure for 3 days prior to each experiment. Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Mean arterial pressure (MAP) and heart rate (HR) data were averaged from 10 different cycles, which were collected between 8 am and 12 am for each animal. These hemodynamic parameters were assessed at the same time-points as those of blood sampling (baseline, 4 weeks, 8 weeks and 12 weeks).

2.6 Leptin and IL-1a measurement

Custom dual-antibody Luminex assays were developed using ProtATonce (Athens, Greece) assay service. Briefly, 2-5 antibodies were selected and cleaned up from amine containing buffers and carrier proteins that interfere with the coupling procedure. All antibodies were tested pair-wise as capture and as detection antibody. Capture antibodies were coupled to the beads whereas detection antibodies were biotinylated. Quality control confirmed biotinylation and coupling efficiency.
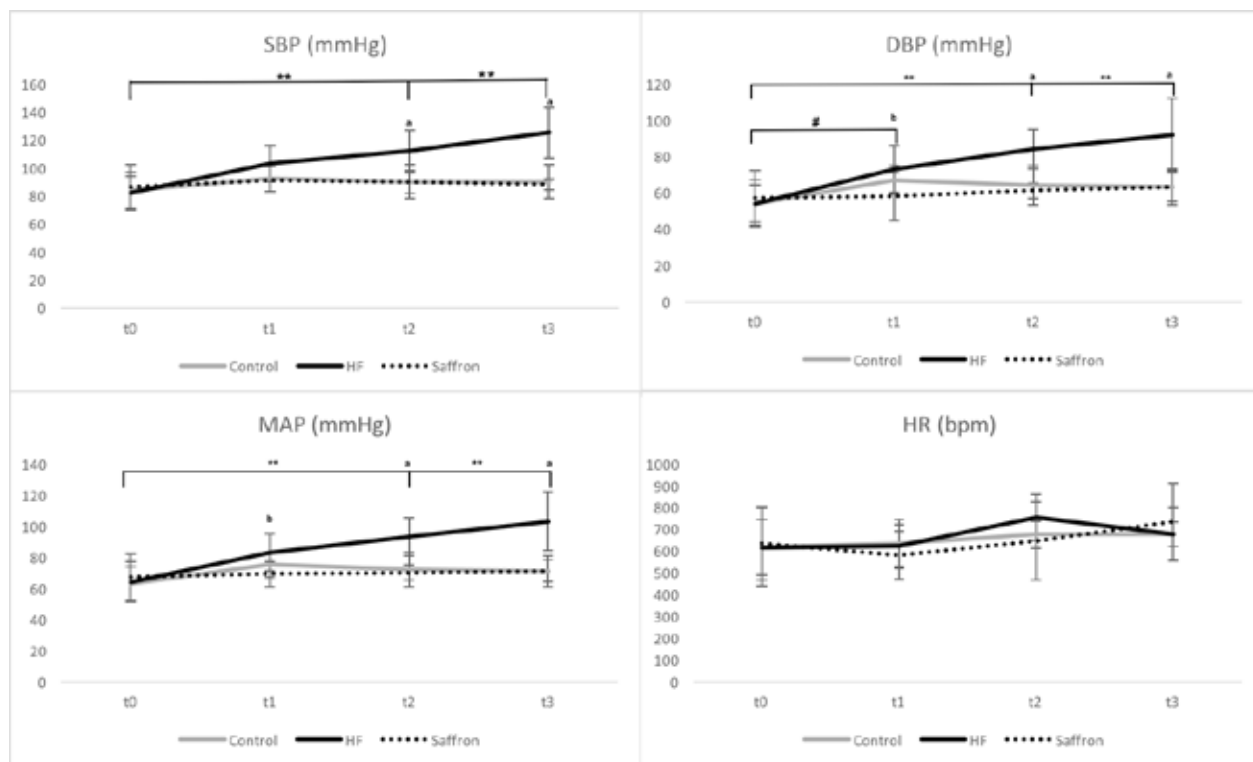
Figure 1. Alternations of SBP, DBP, MAP and HR among groups throughout the study. Data are expressed as mean±SD. P-values for comparisons within the same group between the different time points are generated from Repeated Measures ANOVA followed by Bonferroni's post hoc test. P-values for comparisons among groups at the same time point are generated from One-way ANOVA followed by Bonferroni's post hoc test. In the case of non-normal distributions, non-parametric tests (Kruskal Wallis followed by Mann-Whitney U test) were performed.

*SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; HR: Heart rate

** p<0.001 between the indicated time points for the HF group, #p<0.05 between the indicated time points for the Control group, ap<0.01 between HF-Control and HF-Saffron groups, bp<0.05 between HF-Saffron

For each biomarker the optimal capture/detection antibody pair was selected based on signal-to-noise ratio measurement. Assay validation including Limit of detection (LOD) and reproducibility were performed based on the European medicines Agency EMEA/CHMP/EWP/192217/2009 guideline on bioanalytical method validation.

2.7 Statistical analysis

Data of continuous variables are expressed as mean ± SD and the normality of their distribution was assessed with the use of Kolmogorov-Smirnov's test and graphical methods. In the case of normal distributions, ANOVA was utilized for between-group comparisons followed by Bonferroni's correction for multiple hypothesis testing. Moreover, Kruskal-Wallis's tests was used a non-parametric test for multiple group comparisons, using Mann-Whitney's U test for post hoc multiple testing. Repeated measures ANOVA was utilized for comparisons within the same group for the different time points.

All tests were two-sided. Differences were considered as statistically significant if the null hypothesis could be rejected with >95% confidence interval (*p*<0.05). The IBM SPSS Statistics 22.0 (SPSS Inc. Chicago, Illinois) program was used for all the analyses.

Table 1. Weight, lipidemic and glycemic profile measurements as well as water and food intake of the three groups for the four different time-points

Parameter Group	Baseline (t0) Mean±SD	4 weeks (t1) Mean±SD	8 weeks (t2) Mean±SD	12 weeks (t3) Mean±SD
Weight (g)				
Control	28.0 ± 3.6	25.0 ± 3.1	28.0 ± 2.2	30.0 ± 2.0
HF	28.0 ± 1.2	28.0 ± 0.8	29.0 ± 1.0	33.0 ± 4.1
Saffron	27.0 ± 1.8	26.0 ± 1.2	26.0 ± 1.2	33.0 ± 3.5
p-value				
Between HF - Saffron Groups	NS	NS	0.026	NS
Between Control - HF Groups	NS	NS	NS	NS
Glucose (mg/dL)				
Control	151.0 ± 24.7	155.0 ± 25.8	158.0 ± 24.7	188.0 ± 16.5a
HF	151.0 ± 12.2	146.0 ± 26.8	153.0 ± 26.5	231.0 ± 25.5
Saffron	141.0 ± 13.7	138.0 ± 22.5	123.0 ± 20.6	213.0 ± 27.2b
p-value				
Between HF - Saffron Groups	NS	NS	NS	0.01
Between Control - HF Groups	NS	NS	NS	0.017
Total Cholesterol (mg/dL)				
Control	88.0 ± 12.6	83.0 ± 8.9	88.0 ± 10.6	81.0 ± 4.6
HF	89.0 ± 5.6c	146.0 ± 13.7	133.0 ± 12.5**,d	150.0±5.0
Saffron	89.0 ± 16.5e	148.0 ± 6.5	113.0 ± 6.5	134.0 ± 13.8
p-value	NS	NS	NS	0.03
Between HF - Saffron Groups				
Between Control - HF Groups	NS	<0.001	0.002	<0.001
HDL Cholesterol (mg/dL)				
Control	49.0 ± 3.5	50.0 ± 3.8	50.0 ± 3.7	51.0 ± 4.6
HF	51.0 ± 2.7	51.0 ± 31.5	50.0 ± 2.8	51.0 ± 2.9
Saffron	49.0 ± 5.0	50.0 ± 5.0	51.0 ± 4.6	51.0 ± 4.3
p-value				
Between HF - Saffron Groups	NS	NS	NS	NS
Between Control - HF Groups	NS	NS	NS	NS
LDL Cholesterol (mg/dL)				
Control	24.0 ± 10.0	15.0 ± 10.7	24.0 ± 8.4	13.1 ± 7.0
HF	24.0 ± 7.0f	71.0 ± 13.5	59.0 ± 21.1g	85.0 ± 6.1
Saffron	23.0 ± 14.8h	72.0 ± 10.5**	42.0 ± 7.4i	58.0 ± 14.0**
p-value				
Between HF - Saffron Groups	NS	NS	NS	<0.001
Between Control - HF Groups	NS	<0.001	<0.001	<0.001

Triglycerides (mg/dL)				
Control	73.0 ± 30.5	89.0 ± 21.3	76.0 ± 9.7	91.0 ± 31.5
HF	74.0 ± 27.3	117.0 ± 13.0j	92.0 ± 18.2	70.0 ± 14.5**
Saffron	85.0 ± 40.6k	115.0 ± 30.0	95.0 ± 20.4	100.0 ± 7.5**
p-value				
Between HF - Saffron Groups	NS	NS	NS	NS
Between Control - HF Groups	NS	0.013	NS	NS
Water Intake (mL)				
Control	-	2.6 ± 1.0	2.5 ± 1.0	2.6 ± 0.9
HF	-	2.7 ± 0.8	2.8 ± 0.7	2.9 ± 0.7
Saffron	-	2.7 ± 0.7	2.7 ± 0.6	2.6 ± 0.7
p-value	-			
Between HF - Saffron Groups	-	NS	NS	NS
Between Control - HF Groups	-	NS	NS	NS
Food intake (g)				
Control	-	2.8 ± 1.0	2.8 ± 1.0	2.9 ± 1.0
HF	-	2.4 ± 0.5	2.7 ± 0.5	2.7 ± 0.4
Saffron	-	2.3 ± 0.6	1.7 ± 0.5	2.4 ± 0.5
p-value	-			
Between HF - Saffron Groups	-	NS	0.052	NS
Between Control - HF Groups	-	NS	NS	NS

P-values generated from One-way ANOVA followed by Bonferroni's post-hoc comparisons tests for comparisons between HF-Saffron and Control-HF groups are also presented.

*SD: Standard deviation; HF: High fat; HDL: High density cholesterol; LDL: Low density cholesterol

**Data expressed as Median ± Interquartile range due to the non-normal distribution of the variables.

ap=0.006 *vs.* t0; p=0.021 *vs.* t1; p=0.04 *vs.* t2, bp=0.012 *vs.* t2
cp<0.001 *vs.* t1; p=0.018 *vs.* t2; p<0.001 *vs.* t3, dp=0.015 *vs.* t3
ep<0.001 *vs.* t1; p=0.001 *vs.* t2; p<0.001 *vs.* t3, p<0.001 *vs.* t1; p=0.007 *vs.* t2; p<0.001 *vs.* t3, gp=0.005 *vs.* t3
hp<0.001 *vs.* t1; p=0.016 *vs.* t2; p=0.001 *vs.* t3, ip<0.001 *vs.* t1
jp<0.001 *vs.* t0; p=0.02 *vs.* t2; p=0.001 *vs.* t3, kp=0.006 *vs.* t1

3. Results

3.1 Body weight, lipidemic and glycemic profile

Alternations in body weight, serum lipids and glucose throughout the experiment are cumulatively tabulated in **Table 1.** Baseline measurements did not reveal any difference among groups. Although, in the end of the experiment, body weight did not differ among groups, saffron treated animals exhibited significantly lower body weight than the animals fed the high-fat diet (26.0 ± 1.2g *vs.* 29.0± 1.0g, *p*=0.026, respectively) 8 weeks after the beginning of the study. On the other hand, glycemic and lipid profile seemed to be ameliorated only after long-term treatment with Saffron. More specifically, 12-week administration of Saffron led to decreased levels of glucose, total and LDL cholesterol when compared with the HF group (186 ± 31 mg/dL *vs.* 231± 25 mg/dL, *p*=0.01; 131 ± 14 mg/dL *vs.* 150 ± 5 mg/dL, *p*=0.03; and 64 ± 16 mg/dL *vs.* 85 ± 6 mg/dL, *p*<0.001, respectively). Food and water intake were the similar among all groups, except for a marginally higher (*p*=0.052) food intake in the HF group compared with the Saffron group.

3.2 Arterial blood pressure indices

SBP, DBP, MAP and HR were measured throughout the experiment (**Figure 1**). Baseline measurements were similar among groups, while DBP and MAP
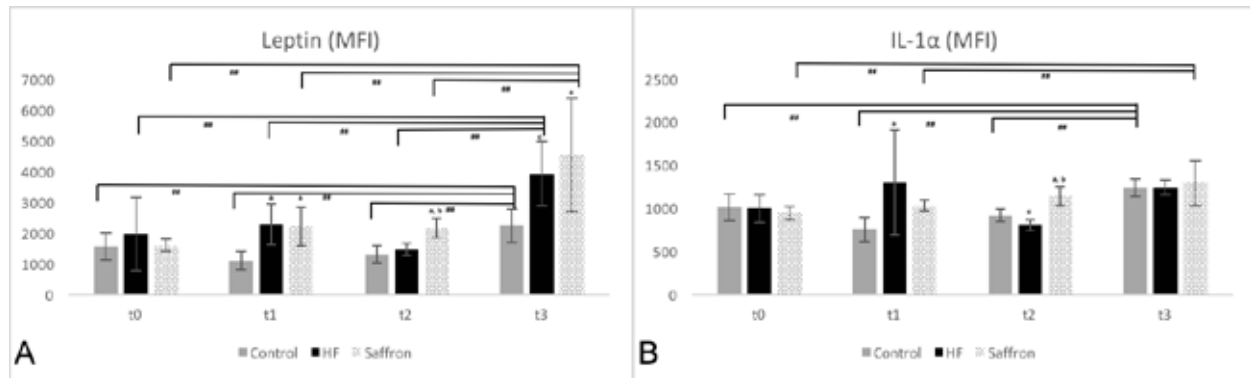
Figure 2. MFIs of leptin (Figure 2A) and IL-1a (Figure 2B) among groups at the beginning, 4 weeks, 8 weeks and 12 weeks afterwards. Data is expressed as mean±SD. P-values for comparisons within the same group between the different time points are generated from Repeated Measures ANOVA followed by Bonferroni's post hoc test. P-values for comparisons among groups at the same time point are generated from One-way ANOVA followed by Bonferroni's post hoc test. ##p<0.001 between the indicated groups and time points

were the first hemodynamic parameters to differ between HF and Saffron group, 4 weeks after the beginning of the study (DBP: 73.3 ± 12.8 mmHg vs 58.1 ± 10,4 mmHg, *p*=0.023 and MAP: 82.8 ± 12 mmHg *vs.* 68.8 ± 8.1 mmHg, *p*=0.021 for HF and Saffron groups, respectively). Later on, all blood pressure indices -except for HR- were significantly lower in the saffron treated group (*p*<0.01 in all cases).

3.3 Leptin and IL-1a
Albeit the lack of difference in leptin (**Figure 2A**) and IL-1α (**Figure 2B**) serum levels between HF and Saffron groups at the beginning and in the end of the experiment, significant differences were noted during the 8th week (MFIs: 1,452 ± 205 *vs.* 2,164 ± 318, *p*<0.001 and 803 ± 65 *vs.* 1,140 ± 114, p<0.001, for leptin and IL-1a in HF and Saffron groups, respectively).

4. Discussion
Crocus sativus is a natural regimen that has been extensively mentioned in the existing literature for its anti-oxidant and anti-inflammatory properties which imply its potent beneficial role in chronic inflammatory diseases [10,11]. Among others, metabolic syndrome is characterized by a chronic and steady low-grade inflammation. This background

is prosperous for the development of certain comorbidities such as insulin resistance, dyslipidemia and hypertension [12]. Our results indicated that saffron plays a substantial role in ameliorating major manifistations of metabolic syndrome induced by high fat diet. Namely, treatment with saffron reduces serum levels of glucose, total and LDL cholesterol, while it is also accompanied with normalization of systolic, diastolic and mean arterial blood pressure. Moreover, it is associated with up-regulation of leptin and a consequent body weight reduction. At the same time, no toxicity or side-effects of saffron administration were observed.

Increased intake of fatty acids leads to adipose tissue accumulation which is associated with lipotoxicity and insulin resistance [13]. 12-week administration of high-fat diet resulted in alternations and metabolic dysregulation equivalent to metabolic syndrome. Serum lipids and glucose as well as arterial blood pressure were elevated in the HF group compared with the animals fed standard chow diet. Additionally, an environment of low-grade inflammation is established which influences satiety via hormone signaling such as leptin. This is an inexpensive, easy and reproducible model of experimental metabolic syndrome.

The protective role of crocin and crocetin against insulin resistance is well-documented [6,14,15].

The glucose-lowering effect of these compounds is evident even when not separately administered, indicative of a synergistic action of saffron's extracts, which is a common attribute of natural herbs [6]. Our results are in accordance with the existing literature suggesting that ameliorated insulin sensitivity may be achieved *via* both an insulin-dependent pathway (PI3-kinase/Akt and mTOR pathway) and insulin-independent one (activation of AMPK/ACC and MAPKs pathway) [15]. Moreover, apart from the insulin-resistance enhancing properties of saffron, it has also been proposed that crocetin upregulates insulin secretion from beta cells of the pancreas due to its antioxidant effect leading to lower levels of reactive oxygen species in Langerhan's cells [16].

The implication of saffron in lipid metabolism has been proposed in both basic and clinical studies [14,17]. Our results indicate the decrease of total and LDL cholesterol levels in mice following a high fat diet and treated with saffron. This relationship is multidimensional and affects the metabolic regulation of adipocytes, gastric, pancreatic and skeletal muscle cells [7]. Saffron suppresses pancreatic and gastric lipase excretion, while it also influences the expression of leptin, adiponectin and tumor necrosis factor-α (TNF- α) focally in the adipocyte [18]. These activities are enhanced by the antioxidant properties of saffron [16]. Consistent with our results, various studies demonstrated the lipid lowering effect of saffron in rodents fed a high fat diet or in a sreptozocin-induced diabetic experimental model [6,16]. Moreover, it is reported that the favorable effects of saffron are evident regardless of the route of administration (per os or intraperitoneal) [19].

Systolic and mean arterial blood pressure were significantly lower in the saffron-treated group. Up to date, the exact pathways linking saffron attributes and its anti-hypertensive activity have not been fully elucidated [11]. It may be presumed that this observation is the result of a dual action of saffron. Firstly, it attenuated the burden of metabolic syndrome by enhancing lipid and glucose metabolism which may contribute to normalization of blood pressure via regulation of energy homeostasis [7]. Secondly, a direct pressure lowering effect may be initiated due to the anti-oxidant and anti-inflammatory properties of saffron [16]. Diminished inflammatory process promotes vascular endothelial function and reduces arterial stiffness, leading, thus, to lower levels of blood pressure. Three are the main compounds responsible for these beneficial effects. Crocin has been reported to decrease malondialdehyde, while increasing superoxide dismutase and antioxidant capacity. Crocetin exerts its antioxidant properties by downregulating thiobarbituric acid reactive substances, while safranal enhances antioxidant system by lowering malondialdehyde levels. Additionally, other studies report the stimulatory effect of saffron on endothelial nitric oxide synthase and the inhibiting effect on calcium influx in the sarcoplasmic reticulum of vascular smooth muscle cells [10,20].

Lastly, an increase in serum leptin levels and a drop in the body weight was noted in the Saffron group. Although, leptin promotes satiety, its levels are up-regulated in obese subjects due to leptin resistance induced by fat accumulation [21]. However, our results seem to be contradictory with the literature, since an up-regulation of leptin was noted in the saffron-treated group. Yet, this can be explained by that leptin measurements may reflect the initial changes with regard to the hormone response to excess fat intake. Moreover, this rationale is supported by the weight loss observed as a consequence of reduced food consumption due to suppressed appetite. Despite the lack of significance in food intake between HF and Saffron groups, even subtle differences may have been adequate for a respective incline in body weight. It should also be mentioned, though, that the weight-lowering effects of saffron were not sustained at the end of the study suggesting that the selected dose of saffron was not adequate to counter-act the detrimental effects of HF diet with respect to weight gain.

Prior to drawing conclusions, certain limitations of our study should be taken into consideration. Rodent experimental models, despite useful and easily reproducible may not reflect identical alternations in

humans. Moreover, the relatively small sample size may be considered a limitation, however based on the power analysis and the observed results, it was adequate for the acquisition of significant results. Administration of saffron *via* drinking water may not allow to determine its exact pharmacokinetics and metabolism, however it is well-documented that long-term administration and stable environmental factors reassure the reliability and reproducibility of the observed outcomes.

5. Conclusion

We suggest that saffron exerts glucose, lipid and pressure lowering properties in animals with HF-diet induced metabolic syndrome. In addition to these findings, leptin levels were also found increased along with body weight reduction. However, further basic and translational research is required in order to verify our findings and elucidate the exact mechanism of action of saffron.◻

Περίληψη

Μείωση παραγόντων του μεταβολικού συνδρόμου, που προκαλείται από διατροφή υψηλής περιεκτικότητας σε λιπαρά, σε τρωκτικά που έχουν λάβει Κρόκο Κοζάνης

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Εισαγωγή: Το μεταβολικό σύνδρομο συνδέεται με αυξημένο κίνδυνο νοσηρότητας και θνησιμότητας. Ο Κρόκος Κοζάνης (σαφράν) είναι μια φυσική ένωση γνωστή για τις ισχυρά αντιφλεγμονώδεις, αντιοξειδωτικές και τις πιθανές δράσεις του αναφορικά με τη μείωση των επιπέδων λιπιδίων και γλυκόζης. Επιδιώξαμε να εξετάσουμε την υπόθεση ότι ο κρόκος ασκεί προστατευτικό ρόλο κατά του μεταβολικού συνδρόμου σε τρωκτικά που ακολουθούν δίαιτα υψηλών λιπαρών.

Υλικό και Μέθοδος: Τριάντα ενήλικα αρσενικά ποντίκια C57BL6 / J χωρίστηκαν τυχαία σε τρεις ομάδες. Ομάδα ελέγχου (*n* = 10), που έλαβε κανονική δίαιτα. Ομάδα υψηλών λιπαρών (HF) (*n* = 10), η οποία έλαβε δίαιτα εμπορίου υψηλής περιεκτικότητας σε λιπαρά (45% λιπαρά). Ομάδα σαφράν (*n* = 10), η οποία ακολούθησε την ίδια δίαιτα με την ομάδα HF και έλαβε επιπλέον σαφράν (100 mg / kg / ημέρα). Το μεταβολικό

προφίλ η αρτηριακή πίεση αίματος, η λεπτίνη ορού και η IL-1α μετρήθηκαν σε όλη τη διάρκεια της μελέτης. *Αποτελέσματα:* Η χορήγηση του σαφράν για 12 εβδομάδες οδήγησε σε μειωμένα επίπεδα γλυκόζης, ολικής και LDL χοληστερόλης σε σύγκριση με την ομάδα HF (186 ± 31 mg / dL έναντι 231 ± 25 mg / dL, $p = 0,01$ · 131 ± 14 mg / dL έναντι 150 ± 5 mg / dL, $p = 0,03$ και 64 ± 16 mg / dL έναντι 85 ± 6 mg / dL, $p < 0,001$, αντίστοιχα). Επιπλέον, στο τέλος της μελέτης, όλοι οι δείκτες αρτηριακής πίεσης -εκτός από την HR- ήταν σημαντικά μειωμένοι στην ομάδα που έλαβε σαφράν σε σύγκριση με την ομάδα HF ($p < 0,01$ σε όλες τις περιπτώσεις). Σημαντικές διαφορές παρατηρήθηκαν στην περίπτωση της λεπτίνης και της IL-1α κατά τη διάρκεια της 8ης εβδομάδας (MFI: 1452 ± 205 έναντι 2164±318, $p < 0.001$ και 803 ± 65 έναντι 1140 ± 114, $p < 0.001$, για τη λεπτίνη και την IL-1α στις ομάδες HF και Saffron, αντίστοιχα). *Συμπεράσματα:* Το σαφράν παρουσιάζει υπογλυκαιμικές, υπολιπιδαιμικές και αντιυπερτασικές δράσεις. Ωστόσο, απαιτούνται περαιτέρω μελέτες για την διερεύνηση των ακριβών μηχανισμών του τρόπου δράσης του σαφράν.

Λέξεις ευρετηρίου: μεταβολικό σύνδρομο, Κρόκος Κοζάνης, δίαιτα υψηλής περιεκτικότητας σε λιπαρά, τρωκτικά

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