Journal of Sports Physiology and Athletic Conditioning (J.S.P.A.C) 2023; 3 (7): 1-11

Research Article

The Effect of Aerobic Training and Octopamine Supplement on Gene Expression Levels of VEGF and PDGFR in the Heart Tissue of Rats Exposed to Deep Fried Oil

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Received: 9 October 2022
Revised: 19 October 2022
Accepted: 16 December 2022

Abstract

Background: Deep-fried oils (DFO) produce toxins that endanger people's health. Using herbal supplements along with exercise training can help improve health. The purpose of this study was to investigate the effect of aerobic training (T) and octopamine (O) supplementation on VEGF and PDGFR gene expression levels in the heart tissue of rats poisoned with DFO.

Materials and Methods: In this experimental study, 25 male Wistar rats were purchased and placed in 5 groups of 5 animals, including: 1) control, 2) DFO, 3) DFO+T, 4) DFO+O and 5) DFO+T+O.

Over a course of 4 weeks, rats in groups 2 to 5 received DFO by gavage, and rats in groups 3 and 5 ran on the treadmill 5 times a week with moderate intensity; also, rats in groups 4 and 5 received 81 μmol/kg octopamine supplement intraperitoneally 5 days a week. The Kolmogorov-Smirnov statistical test, independent samples t-test and two-way analysis of variance were used to analyze the research findings ($p<0.05$).

Results: DFO had a significant effect on increasing the gene expression levels of VEGF ($p=0.001$) and PDGFR ($p=0.002$); training had a significant effect on the reduction of VEGF ($p=0.001$) and PDGFR ($p=0.012$); also, octopamine consumption had a significant effect on the reduction of VEGF ($p=0.001$) and PDGFR ($p=0.045$).

Conclusion: It seems that aerobic training and octopamine consumption alone have anti-inflammatory effects in the heart tissue of DFO-poisoned rats, however they do not have significant anti-inflammatory interactive effects.

Keywords:
Deep Fried Oils, Aerobic Training, Octopamine, VEGF, PDGFR.

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1. Introduction

Cardiovascular disease (CVD) is the most common cause of death in most countries of the world, including Iran, and is the most important cause of disability as well. In most cases, premature coronary artery disease is directly related to the number and severity of atherosclerosis risk factors. Heart failure is one of the most common heart diseases, which is considered as a clinical syndrome in which an abnormality in the structure or function of the heart causes its inability to empty or fill with blood at a rate to meet the metabolic needs of the body (1).

Today, deep frying is a general cooking method in which fat is used as a heat transfer medium and during which foods with unique characteristics in terms of taste, texture and appearance are produced (2). In this method, during the frying process, simultaneously with the dislocation and transfer of temperature, the transfer of oil into the product and the exit of water from it can be envisaged (3). One of the compounds formed during high heating of foods, especially foods with high fat, is acrolein. Propenal-1 or acrolein is an unsaturated aldehyde electrophile belonging to the group of α and β aldehydes (4). The toxins produced during the fraying process cause the production of free radicals. The production of free radicals causes the initiation of inflammatory pathways related to cell death in vessels and the reduction of angiogenesis (5).

A set of factors such as increased blood flow and hemodynamic forces, increased shear stress, muscle contraction, hypoxia and some cytokines are angiogenic stimulants that cause the release of angiogenic factors and as a result angiogenesis (5).

Several angiogenic factors have been identified so far, but much attention has been paid to vascular endothelial growth factor (VEGF) and plate-derived growth factor (PDGF) (6). VEGF, as the most important angiogenic factor, causes proliferation of endothelial cells, migration and cell differentiation (6). Also, platelet-derived growth factor (PDGF) plays a role in collagen synthesis, production of extracellular matrix components, and contraction, and is also an angiogenesis regulatory factor (7). Recently, to reduce the effects of apoptosis, the role of exercise training in interaction with supplementation has been investigated. Today, herbal supplements are considered as one of the most effective supplements available.

Among these, we can refer to the antioxidant effects of octopamine supplement (8). Citrus fruit extracts, including sour orange, are traditionally used as weight loss and appetite suppressant products and sometimes as a food ingredient, but mostly as a medicinal or dietary supplement (9). One of the components of these extracts is octopamine, which mimics the sympathetic function and is considered an adrenergic substance. The effects of octopamine include antioxidant and anti-inflammatory effects as well as weight loss and fat burning effects (10). The difference in adrenergic receptor is one of the factors that causes the difference in the pharmacological effects when comparing octopamine with other biogenic amines such as norepinephrine and ephedrine (11).

The active ingredients in octopamine include various alkaloids with adrenergic activity, including synephrine. Based on the evidence, this substance affects the adrenaline system of the body, increases the rate of basic metabolism and rises the metabolism of the body to a great extent. Having the ability to generate heat is another characteristic of octopamine (12).

Several studies have shown that increasing physical activity as well as using antioxidant supplements is one of the ways to prevent cardiovascular diseases caused by nutritional errors (13).

It has been reported that regular aerobic physical activity with low to moderate intensity improves the physiological function of skeletal and cardiac muscles, reduces the incidence of a wide range of diseases, including cardiovascular diseases, and improves inflammatory factors (14). On the other hand, performing exercise training individually can offset the negative effects of fatty tissue, and also make brown fat tissue more efficient (15).

Recent evidence shows that exercise leads to major adaptations in adipose tissue, especially turning white fat into brown and making brown adipose tissue more efficient, which plays an important role in the metabolic effects of exercise on health (15).

Due to the importance and criticality of damage to the vital organs of the human body induced by fast foods and deep fried oils, as well as the anti-inflammatory effects of exercise training and octopamine supplementation, the present study was conducted to investigate the effect of aerobic training and octopamine supplementation on VEGF and PDGFR gene expression levels in the heart tissue of rats poisoned with deep-fried oils.

2. Materials and Methods

Animals selection

In this experimental study, 25 male Wistar rats, approximately 20 weeks old and with a weight range of 300 to 350 grams, were purchased from the Histogen Research Center and transferred to the laboratory and were kept under standard conditions for one week in order to adapt to the laboratory environment.

Then, on the eighth day, according to body weight, they were placed in 5 groups of 5 animals, including: 1) control, 2) DFO, 3) DFO+ T, 4) DFO + O and 5) DFO + T + O. Over a course of 4 weeks, rats in groups 2 to 5 received DFO by gavage; also, rats in groups 3 and 5 ran on a treadmill with moderate intensity 5 times a week, and rats in groups 4 and 5 received 81μmol/kg O supplement intraperitoneally for 5 days a week.

Exercise protocol

The aerobic training protocol was performed with moderate intensity so that the rats ran at a speed of 16 m/min (50% Vo_{2max}) in the first week, and the running speed reached 26 m/min (65% Vo_{2max}) in the last week. The duration of running in the whole research period was 20 minutes.

It is worth noting that in order to acclimate the rats to running on the treadmill, before starting the main training program, the rats ran at a speed of 9 m/min for 20 minutes for one week. Also, before starting each training session, they warmed up for 5 minutes at a speed of 7 m/min and cooled down for 5 minutes at a speed of 5 m/min after the end of the main training (16).

Supplement preparation and consumption

In the present study, octopamine supplement was prepared from Sigma Aldrich Co. Rats in groups 4 and 5 received 81 μmol/kg octopamine supplement peritoneally 5 days a week.

It is worth mentioning that in order to prepare octopamine for injection, it was dissolved in 9% normal saline solution (17). Based on previous studies, 8 liters of sunflower oil were used to prepare DFO. The oil was heated for 4 consecutive days, 8 hours a day at a temperature of 190 to 200° C, and depending on the available sources, food items (chicken nuggets, potatoes, chicken and protein products such as sausages and salami) were immersed in the frying oil every 30 minutes, and finally, on the fourth day, the oil was fed to rats by gavage (18).

Blood sampling and laboratory analysis

48 hours after the last training session and O supplement injection, rats were anesthetized by chloroform inhalation (15). In order to measure VEGF and PDGFR gene expression levels, the heart tissue of rats was extracted and placed inside special microtubes.

The microtubes were transferred into a nitrogen tank and kept in a -80° C freezer until cell analysis. The desired factors were measured by real-time PCR. The sequence of primers is presented in Table 1.

Table 1: Sequence of primers used in the present study

Gene	Forward (5'-3')	Reverse (5'-3')
PDGFR	*ACAGCACAGGGGTAGAAGAGTTG*	*GAGGATGGTTTTGGAGTGAGGAGG*
VEGF	*TGT GTG TGT GAG TGG CTT*	*ACC GAG AAT ACT GAA AAA AAC CC*
Gap	*AAG TTC AAC GGC ACA GTC AAG G*	*CAT ACT CAG CAC CAG CAT CAC C*

Statistical analysis

The Kolmogorov-Smirnov statistical test, independent samples t-test and two-way analysis of variance were used to analyze the research findings ($P<0.05$).

3. Results

VEGF and PDGFR gene expression levels in the five research groups are presented in Figures 1 and 2. The results of independent samples t-test showed that the gene and protein expression levels of VEGF ($p=0.005$) and PDGFR ($p=0.001$) in the DFO group were significantly higher than the control group.

The results of two-way analysis of variance showed that the interaction of training and octopamine supplementation had no significant effect on VEGF gene expression levels, but training had a significant effect on VEGF gene expression levels ($F=32.28$, $P=0.001$, $\eta=0.617$). Octopamine supplementation also had a significant effect on VEGF gene expression levels ($F=12.61$, $P=0.002$, $\eta=0.387$). Besides, training ($F=16.56$, $P=0.001$, $\eta=0.453$) and octopamine supplementation ($F=4.57$, $P=0.045$, $\eta=0.186$) had a significant effect on the reduction of PDGFR. However, the interaction of training and octopamine supplementation had no significant effect on VEGF gene expression levels ($F=0.236$, $P=0.632$, $\eta=0.012$).

The results of two-way analysis of variance test showed that training ($F=6.83$, $P=0.01$, $\mu=0.29$) and octopamine supplementation ($F=17.18$, $P=0.001$, $\mu=0.51$) had a significant effect on the reduction of NFkB, however the effect of training and octopamine supplementation was not significant in the reduction of NFkB ($F=0.33$, $P=0.57$, $\mu=0.02$). Also, training ($F=6.68$, $P=0.007$, $\mu=0.37$) and octopamine supplementation ($F=20.08$, $P=0.001$, $\mu=0.55$) had a significant effect on the reduction of TNF-α, however the effect of training and octopamine supplementation on the reduction of TNF-α α was not significant ($F=0.41$, $P=0.20$, $\mu=0.02$).

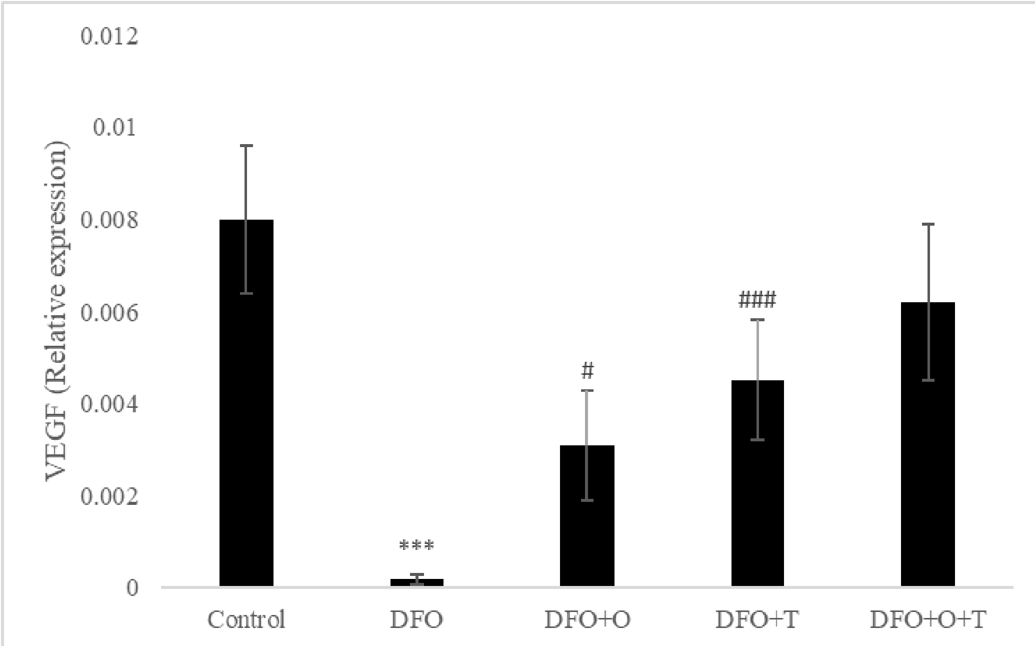

Figure 1: VEGF gene expression levels in the five research groups

*Significant reduction compared to the control group

#and ### Significant effect on the reduction of VEGF compared to the DFO group

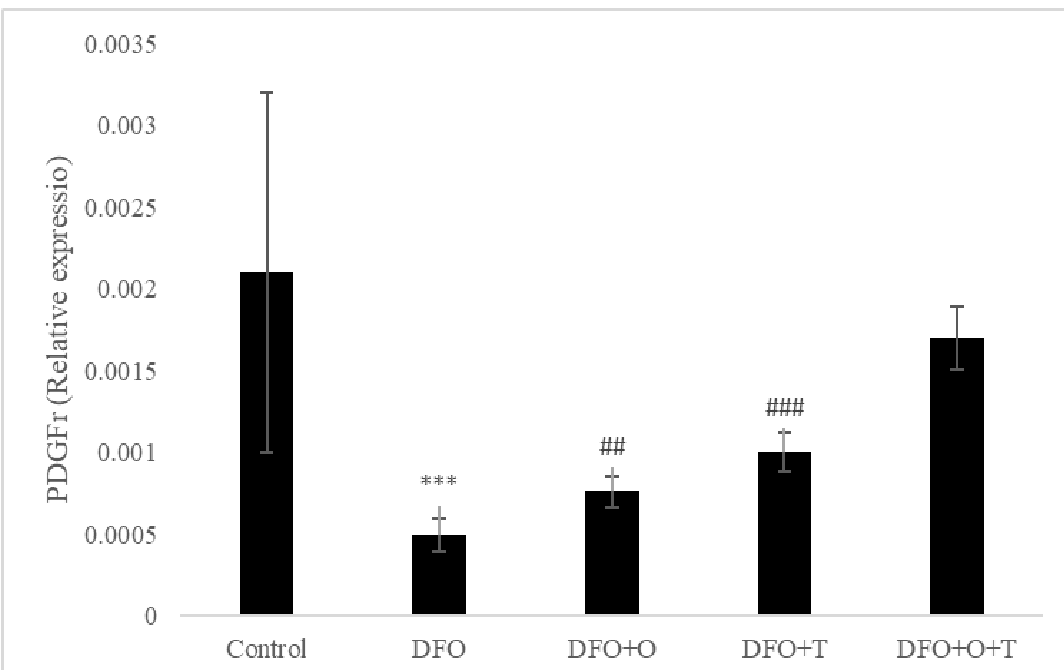

Figure 2: PDGFR gene expression levels in the five research groups

*Significant reduction compared to the control group

#and ### Significant effect on the reduction of PDGFR compared to the DFO group

4. Discussion

The results of the current research indicated that there was a significant difference in VEGF and PDGFr gene expression levels between the healthy control group and those poisoned with deep-fried oil, and as a result of poisoning with deep-heated oil, VEGF and PDGFr gene expression levels significantly decreased.

In line with the present study, many studies have been conducted regarding the effect of deep-fried oils on the vascular endothelial growth factors, which have reported similar results. For example, Zhao et al. conducted a study on the effect of four weeks of aerobic training and octepamine on the levels of malondialdehyde and caspase-3 in the brown fat tissue of male rats fed with deep-fried oils. The findings of their study showed that the concentration of malondialdehyde increased significantly as a result of poisoning with deep fried oil.

Also, the results of the above study showed that training and octopamine supplementation had a compensatory effect on the rats that were induced by poisoning, also these interventions had a significant effect on increasing VEGF and PDGFr levels in the rats poisoned with deep-fried oils; thus, it confirms the hypothesis that training and octopamine supplementation can reduce the negative effect of fried oil on the heart tissue of poisoned rats (19).

In a study, Zarezadeh Mehrizi et al investigated the effect of eight weeks of aerobic training on the gene expression of hypoxia-inducible factor-1 (HIF-1α), vascular endothelial growth factor (VEGF) and angiostatin in the hippocampus of male Wistar rats. The result of their study showed that aerobic training caused a significant increase in the levels of HIF-1α and VEGF.

Given the changes made in the levels of HIF-1α and VEGF, aerobic training had beneficial effects on the function of the hippocampus region of the brain. The results of this study are in line with the present study. This consistency may be due to the implementation of similar feeding, maintenance and aerobic training conditions in the two above-mentioned studies (20).

In another study, Wang investigated the effect of exercise training on age-related changes in improving cerebral blood flow and capillary vessels through the re-regulation of VEGF and eNOS. The results of this study indicated that exercise can improve vascular changes caused by aging and decreased perfusion, which is associated with the re-regulation of VEGF and eNOS.

The findings of this research showed that the effective mechanisms of exercise training on the changes in cerebrovascular vessels caused by aging included the re-regulation of VEGF and eNOS gene expression in connection with the change in the oxidant and antioxidant balance, which is in line with the present study (21).

The present study showed that octopamine supplementation had a significant effect on VEGF and PDGFr gene expression levels. In line with this research, Shokri et al. investigated the effect of aerobic exercise and octopamine supplementation on the angiogenesis of visceral fat tissue of rats fed with fried oil and concluded that consumption of DFO significantly increased visceral fat, while octopamine supplementation significantly increased VEGF. This agreement can be due to similar dosage of supplementation and implementation of similar procedures in keeping and feeding the rats (22).

Another result of the present study was that aerobic training and octopamine supplementation alone had a significant effect on VEGF and PDGFr gene expression, but the interaction of aerobic training and octopamine supplementation had no significant effect on the heart tissue of rats poisoned with deep-fried oil.

Also, the results of this study showed that exercise training and supplementation had a compensatory effect on the rats induced by poisoning, and these interventions had a significant effect on increasing VEGF and PDGFr levels in rats poisoned with deep-fried oils; it confirms the hypothesis that exercise training and octopamine supplementation can reduce the negative effect of fried oil on the heart tissue of poisoned rats (23).

Many studies have been carried out in line with the present study regarding the effect of aerobic exercise and octopamine supplementation on VEGF and PDGFr gene expression levels. For example, Shokri et al. in a study investigated the effect of aerobic exercise and octopamine supplementation on the angiogenesis of rat visceral adipose tissue with fried oil and concluded that DFO intake significantly increased visceral fat, while it significantly decreased VEGF. Aerobic exercise significantly increased HIF-1 and VEGF levels, while octopamine decreased HIF-1 and VEGF levels. On the other hand, octopamine along with aerobic exercise had no significant interactive effect on HIF-1 and VEGF levels. Octopamine and aerobic exercise appear to improve the process of visceral adipose tissue angiogenesis, which is impaired by DFO, and hence reduce the damage caused by DFO feeding (22).

Conclusion

The results of the present study showed that deep-fried oils lead to an increase in VEGF and PDGFR gene expression levels in the heart tissue of rats poisoned with deep-fried oil, however training and octopamine supplementation alone lead to a decrease in VEGF and PDGFR gene expression levels in the heart tissue of rats poisoned with deep-fried oil.

Acknowledgements

The authors would like to thank all the people who helped in different steps of the present research.

Funding

This study did not have any funds.

Compliance with ethical standards

Conflict of interest None declared.

Ethical approval The present study followed the ethical principles of working with laboratory animals in accordance with international laws and according to the rules of the Ethical Committee of Laboratory Animals of Islamic Azad University.

Informed consent Informed consent was obtained from all participants.

Author contributions

Conceptualization: M.A.A.; Methodology: F.J.A.; Software: S.A.H., F.J.A., P.F.; Validation: P.F., M.A.A., S.A.H.; Formal analysis: P.F., M.A.A., S.A.H.; Investigation: M.T., M.A.A., M.P.; Resources: S.A.H., F.J.A., P.F.; Data curation: P.F., M.A.A., S.A.H.; Writing - original draft: S.A.H., F.J.A., P.F.; Writing - review & editing: F.J.A., M.A.A.; Visualization: S.A.H., F.J.A., P.F.; Supervision: S.A.H., F.J.A., P.F.; Project administration: S.A.H., F.J.A., P.F.; Funding acquisition: S.A.H., F.J.A., P.F.;

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