RESEARCH ARTICLE Indian Journal of Animal Research, Volume 59 Issue 12: 2133-2137 (December 2025)

Effects of Varying Ratios of Hawthorn Fruit Extract on Nesfatin-1, GLP-1 and cTnI Response in Streptozotocin-induced Diabetic Rats

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10.18805/IJAR.BF-2045

ABSTRACT

Background: The aim of this study was to investigate the effects of Hawthorn (Crataegus oxyacantha) Fruit Extract on the response of nesfatin-1, Glucagon-like peptide 1 (GLP-1) and cardiac troponin I (cTnI) in STZ-induced diabetic rats.

Methods: This study utilized 64 adult male Wistar albino rats, aged 8-10 weeks and weighing an average of 195-215 g. Eight groups were randomly selected, each comprising eight rats designated as Control (C), H100, H200, H300; Diabetes Control (DC), DH100, DH200, DH300. Blood samples were collected from the tail vein (vena caudalis) of all individuals on days 0 and 21 of the research. The serum levels of Nesfatin-1, GLP-1 and cTnI were quantified and assessed using the ELISA technique.

Result: In diabetic groups, the increase in serum mean nesfatin-1 and cTnI levels was most pronounced in DC groups, while the most significant decrease due to increased HFE supplementation was observed in DR200 groups ($p<0.01$); whereas in diabetic groups, the decrease in serum mean GLP-1 levels was observed in DC group, while the most significant increase due to increased HFE supplementation was detected in DG200 group. As a result, it was concluded that 200 mg/kg RPE administration to healthy and diabetic rats did not cause any side effects. It was concluded that HFE, which has an anti-diabetic effect by regulating the inflammatory response that plays a role in the development of diabetes, decreasing nesfatin-1 levels and increasing GLP-1 levels, may be useful in supporting the impaired pancreatic beta cell function that occurs in diabetes.

Key words: Cardiac troponin I, Glucagon-like peptide 1, Hawtorn fruit extract, Nesfatin-1, Rat, Type 1 diabetes mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder that characterized by abnormalities carbohydrate, protein and fat metabolism and causes hyperglycemia. This condition arises from either an absolute or relative insufficiency of the insulin hormone secreted by the pancreas and/or decreased effect of insulin on cells (Çelikel *et al.,* 2024; Orkun Erkılıç and Bayraktar, 2025a; Orkun Erkılıç and Bayraktar, 2025b). Type 1 (insulin-dependent) diabetes mellitus is a chronic autoimmune disease, most common in childhood or adolescence, in which the body attacks its own insulin-producing beta cells, requiring lifelong insulin supplements (Bielka *et al.,* 2024).

Hormones are biomolecules produced by the endocrine glands and transported to target cells or organs *via* the bloodstream, regulating and coordinating biological functions (Bayraktar, 2020). Nesfatin-1, originating from the precursor protein of Nucleobindin-2 (NUCB2), is an adipokine secreted from adipose tissue that exhibits anti-apoptotic, anti-inflammatory, antioxidant and anorexigenic effects (Gharanei *et al.,* 2022). Nesfatin-1 has an effect of enhances glucose-dependent insulin secretion from beta (β) cells in the pancreas (de Oliveira dos Santos *et al.,* 2021). It is reported that nesfatin-1 plays an indirect role in preventing or reducing the complications of diabetes due to its anti-inflammatory and antioxidant properties (Nazarnezhad *et al.,* 2019). GLP-1 is a peptide hormone generated through the enzymatic breakdown of proglucagon, which is secreted from L cells in the small intestines depending on food intake and causes glucose-dependent insulin secretion (Sandoval and D'Alessio, 2015). The main effect of GLP-1 is to stimulate insulin secretion from beta cells in the pancreas when blood glucose rises, reduce glucagon secretion from alpha cells and also improve the function of beta cells by extending their lifespan (Buteau, 2008; Liu *et al.,* 2011; Lee and Jun, 2014). Troponins are a protein complex found specifically in heart muscle cells that play a vital role in muscle contraction (Bayraktar *et al.,* 2020a; Bayraktar and Tekce, 2021). There are three main types of troponin in the human body, Troponin I (TnI) and Troponin T (TnT), which play a role in muscle contraction and in the diagnosis of heart

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How to cite this article: Özcan, G.B. and Kaya, H. (2025). Effects of Varying Ratios of Hawthorn Fruit Extract on Nesfatin-1, GLP-1 and cTnI Response in Streptozotocin-induced Diabetic Rats. *Indian Journal of Animal Research*. **59(12):** 2133-2137. doi: 10.18805/IJAR.BF-2045.

Submitted: 11-07-2025 **Accepted:** 17-09-2025 **Online:** 10-12-2025

muscle damage (Orkun Erkılıç and Bayraktar, 2025c). Cardiac troponin I (cTnI) is a highly specific cardiac biomarker that is released into plasma from cardiac myocytes due to cardiac damage and is used to evaluate myocardial damage and diseases (Wu *et al.,* 1996; Bayraktar *et al.,* 2020b).

Medicinal and aromatic plants stand out as an important alternative in traditional and complementary medicine practices in the treatment and prevention of diseases, thanks to their antioxidant, antidiabetic and antimicrobial effects and valuable phytochemicals (Bayraktar and Tekce, 2019; Ozcan Böyük *et al.,* 2024; Orkun Erkılıç and Bayraktar, 2025d). Hawthorn fruit is a small, red, slightly sour sweet fruit produced by plants belonging to the Crataegus genus. Hawthorn (*Crataegus* spp.) extract is a promising plant in the management of diabetes and the prevention of diabetic complications due to presence of its bioactive compounds, especially phenolic compounds (chlorogenic acid, proanthocyanidins, flavonoids) and triterpenoids (Nazhand *et al.,* 2020; Martinelli *et al.,* 2021). There are no studies investigating the changes in mean serum nesfatin-1, GLP-1 and cTnI levels in diabetic rats with different amounts of Hawthorn (*Crataegus oxycantha*) fruit extract (HFE). Therefore the study has been conducted to investigate the effect of STZ and HFE on adipokine (nesfatin-1), intestinal (GLP-1) and cardiac response in type 1 DM rats.

MATERIALS AND METHODS

The study was conducted on 64 male Wistar rats, aged 8-10 weeks old and averaging 195-215 grams in weight. Before starting the study, ethics committee approval was obtained from the Veterinary Control Research Institute Ethics Committee (Decision number 2025/89). The research was carried out in accordance with ethical principles and rules, considering animal welfare and rights. All rats were kept in a controlled room with 50-60% humidity, 22°C temperature and 12 hours of light (06:00, 18:00) and 12 hours of darkness, with 2 cages in each group and 4 animals in each cage. The study spanned a total of 31 days, comprising a 7-day adaptation phase, a 3-day diabetes induction period and a 21-day trial phase. Those with fasting blood glucose levels of ≥250 mg/dL after 3 days of the application were evaluated as diabetic. All applications during the study were performed in the same time periods (09:00-10:00). This investigation involved the addition of the extract to the experimental meals of diabetic rats at varying dosages to assess its impact on serum nesfatin-1, intestinal GLP-1 and cardiac responses. Hawthorn berry extract was obtained from a previous study.

The experimental protocol was formed as follows:

Control group (C)

Only physiological saline was administered to rats *via* i.p.

HFE 100 mg/kg group (H100)

100 mg/kg of HFE was added to the rats' diet.

HFE 200 mg/kg group (H200)

200 mg/kg of HFE was added to the rats' diet.

HFE 300 mg/kg group (H300)

300 mg/kg of HFE was added to the rats' diet.

Diabetic control group (DC)

50 mg/kg of STZ solution prepared in citrate buffer (pH 4.5) was administered to rats *via* i.p.

Diabetic HFE 100 mg/kg group (DH100)

Rats were given a single intraperitoneal (i.p.) dosage of 50 mg/kg of STZ citrate buffer (pH 4.5) solution. HFE was added to the rats' diet at a level of 100 mg/kg.

Diabetic HFE 200 mg/kg group (DH200)

Rats were given a single intraperitoneal (i.p.) dosage of 50 mg/kg of STZ citrate buffer (pH 4.5) solution. HFE was added to the rats' diet at a level of 200 mg/kg.

Diabetic HFE 300 mg/kg group (DH300)

Rats were given a single intraperitoneal (i.p.) dosage of 50 mg/kg of STZ citrate buffer (pH 4.5) solution. HFE was added to the diet of rats at a level of 300 mg/kg.

Collection of serum samples

Blood samples were taken from the tail vein of rats on day 0 of the study and intracardially on day 21. Blood samples were collected in tubes without anticoagulant (VACUETTE® TUBE Z Serum Clot Activator) and centrifuged in a refrigerated centrifuge (NF 1200R, NÜVE, Türkiye) for 10 minutes at 3000 rpm in the laboratory and the resulting sera were separated.

Measurement of serum visfatin and cTnI level

In measuring serum nesfatin-1, GLP-1 and cTnI levels obtained in the study, ELISA kit type-specific for rat nesfatin-1 Elisa Kit (BT LAB, Cat. No: E0878Ra, China), GLP-1 Elisa Kit (Sinogeneclon, Cat. No: SG-20242, China) and cTnI ELISA kit (BT LAB, Cat. No SG-20697, China) an intra-assay coefficient of 8.0% and an inter-assay coefficient of 10.0% was utilized under the manufacturer's protocol. The results were evaluated by reading absorption values at 450 nm under the procedure reported in the kit.

Statistical analysis

Statistical analyses were conducted utilizing graph pad prism (version 8). The data are presented as mean ± standard error of the mean (SEM). After observing significant effects in the ANOVA, Tukey's multiple comparison test was employed to evaluate pairwise differences between the groups. Statistical comparisons encompassed intra-group evaluations (Day 0 vs. Day 21) and inter-group assessments (*e.g.*, Control Day 0 vs. H200 Day 21). The significance level in the analysis results was established at $p<0.05$.

RESULTS AND DISCUSSION

While adipokines secreted from adipose tissue regulate physiological processes including energy balance,

glucose homeostasis, lipid metabolism and inflammation, the release profile of adipokines is impaired in diabetes (Bayraktar, 2020; Dilworth *et al.,* 2021). Therefore, adipokines significantly contribute to the pathogenesis of diabetes and diabetes-related complications (Błażejewska *et al.,* 2025). Nesfatin-1 is an adipokine involved in energy metabolism and glucose homeostasis and has anorexigenic, anti-hyperglycemic and anti-inflammatory effects (Xu and Chen, 2020). While the increase in mean serum nesfatin-1 levels due to diabetes was mostly seen in DC groups, similarly, mean serum nesfatin-1 levels notable decreased in all groups due to the addition of antioxidant HFE in DH groups, with the most significant decrease being determined in DH200 groups (Table 1), ($p<0.01$). Although the current results of our study are limited in terms of studies examining the effect of HFE on serum nesfatin-1 levels, they are consistent with similar research literature reporting that its use in diabetes groups reduces mean serum nesfatin-1 levels (Kargarfard *et al.,* 2023). We believe that this is due to the phytochemicals contained in HFE, which have an antioxidant effect.

DM has an active role in the development of cardiovascular diseases and cTnI is a highly specific cardiac biomarker used in the diagnosis of heart muscle damage (Erkılıç Orkun and Bayraktar, 2025b). While the increase in diabetes-related cardiac damage was mostly seen in DC groups, the most significant decrease in mean serum cTnI levels associated with HFE addition, purported to have a cardioprotective effect, was determined in DH200 groups, despite lacking statistical significance ($p>0.05$). Although studies examining the effect of HFE on serum cTnI levels in diabetes are limited, in our study, it was observed that the use of HFE at different rates decreased the serum cTnI level, However, this decrease was not statistically significant (Table 2), ($p>0.05$), aligning with previous studies indicating an increase in serum cTnI levels in diabetic patients (Berndt *et al.,* 2005; Brouwers *et al.,* 2013) and that HFE, which is reported to have a cardioprotective effect, reduces the mean serum cTnI level (Sadek *et al.,* 2018). We believe that this is due to differences in individual physiological responses to HFE.

The most important effect of GLP-1 in the treatment of diabetes is that it increases insulin secretion from pancreatic beta (β) cells when blood glucose levels are high (Vilsbøll, 2009). In diabetic groups, the most notable reduction in serum mean GLP-1 levels occurred in DC groups, whereas the most significant increase attributed to HFE addition was observed in DH200 groups (Table 3), ($p<0.05$). Although the current results of our study are limited in terms of studies examining the effect of HFE on serum GLP-1 levels, they are consistent with similar research literature reporting that its use in diabetic groups reduces

Table 1: Mean serum nesfatin-1 values (ng/ml) and statistical comparisons (Mean±SH) of the study groups.

Group	Day 0	Day 21	Mean difference	Significance
	(Mean ± SEM)	(Mean ± SEM)	(Day 21 - Day 0)	
C	2.03±0.10	2.41±0.12	+0.37	p>0.05
H100	2.10±0.07	2.62±0.07	+0.52	**(p<0.01)
H200	2.20±0.09	3.07±0.11	+0.87	***(p<0.001)
H300	2.15±0.12	2.86±0.10	+0.71	***(p<0.001)
DC	1.36±0.04	0.98±0.06	-0.37	***(p<0.001)
DH100	1.41±0.05	1.63±0.05	+0.22	p>0.05
DH200	1.38±0.04	1.70±0.04	+0.31	**(p<0.01)
DH300	1.40±0.05	1.67±0.05	+0.27	*(p<0.05)

*Means within a column showing different superscripts are significantly different ($p<0.05$). SEM = standard error of the mean. C:Control, H: Hawthorn fruit extract, DC: Diabetic Control and DH:Diabetic rats given Hawthorn fruit extract.

Table 2: Mean serum cTn1 values (ng/ml) and statistical comparisons (Mean±SH) of the study groups.

Group	Day 0	Day 21	Mean difference	Significance
	(Mean ± SEM)	(Mean ± SEM)	(Day 21 - Day 0)	
C	0.38±0.03	0.41±0.06	+0.0250	P>0.05
H100	0.37±0.0	0.38±0.02	+0.0125	P>0.05
H200	0.38±0.03	0.33±0.05	-0.0500	P>0.05
H300	0.37±0.03	0.35±0.04	-0.0250	P>0.05
DC	0.67±0.19	0.78±0.24	+0.1125	P>0.05
DH100	0.66±0.16	0.65±0.11	-0.0125	P>0.05
DH200	0.70±0.13	0.57±0.18	-0.1250	P>0.05
DH300	0.67±0.16	0.62±0.21	-0.0500	P>0.05

*cTnI (Cardiac Troponin I), Means within a column showing different superscripts are significantly different ($p<0.05$): SEM = standard error of the mean. C:Control, H: Hawthorn fruit extract, DC: Diabetic Control and DH:Diabetic rats given Hawthorn fruit extract.

Table 3: Mean serum GLP-1 values (ng/ml) and statistical comparisons (Mean±SH) of the study groups.

Group	Day 0	Day 21	Mean difference	Significance
	(Mean ± SEM)	(Mean ± SEM)	(Day 21 - Day 0)	
C	11.86±0.27	12.35±0.36	+0.49	p>0.05
H100	11.95±0.25	12.45±0.32	+0.50	p>0.05
H200	12.76±0.32	13.69±0.46	+0.93	*(p<0.05)
H300	12.11±0.27	12.88±0.40	+0.77	p>0.05
DC	5.65±0.15	5.25±0.12	-0.40	p>0.05
DH100	5.44±0.24	5.64±0.24	+0.20	p>0.05
DH200	5.74±0.29	6.64±0.26	+0.90	*(p<0.05)
DH300	5.46±0.17	6.15±0.24	+0.69	p>0.05

*Means within a column showing different superscripts are significantly different (p<0.05): SEM= Standard error of the mean. C:Control, H: Hawthorn fruit extract, DC: Diabetic control and DH: Diabetic rats given Hawthorn fruit extract.

mean serum GLP-1 levels (González-Abuín *et al.,* 2014; Bhat *et al.,* 2018). We think that this is due to the phytochemicals found in HFE, which have antioxidant effects.

CONCLUSION

In conclusion, it is thought that HFE, which has been reported to have antioxidant and anti-inflammatory effects in the regulation of impaired metabolic and inflammatory responses in healthy individuals and in diabetes, is safe and beneficial when administered at a dose of 200 mg/kg in diabetic groups.

ACKNOWLEDGEMENT

The views and conclusions expressed in this article are solely those of the authors and do not necessarily represent the views of their affiliated institutions. The authors are responsible for the accuracy and completeness of the information provided, but do not accept any liability for any direct or indirect losses resulting from the use of this content.

Informed consent

All animal procedures for experiments Veterinary Control Central Research were approved by the Committee of Experimental Animal Care and Handling Techniques were approved by the University of Animal Care Committee.

Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this article. No funding or sponsorship influenced the design of the study, data collection, analysis, decision to publish or preparation of the manuscript.

REFERENCES

Bayraktar, B. (2020). Endocrine System. In: Taşkin E, Kocahan S, editors. Physiology for Health Sciences. *Akademisyen Yaynevi: Ankara. Türkiye*. pp. 239-270.

Bayraktar, B. and Tekce, E. (2019). Sıcaklık stresi ile indüklenen broilerde farklı oranlarda uygulanan bitkisel eksraktların bazı kan parametrelerine etkisinin incelenmesi. *Etlik Veteriner Mikrobiyoloji Dergisi*. **30(2):** 143-148. doi: 10.35864/evmd.579922.

Bayraktar, B. and Tekce, E. (2021). Investigation of the relationship of asprosin and cardiac troponin response with some physiological and biochemical parameters in Anatolian native horse. *Pferdeheilkunde*. **37(5):** 518-524. doi: 10.21836/PEM20210508.

Bayraktar, B., Tekce, E., Çiğdem, T., Bayraktar, S.B., Kilinç, A.A., Ülker, U. and Kurtdede, E. (2020a). Investigating the adipokine and cardiac troponin response ın experimental thyroid dysfunction. *Veterinarski Arhiv*. **90(3):** 289-296. doi: 10.24099/vet.arhiv.0783.

Bayraktar, B., Tekce, E., Kaya, H., Karaalp, M. and Turunc, E. (2020b). The impact of dietary tarragon (Artemisia dracun-culus) on serum apelin, brain-derived neurotrophic factor, cardiac troponin concentrations and histopathology of liver tissue in laying hens housed at different stocking densities. *Vet. Med-Czech*. **65:** 269-279. doi:10.17221/9/2020-VETMED.

Berndt, J., Kloting, N., Kralisch, S., Kovacs, P., Fasshauer, M., Schon, M.R., Bluher, M. (2005). Plasma visfatin concentrations and fat depot-specific mRNA expression in humans. *Diabetes*. **54(10):** 2911-2916. doi: 10.2337/diabetes.54.10.2911.

Bhat, G.A., Khan, H.A., Alhomida, A.S., Sharma, P., Singh, R. and Paray, B.A. (2018). GLP-I secretion in healthy and diabetic wistar rats in response to aqueous extract of *Momordica charantia*. *BMC Complementary and Alternative Medicine*. **18:** 1-8. doi: 10.1186/s12906-018-2227-4.

Bielka, W., Przezak, A., Molêda, P., Pius-Sadowska, E. and Machaliñski, B. (2024). Double diabetes-when type 1 diabetes meets type 2 diabetes: definition, pathogenesis and recognition. *Cardiovascular Diabetology*. **23(1):** 62. doi:10.1186/s12933-024-02145-x.

Błażejewska, W., Dąbrowska, J., Michałowska, J. and Bogdañski, P. (2025). The role of adiponectin and ADIPOQ variation in metabolic syndrome: A narrative review. *Genes*. **16(6):** 699. doi: 10.3390/genes16060699.

Brouwers, O., de Vos-Houben, J.M., Niessen, P.M., Miyata, T., Nieuwenhoven, F.V., Janssen, B.J., Schalkwijk, C.G. (2013). Mild oxidative damage in the diabetic rat heart is attenuated by glyoxalase-1 overexpression. *International Journal of Molecular Sciences*. **14(8):** 15724-15739. doi: 10.3390/ijms140815724.

Buteau, J. (2008). GLP-1 receptor signaling: Effects on pancreatic β-cell proliferation and survival. *Diabetes and Metabolism*. **34:** S73-S77. doi: 10.1016/S1262-3636(08)73398-6.

Çelikel Taşci S., Bayraktar B., Bülbül A.S., Sait A., Korkmaz S. (2024). Effect of different rates of rambutan peel extract on visfatin and cardiac troponin I response in type 2 diabetic rats induced with streptozotocin. *Indian Journal of Animal Research*. **58(11):** 1969-1974. doi: 10.18805/IJAR.BF-1899.

de Oliveira dos Santos, A.R., de Oliveira Zanuso, B., Miola, V.F.B., Barbalho, S.M., Santos Bueno, P.C., Flato, U.A.P. and dos Santos Haber, J.F. (2021). Adipokines, myokines and hepatokines: Crosstalk and metabolic repercussions. *International Journal of Molecular Sciences*. **22(5):** 2639. doi: 10.3390/ijms22052639.

Dilworth, L., Facey, A. and Omoruyi, F. (2021). Diabetes mellitus and its metabolic complications: The role of adipose tissues. *International Journal of Molecular Sciences*. **22(14):** 7644.doi: 10.3390/ijms22147644.

Erkılıç Orkun T. and Bayraktar, B. (2025a). Effect of jackfruit pulp extract on serum nesfatın-1 and Vısfatın levels in streptozotocın-induced rats. *Indian Journal of Animal Research*. **59(2):** 293-298. doi: 10. 18805/IJAR.BF-1902.

Erkılıç Orkun T. and Bayraktar, B. (2025b). Effect of *Moringa oleifera* oil extract on adipokine (Apelin, Visfatin and Nesfatin-1) and cardiac (cTnI) response in streptozotocin-induced rats. *Indian Journal of Animal Research*. **59(1):** 108-113. doi: 10.18805/IJAR.BF-1904.

Erkılıç Orkun T. and Bayraktar, B. (2025c). The effect of cannabidiol on myokine, cerebral and cardiac response in rats with sepsis induced by cecal ligation and punture method. *Indian Journal of Animal Research*. **59(3):** 497-502. doi: 10.18805/IJAR.BF-1905.

Gharanei, S., Ramanjaneya, M., Patel, A.H., Patel, V., Shabir, K., Auld, C. and Randeva, H.S. (2022). NUCB2/Nesfatin-1 reduces obesogenic diet induced inflammation in mice subcutaneous white adipose tissue. *Nutrients*. **14(7):** 1409. doi: 10.1016/j.neuro.2019.07.001.

González-Abuín, N., Martínez-Micaelo, N., Margalef, M., Blay, M., Arola-Arnal, A., Muguerza, B. and Pinent, M. (2014). A grape seed extract increases active glucagon-like peptide-1 levels after an oral glucose load in rats. *Food and Function*. **5(9):** 2357-2364.

Kargarfard, M., Mokhtaba, M., Chehelcheraghi, F. and Nazari, A. (2023). The effect of high-intensity interval training in combination with hawthorn extract consumption on cardiac fibrosis and inflammatory markers in heart tissue of elderly rats. *Sport Physiology*. **15(60):** 35-54. doi: 10.22089/spj.2023.5105.2283.

Lee, Y.S. and Jun, H.S. (2014). Anti-diabetic actions of glucagon-like peptide-1 on pancreatic beta-cells. *Metabolism*. **63(1):** 9-19. doi: 10.1016/j.metabol.2013.09.010.

Liu, Z., Kim, W., Chen, Z., Shin, Y.K., Carlson, O.D., Fiori, J.L. and Egan, J.M. (2011). Insulin and glucagon regulate pancreatic β-cell proliferation. *PloS one*. **6(1):** e16096. doi: 10.1371/journal.pone.0016096.

Martinelli, F., Perrone, A., Yousefi, S., Papini, A., Castiglione, S., Guarino, F. and Salami, S. A. (2021). Botanical, phytochemical, anti-microbial and pharmaceutical characteristics of hawthorn (*Crataegus monogyna* Jacq.), Rosaceae. *Molecules*. **26(23):** 7266. doi: 10.3390/molecules26237266.

Nazarnezhad, S., Rahmati, M., Shayannia, A., Abbasi, Z., Salehi, M. and Khaksari, M. (2019). Nesfatin-1 protects PC12 cells against high glucose-induced cytotoxicity *via* inhibiting oxidative stress, autophagy and apoptosis. *Neurotoxicology*. **74:** 196-202. doi: 10.1016/j.neuro.2019.07.001.

Nazhand, A., Lucarini, M., Durazzo, A., Zaccardelli, M., Cristarella, S., Souto, S.B. and Santini, A. (2020). Hawthorn (*Crataegus* spp.): An updated overview on its beneficial properties. *Forests*. **11(5):** 564. doi: 10.3390/f11050564.

Orkun Erkılıç, T. and Bayraktar, B. (2025d). Effect of graviola oil extract on anti-obesity effect and adipokine (Apelin and Adiponectin) response in high fat diet-induced obese rats. *Indian Journal of Animal Research*. **59(2):** 316-320. doi: 10.18805/IJAR.BF-1907.

Ozcan, G.B., Bozok, U.G., Battal, F. and Bayraktar, B. (2024). The impact of aromatherapy on glossophobia among medical students: A study on cortisol levels and stress reduction. *Medicine Science*. **13(3):** 610-615. doi: 10.5455/medscience.2024.06.053.

Sadek, M.A., Mousa, S., El-Masry, S. and Demain, A. (2018). Influence of hawthorn (*Crataegus oxyacantha*) leaves extract administration on myocardial infarction induced by isoproterenol in rats. *Cardiology and Angiology: An International Journal*. **7(1):** 1-12.

Sandoval, D.A. and D'Alessio, D.A. (2015). Physiology of proglucagon peptides: Role of glucagon and GLP-1 in health and disease. *Physiological Reviews*. **95(2):** 513-548. doi: 10.1152/physrev.00013.2014.

Vilsbøll, T. (2009). The effects of glucagon like peptide 1 on the beta cell. *Diabetes, Obesity and Metabolism*. **11:** 11-18. doi: 10.1111/j.1463-1326.2009.01073.x.

Wu, A.H., Feng, Y.J., Contois, J.H. and Pervaiz, S. (1996). Comparison of myoglobin, creatine kinase-MBand cardiac troponin I for diagnosis of acute myocardial infarction. *Annals of Clinical and Laboratory Science*. **26(4):** 291-300.

Xu, Y. and Chen, F. (2020). Antioxidant, anti-inflammatory and anti-apoptotic activities of nesfatin-1: A review. *Journal of Inflammation Research*. pp: 607-617.