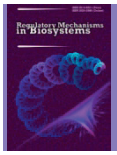

Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.

Relationship between asprosin and certain biochemical parameters in obese patients

N. S. Humadi*, N. A. Saleh**

*Aliraqia University, Baghdad, Iraq
**Tikrit Unversity, Tikrit, Iraq

Article info

Received 17.02.2025
Received in revised form 10.03.2025
Accepted 09.04.2025

Department of Basic Science, College of Dentistry, Aliraqia University, Baghdad, 10001, Iraq. E-mail: nada.subhi@aliraqia.edu.iq.com

Department of Chemistry, College of Education of Pure Science, Tikrit University, Tikrit, 34001, Iraq. E-mail: nadea.saleh@tu.edu.iq

Humadi, N. S., & Saleh, N. A. (2025). Relationship between asprosin and certain biochemical parameters in obese patients. Regulatory Mechanisms in Biosystems, 16(2), e25059. doi:10.15421/0225059

Obesity is a widespread health issue among children and adolescents, driven by genetic and environmental factors. It results from low energy expenditure and excessive caloric intake, leading to complications like hypertension, metabolic disorders, cardiovascular disease, diabetes, and arthritis. The current study aimed to estimate the levels of asprosin, leptin, adiponectin, and zinc in obese individuals and to analyze their correlation with obesity-related metabolic disorders. The study collected 60 blood samples from obese individuals (30 males, 30 females) and 60 from healthy controls in Baghdad, Iraq. Asprosin, leptin, and adiponectin levels were measured using ELISA, involving antibody reactions and spectrophotometric detection at 450 nm. Zinc concentration was determined through its reaction with 5-Br-PADAP, forming a color complex measured at 560 nm. The findings revealed an increase in asprosin levels in obese individuals, supporting its role as a potential biomarker for obesity and metabolic disorders. Additionally, leptin levels were elevated in obese subjects, while adiponectin and zinc levels were significantly lower in comparison to healthy controls. This study highlights the potential role of asprosin as a biomarker and therapeutic target for obesity. The observed alterations in leptin, adiponectin, and zinc levels further emphasize the metabolic dysregulation associated with obesity.

Keywords: asprosin; obesity; leptin; adiponectin; zinc; metabolic disorders.

Introduction

The accumulation of excess body fat is called obesity, a condition characterized by an excessive increase in triacylglycerol in adipose tissue (Oussaada et al., 2019). Many factors influence obesity, including age, reactive oxygen species damage, environmental pollution, hormonal changes and immunological variables (Pérez-Torres et al., 2021; Nguyen et al., 2022). It may also have uncontrollable genetic or metabolic reasons, although it frequently stems from a sedentary lifestyle, poor nutrition, and insufficient physical exercise (Loos et al., 2022). Many comorbidities, including type 2 diabetes and hypertension, which are risk factors for cardiovascular disease and the world's leading cause of death, are typically present in people who are obese (Kosmas et al., 2023). Furthermore, decreased insulin receptors, which account for the incapacity to lower hepatic glucose synthesis, are linked to insulin resistance and obesity. Although primary hypertension has increased in prevalence with the spread of the obesity pandemic, hypertension is a secondary consequence of renal disease. Furthermore, compared to non-obese groups, obese populations have been shown to have higher fluctuations in blood pressure and heart rate. While obesity is frequently linked to psychological issues and its low social standing can result in total social isolation and melancholy, physical inactivity may be the result of physical handicaps brought on by excess body weight (Sagar et al., 2018). Asprosin is a newly recognised fasting-induced hormone that has received considerable attention in scientific research since its discovery and first description in 2016 (Feng et al., 2020). Recently, the newly discovered adipokine asprosin entered the codeine subclass of protein hormones. Exons 65 and 66 of the fibrillin-1 gene (FBN1), which is found on chromosome 15q21.1, encode profibroline-1, the 320 kDa glycoprotein that is produced when the C-terminus of the parent protein profibroline-1 is cleaved by an enzyme to produce the new peptide hormone asprosin. The protein known as mammalian asprosin has 140 amino acids and weighs around 30 kDa (Ovali et al., 2022). It is synthesized primarily in white adipose tissue during fasting. However, it can also be produced by other tissues such as the lungs, heart, and pancreatic beta cells under certain conditions, and it plays a critical role in the regulation of metabolism and energy and also in the regulation of appetite. It is a key factor in the body's response during periods of fasting. Asprosin is secreted into the circulation and then polarised by the liver, where it binds to the surface of liver cells and promotes high levels of blood glucose, which is vital for the survival and function of the brain (Shabir et al., 2021). Elevated asprosin levels are associated with several metabolic disorders, including T2DM (Zhang et al., 2024). Studies suggest that asprosin regulates insulin sensitivity and promotes inflammation in pancreatic tissue. Thus, understanding these pathways may provide insight into potential therapeutic targets for treating T2DM and other related diseases. Despite its promise as a biomarker or therapeutic target for metabolic diseases, challenges remain in determining its levels in clinical settings, and continued research into this newly discovered hormone may open new avenues for the effective treatment of metabolic syndrome. Leptin is a body weight-regulating hormone composed of (167) amino acids that regulate body weight, metabolism, and reproductive function. Studies have confirmed that leptin mRNA expression in white and brown fat cells is controlled by food-related hormones, including insulin, and metabolic factors, including glucose and its metabolites. Fasting has been shown to reduce glucose and insulin concentrations, and thus plasma leptin concentrations, in obese and lean individuals. Subcutaneous injection of leptin in congenitally leptin-deficient subjects has been found to reduce total cholesterol, triglycerides, and LDL while increasing adipose tissue HDL concentration, as leptin lowers triglyceride levels (Picó et al., 2022; Peelman et al., 2004). Therefore, when leptin deficiency or mutation in the leptin receptor gene or resistance to its receptor occurs, triglycerides are increased and stored in non-adipose tissues, and leptin also acts on lipolysis by increasing the concentration of the lipolytic hormone lipase (Ahmed et al., 2021). Adiponectin is a newly discovered cytokine that increases insulin sensitivity in various surface and epithelial cells. Adipocytes secrete various proteins called adipokines, which have different biological functions. Adipose tissue can regulate energy balance through the action of secreted adipokines, and one of these secreted proteins is adiponectin (Clemente-Suárez et al., 2023). Adiponectin is mainly produced in adipose tissue and consists of 224 amino acids. It is secreted into the circulation in three primary forms: low molecular weight trimer (LMW), medium molecular weight hexamer (MMW), which can be converted to globular adiponectin, and high molecular weight protein (HMW). Low levels of adiponectin's high molecular

weight form, the most bioactive form in humans, are frequently linked to the onset of type 2 diabetes. Because of its anti-inflammatory, anti-fibrotic, and antioxidant properties, adiponectin is a well-known homeostatic factor that regulates blood sugar, lipid metabolism, insulin sensitivity, and immunological response. It also protects neurons and stem cells (Ramakrishnan et al., 2023). After iron, zinc is the second most prevalent mineral in living things. Throughout the body, zinc is primarily present in bone (~30%) and skeletal muscle (~60%), followed by the skin, liver, prostate, pancreas, heart, kidney, and brain. Zinc plays a crucial role in nerve signalling, cell autolysis, differentiation, and proliferation. Zinc is a structural element of thousands of protein domains and a catalytic cofactor for 300 enzymes of all types. Many proteins depend on zinc to function (Hernández-Camacho et al., 2020; Abdulmajeed et al., 2024), zinc deficiency primarily affects the immune, skeletal, gastrointestinal, skin, and nervous systems. The body reacts to inadequate zinc intake with quick metabolic changes to minimise endogenous losses by lowering zinc-dependent processes, such as growth and immune system functions. Therefore, severe zinc deficiency causes significant problems such as growth retardation, weight loss, diarrhoea, dermatitis, hypogonadism, blood abnormalities, mental disorders, immunological malfunction with recurrent infections, and increased oxidative stress (Franco et al., 2024).

Matherials and methods

The study was approved by the human ethics committee of Department of Chemistry / College of Education for Pure Sciences / Tikrit University, Everyone who took part in the study was told about it and asked to sign a consent form. The patient was also guaranteed that his information would be kept private.

The present study involved collecting 60 blood samples from obese subjects (30 males and 30 females) and 60 blood samples from healthy subjects (30 males and 30 females) who were considered the control group in the Baghdad-Iraq governorate. 5mL of venous blood was collected in gel tubes. The samples were left at room temperature and then centrifuged at 3000 r.p.m. to obtain the serum, which was stored in Eppendorf tubes at -20 °C until the biochemical measurements under investigation were carried out.

Determination of asprosin, leptin and adiponectin levels: asprosin, leptin and adiponectin levels were estimated using a sandwich ELISA kit. Samples (or standards) were added to the wells of the ELISA plate and allowed to react with the antibody. Each plate well was filled with an avidin-horseradish peroxidase (HRP)-conjugated antibody and a hormone-specific biotinylated detection antibody, which are then incubated. The unbound components were cleaned and each well filled with the substrate solution. Only wells that looked blue contained the antibody needed to identify the target hormone. When the Stop Solution was added, the enzyme-base reaction was stopped, and the colour turned yellow. The optical density (OD) was determined using spectrophotometry at a wavelength of 450 nm. The amount of hormone being measured was directly correlated with the OD value. The determination of zinc concentration was based on the reaction of zinc in the sample with 5-Br-PADAP to form a colour complex; the colour depth of the complex was directly proportional to the zinc ion concentration, which is measured at a wavelength of 560 nm.

The results of the current study were statistically analysed using the statistical program (GraphPad Prism 9.2.0.332) to extract the arithmetic mean and standard deviation and by ANOVA and t-test, and the arithmetic means were compared by t-test with a probability level of $P < 0.05$. The Pearson correlation coefficient was also used to find the correlation between the glutamate carboxypeptidase enzyme and the chemical variables studied.

Results

Statistical analysis of the results showed significant differences in the levels of biochemical markers between obese patients and the control group. A significant decrease in the mean zinc concentration was observed in patients (0.32 ± 0.06 mmol/L) compared to the control group (0.54 ± 0.06 mmol/L, $P < 0.0001$). Adiponectin concentration was also significantly lower in obese patients (1.28 ± 0.47 ng/mL) compared to healthy controls (3.15 ± 0.82 ng/mL). Conversely, asprosin concentration was significantly higher in patients (4.45 ± 1.71 ng/mL) compared to the control group (2.63 ± 0.80 ng/mL). Furthermore, leptin levels were significantly higher in obese patients (332.7 ± 74.7 pg/mL) compared to healthy controls (143.7 ± 51.9 pg/mL). These findings reflect the metabolic disturbances associated with obesity, suggesting a role for these markers in the biochemical interaction associated with obesity and its subsequent metabolic complications.

Table 1
Comparison of zinc, adiponectin, asprosin, and leptin levels between obese patients and healthy controls (mean ± SD, n = 60)

Parameter	Control	Patients	P-value
Zinc, mmol/L	0.54 ± 0.06	0.32 ± 0.06	<0.0001
Adiponectin, ng/mL	3.15 ± 0.82	1.28 ± 0.47	<0.0001
Asprosin, ng/mL	2.63 ± 0.80	4.45 ± 1.71	<0.0001
Leptin, pg/mL	143.68 ± 51.85	332.65 ± 74.66	<0.0001

ROC curve analysis results showed the varying discriminatory ability of the studied biochemical variables in predicting obesity. Asprosin showed an area under the curve (AUC) of 0.8 at a cutoff value of 3.7 pg/mL, with a sensitivity of 56% and a specificity of 97%. Leptin, on the other hand, had the highest discriminatory ability with an AUC of 0.971 and a cutoff value of 187 ng/mL, achieving a sensitivity of 98.3% and a specificity of 95%. Conversely, adiponectin and zinc had the lowest discriminatory ability, with AUCs of 0.013 and 0.011, respectively, at a cutoff value of 0.4 ng/mL for adiponectin and 0.75 mmol/L for zinc, with a sensitivity of 98% and a specificity of 98.3% for zinc. These results indicate the important role of lipoproteins in distinguishing obese from healthy individuals, with leptin being superior as a reliable diagnostic tool.

Table 2
Diagnostic performance of asprosin, leptin, adiponectin, and zinc in obese patients

Variable	AUC	Cutoff	SE	P-value	95% CI (lower)	95% CI (upper)	Sensitivity, %	Specificity, %
Asprosin, pg/mL	0.800	3.7	0.040	<0.001	0.715	0.874	56.0	97.0
Leptin, ng/mL	0.971	187.0	0.020	<0.001	0.933	1.000	98.3	95.0
Adiponectin, ng/mL	0.013	0.4	0.012	<0.001	0.000	0.036	98.0	0.0
Zinc, mmol/L	0.011	0.75	0.009	<0.001	0.000	0.028	0.0	98.3

Correlation analysis results showed a statistically significant positive correlation between asprosin and levels of both zinc ($r = 0.356$, $P = 0.005$) and adiponectin ($r = 0.392$, $P = 0.002$), suggesting that higher asprosin levels may be associated with a slight increase in these markers. In contrast, a strong negative correlation was observed between asprosin and leptin ($r = –0.583$, $P = 0.0001$), suggesting that higher asprosin levels may coincide with lower leptin levels. These findings reflect the potential role of asprosin in the metabolic interactions associated with obesity, which may help understand the mechanisms of bioregulation of these proteins and their impact on metabolic disorders.

Table 3
Relationship of asprosin with zinc, adiponectin, and leptin levels

Test variable	Correlation coefficient (r)	P-value
Zinc	0.356	0.005
Adiponectin	0.392	0.002
Leptin	–0.583	0.0001

Correlation analysis results showed a statistically significant positive correlation between adiponectin and zinc levels ($r = 0.382$, $P = 0.003$), suggesting that higher adiponectin levels may be associated

with higher zinc levels. Conversely, a negative correlation was observed between adiponectin and leptin (r = –0.351, P = 0.006), suggesting that higher adiponectin levels may coincide with lower leptin levels. These findings reflect the overlapping effects of these markers in obesity-related metabolic disorders, which may help explain the role of adiponectin in metabolic homeostasis and its relationship to body fat and inflammation.

Table 4
Relationship of adiponectin with zinc and leptin levels

Test Variable	Correlation coefficient (r)	P-value
Zinc	0.382	0.003
Leptin	–0.351	0.006

Correlation analysis results showed no statistically significant relationship between leptin and zinc levels (r = -0.209, P = 0.109), indicating no clear association between these two variables in the study. This suggests that changes in zinc levels may not directly affect leptin levels in obese individuals, warranting further studies to understand the relationship between these factors and their impact on metabolic balance and obesity-related inflammation.

Discussion

Zinc, adiponectin, asporsine, and leptin are in each subject's blood. The results showed that there were some differences between the patients and the control group, as shown in Table 1. Some studies have found a higher concentration of asprosin in obese people compared to a standard weight control group, which is consistent with the results of our current study. Studies have also reported a positive correlation between asprosin and various obesity-related indices, including BMI and insulin resistance. Asprosin has been proposed as a biomarker for obesity and metabolic disorders and as a therapeutic target for obesity (Beutler et al., 2018; Zhang et al., 2019). Plasma asprosin levels are elevated in insulin-resistant individuals. Individuals with insulin resistance experience rapid hunger and delayed satiety (Wang et al., 2018). Asprosin enhances food intake by stimulating agRP peptide neurons through cAMP, promoting appetite (Ma et al., 2018). Asprosin is primarily released into the bloodstream at nanomolar levels by white adipose tissue, which rises with obesity. It can also pass through the blood-brain barrier and activate AgRP neurons by cAMP, which increases appetite, food intake, absorption, and energy conversion into fat mass as obesity increases in this cycle (Coelho et al., 2013). This mechanism is supported by the extremely high asprosin levels found in obesity. This is how many comorbidities (such as cardiovascular disease) may arise, depending on the metabolic implications of obesity. Additionally, it has been proposed that the sole reason for fasting hyperglycemia is elevated hepatic glucose production. Asprosin may be the source of this increased hepatic glucose production since asprosin enhances appetite, which in turn causes the release of glucose into the liver (Ugur et al., 2019). Since it is unclear if elevated asprosin levels represent a preventive mechanism following obesity or the outcome of obesity, more research is necessary to determine whether asprosin might be a novel therapeutic target for problems associated with obesity (Wang et al., 2020). The higher leptin level in obese patients compared to non-obese patients is consistent with previous studies. In a survey of cardiovascular patients, leptin levels were found to be elevated in obese patients with cardiovascular disease (Andleeb et al., 2020). In another study (Smith et al., 2006), leptin resistance did not increase leptin levels in non-obese cardiac patients over 65. Furthermore, in response to leptin, adipose tissue releases inflammatory mediators such as adiponectin, TNF-a, interleukin 6 (IL-6), and CRP (Guerre-Millo et al., 2004). Leptin has also been demonstrated to influence how the body reacts to specific acute stressors. Leptin has been shown to boost pro-inflammatory cytokines; in other words, it may contribute to the development of inflammation. As a result, leptin levels may be a useful indicator of an individual's risk of obesity (Andleeb et al., 2020). In line with other research that found that fat reduction was linked to a significant drop in inflammatory markers and a nonsignificant rise in total adiponectin levels, our findings imply an inverse relationship between fat and adiponectin levels (Gariballa et al., 2014). This means that obese people have higher levels of inflammation and lower levels of antioxidants (Gariballa et al., 2017). Since evidence indicates that fat growth is linked to reduced adiponectin levels, adiponectin is also adversely connected with insulin resistance and type 2 diabetes linked to obesity (Shah et al., 2012; Prakash et al., 2013). Adiponectin is one of the many adipokine hormones secreted by adipose tissue. It plays a significant role in obesity and related disorders, with several effects on the cardiovascular system. One study found a positive association between adiponectin and HDL levels (Barter et al., 2013), and an increased risk of cardiovascular disease. Adiponectin was also linked to obesity and insulin resistance (Ferris et al., 2005). Low adiponectin levels and the risk of type 2 diabetes are strongly correlated with high inflammatory indicators, according to a study on the link between adiponectin levels and other inflammatory markers and the risk of T2DM (Liu et al., 2016). Because of its insulin-sensitive qualities, adiponectin is believed to decrease hepatic glucose production, increase insulin sensitivity, and enhance cellular glucose absorption. Adiponectin is also shown to lower cardiovascular oxidative stress and have anti-inflammatory properties. Given that visceral fat reduction has been linked to a drop in inflammatory markers, adiponectin's anti-inflammatory qualities raise the possibility that it might serve as a mediator between inflammation and obesity (Wang et al., 2016; Woodward et al., 2017). A previous study that discovered a negative connection between mean serum zinc level, waist circumference, and BMI supports our current findings. These findings are associated with a build-up of adipose tissue and elevated cortisol and adipocytokine production, which ultimately results in chronic inflammation. The negative relationship between blood zinc levels and BMI in obese people may have been caused by inflammation, which encourages zinc accumulation in the liver and adipocytes (Ferro et al., 2011). Given the strong inverse relationship between zinc and TNF-a, the reduction in zinc concentration in obese individuals may be the result of the impact of the inflammatory process on zinc metabolism (Feitosa et al., 2013). ROC curve analysis was performed for adiponectin, leptin and asprosin in obese patients. A reasonable and good prediction was observed for the AUC values of adiponectin, leptin and asprosin (0.013, 0.971 and 0.800, respectively). The sensitivity was 98%, 98% and 56%, and the specificity was 0%, 95%, and 97%, respectively, at an optimal cutoff of greater than 0.4 ng/mL, 187 pg/mL, and 3.7ng/mL, 3 and 56%, respectively, and the specificity was 0%, 95% and 97%, respectively, at the optimal cut-off of greater than 0.4 ng/mL, 187 pg/mL and 3.7 ng/mL, which discriminates patients from controls. In addition, the results of ROC analysis showed that the area under the zinc curve value was 0.0110. The sensitivity, specificity were 0% and 98.3% at a cut-off value of more than 0.75 mmol/L, which discriminated patients from the control group (probability value P < 0.0001), as shown in Table 2. Furthermore, the results of the correlational relationships of the current study showed a statistically significant negative correlation between asprosin and leptin (r = –0.583), leptin and adiponectin (r = –0.351), and leptin and zinc (r = –0.209), while there was a statistically significant positive correlation between asprosin and zinc (r = –0.356) and asprosin and adiponectin (r = –0.392), while there was a statistically significant positive correlation between asprosin and zinc (r = 0.356) and asprosin and adiponectin (r = 0.392), as well as a positive correlation for adiponectin and zinc (r = 0.383), as shown in Figure 1 and Tables 3–5. There is limited research on the correlation between adiponectin and asprosin, so more comprehensive studies are needed to elucidate potential interactions and relationships between adiponectin and asprosin, especially considering their roles in metabolic processes. Body fat levels are associated with increased leptin levels and decreased adiponectin concentrations. This inverse relationship is essential in obesity because high leptin levels indicate increased fat stores, while low adiponectin levels are associated with insulin resistance and other metabolic disorders. Therefore, increasing adiponectin levels may be a potential therapeutic approach to address metabolic disorders related to obesity (Nigro et al., 2014; Luo et al., 2022). Previous studies suggest a complex relationship between adiponectin and zinc in obesity.

Zinc alpha-2-glycoprotein (ZAG) positively correlates with adiponectin and has enhanced adiponectin production in human adipocytes (Ceperuelo-Mallafré et al., 2009; Mracek et al., 2010). This suggests that zinc may play a role in regulating adiponectin levels. In addition, some studies have shown that zinc supplementation partially restores adiponectin concentrations and increases high-density lipoprotein (HDL) levels (Tabatabaie et al., 2021). Research has also demonstrated a negative correlation between zinc levels and leptin concentration, suggesting that as zinc levels decrease, leptin levels tend to increase, which may contribute to obesity-related metabolic changes (Konukoglu et al., 2004; Baltaci et al., 2012). Zinc supplementation has also been shown to reduce leptin levels, suggesting a regulatory role for zinc, as zinc promotes the production of various cytokines that mediate leptin secretion. Finally, the results of our current study showed a positive correlation between asprosin and zinc (r = 0.356), consistent with a previous study showing a positive correlation between asprosin and zinc (García et al., 2012). Previous studies do not provide conclusive evidence of the direct effect of zinc supplementation on asprosin levels. Still, zinc plays an essential role in insulin signalling and glucose metabolism, which may indirectly affect asprosin. Thus, changes in zinc levels may have downstream effects on asprosin (Senyigit et al., 2024).

Conclution

The findings revealed a considerable rise in the hormone asprosin levels, which may be regarded as a biomarker for obesity because the hormone is positively connected with body mass index and rises when one is hungry, making it a potential target for treatment. Very high levels of asprosin in obesity support such a mechanism, as it activates peptide neurons (AgRP) through cAMP to increase appetite, increasing food intake, which leads to increased absorption, converting energy into fat mass, and continuing to increase obesity in this cycle. The present study's findings also revealed that obese participants had significantly higher leptin levels, which may be the result of leptin resistance, and the low levels of adiponectin in obese subjects in the current study indicate an inverse association between fat and adiponectin, which could explain the role of adiponectin in inflammation. In addition, low zinc levels in obese subjects may be due to obesity-induced inflammation, and zinc supplementation may be a new therapeutic strategy for obesity. Furthermore, the correlations of the present study revealed a statistically significant negative correlation between asprosin and leptin, and between leptin and adiponectin and leptin and zinc, while a statistically significant positive correlation was found between asprosin and zinc, indicating that zinc may indirectly affect the secretion of asprosin and between asprosin and adiponectin, as well as a positive correlation of adiponectin and zinc due to zinc alpha protein enhancing adiponectin production.

References

Abdulmajeed, A. Z., & Nazhan, W. (2024). Kinetic properties of glutamate carboxypeptidase II partially purified from leukodystrophy patient's serum. ACS Chemical Neuroscience, 15(18), 3384–3390.

Ahmed, B., Sultana, R., & Greene, M. W. (2021). Adipose tissue and insulin resistance in obese. Biomedicine and Pharmacotherapy, 137, 111315.

Andleeb, J., Javaid, S., & Karim, R. A. (2020). Correlation of leptin level with obesity. The Professional Medical Journal, 27(6), 1139–1142.

Baltaci, A., & Mogulkoc, R. (2012). Leptin and zinc relation: In regulation of food intake and immunity. Indian Journal of Endocrinology and Metabolism, 16(9), 611–616.

Barter, P. J. (2013). High density lipoprotein: A therapeutic target in type 2 diabetes. Endocrinology and Metabolism, 28(3), 169–177.

Beutler, L. R., & Knight, Z. A. (2018). A spotlight on appetite. Neuron, 97(4), 739–741.

CeperuelɵMallafrę V., Näf, S., Escoté X., Caubet, E., Gomez, J. M., Miranda, M., Chacon, M. R., Gonzalez-Clemente, J. M., Gallart, L., Gutierrez, C., & Vendrell, J. (2009). Circulating and adipose tissue gene expression of zinc-α_2-glycoprotein in obesity: Its relationship with adipokine and lipolytic gene markers in subcutaneous and visceral fat. The Journal of Clinical Endocrinology and Metabolism, 94(12), 5062–5069.

Clemente-Suárez, V. J., Redondo-Flórez, L., Beltrán-Velasco, A. I., Martín-Rodríguez, A., Martínez-Guardado, I., Navarro-Jiménez, E., Laborde-Cárdenas, C. C., & Tornero-Aguilera, J. F. (2023). The role of adipokines in health and disease. Biomedicines, 11(5), 1290.

Coelho, M., Oliveira, T., & Fernandes, R. (2013). State of the art paper biochemistry of adipose tissue: An endocrine organ. Archives of Medical Science, 2, 191–200.

Ennes Dourado Ferro, F., de Sousa Lima, V. B., Mello Soares, N. R., Franciscato Cozzolino, S. M., & do Nascimento Marreiro, D. (2011). Biomarkers of metabolic syndrome and its relationship with the zinc nutritional status in obese women. Nutricion Hospitalaria, 26(3), 650–654.

Feitosa, M. C. P., Lima, V. B. de S., Neto, J. M. M., & Marreiro, D. do N. (2013). Plasma concentration of IL-6 and TNF-α and its relationship with zincemia in obese women. Revista Da Associação Médica Brasileira, 59(5), 429–434.

Feng, B., Xu, P., & He, Y. (2020). Novel targets in glucose homeostasis and obesity – lesson from rare mutations. Current Diabetes Reports, 20, 66.

Ferris, W. F., Naran, N. H., Crowther, N. J., Rheeder, P., van der Merwe, L., & Chetty, N. (2005). The relationship between insulin sensitivity and serum adiponectin levels in three population groups. Hormone and Metabolic Research, 37(11), 695–701.

Franco, C., & Canzoniero, L. M. T. (2024). Zinc homeostasis and redox alterations in obesity. Frontiers in Endocrinology, 14, 1273177.

García, O. P., Ronquillo, D., Caamaño, M. del C., Camacho, M., Long, K. Z., & Rosado, J. L. (2012). Zinc, vitamin A, and vitamin C status are associated with leptin concentrations and obesity in Mexican women: Results from a cross-sectional study. Nutrition and Metabolism, 9(1), 59.

Gariballa, S., Alkaabi, J., Yasin, J., & Al Essa, A. (2017). Oxidative damage and associated inflammatory risk factors in obese Emirati women. Saudi Medical Journal, 38(9), 960–964.

Gariballa, S., Kosanovic, M., Yasin, J., & Essa, A. (2014). Oxidative damage and inflammation in obese diabetic Emirati subjects. Nutrients, 6(11), 4872–4880.

Guerre-Millo, M. (2004). Adipose tissue and adipokines: For better or worse. Diabetes and Metabolism, 30(1), 13–19.

Hernández-Camacho, J. D., Vicente-García, C., Parsons, D. S., & Navas-Enamorado, I. (2020). Zinc at the crossroads of exercise and proteostasis. Redox Biology, 35, 101529.

Konukoglu, D., Turhan, M. S., Ercan, M., & Serin, O. (2004). Relationship between plasma leptin and zinc levels and the effect of insulin and oxidative stress on leptin levels in obese diabetic patients. The Journal of Nutritional Biochemistry, 15(12), 757–760.

Kosmas, C. E., Bousvarou, M. D., Kostara, C. E., Papakonstantinou, E. J., Salamou, E., & Guzman, E. (2023). Insulin resistance and cardiovascular disease. Journal of International Medical Research, 51(3), 1–49.

Liu, C., Feng, X., Li, Q., Wang, Y., Li, Q., & Hua, M. (2016). Adiponectin, TNF-α and inflammatory cytokines and risk of type 2 diabetes: A systematic review and meta-analysis. Cytokine, 86, 100–109.

Loos, R. J. F., & Yeo, G. S. H. (2021). The genetics of obesity: From discovery to biology. Nature Reviews Genetics, 23(2), 120–133.

Luo, L., & Liu, M. (2022). Adiponectin: friend or foe in obesity and inflammation. Medical Review, 2(4), 349–362.

Ma, H., Zhang, G., Mou, C., Fu, X., & Chen, Y. (2018). Peripheral CB1 receptor neutral antagonist, AM6545, ameliorates hypometabolic obesity and improves adipokine secretion in monosodium glutamate induced obese mice. Frontiers in Pharmacology, 9, 156.

Mracek, T., Ding, Q., Tzanavari, T., Kos, K., Pinkney, J., Wilding, J., Trayhurn, P., & Bing, C. (2010). The adipokine zinc-α_2-glycoprotein (ZAG) is downregulated with fat mass expansion in obesity. Clinical Endocrinology, 72(3), 334–341.

Nguyen, T. D. (2020). Adiponectin: Role in physiology and pathophysiology. International Journal of Preventive Medicine, 11(1), 136.

Nigro, E., Scudiero, O., Monaco, M. L., Palmieri, A., Mazzarella, G., Costagliola, C., Bianco, A., & Daniele, A. (2014). New insight into adiponectin role in obesity and obesity-related diseases. BioMed Research International, 2014, 658913.

Oussaada, S. M., van Galen, K. A., Cooiman, M. I., Kleinendorst, L., Hazebroek, E. J., van Haelst, M. M., ter Horst, K. W., & Serlie, M. J. (2019). The pathogenesis of obesity. Metabolism, 92, 26–36.

Ovali, M. A., & Bozgeyik, I. (2022). Asprosin, a C-terminal cleavage product of fibrillin 1 encoded by the FBN1 gene, in health and disease. Molecular Syndromology, 13(3), 175–183.

Peelman, F., Waelput, W., Iserentant, H., Lavens, D., Eyckerman, S., Zabeau, L., & Tavernier, J. (2004). Leptin: Linking adipocyte metabolism with cardiovascular and autoimmune diseases. Progress in Lipid Research, 43(4), 283–301.

Pérez-Torres, I., Castrejón-Téllez, V., Soto, M. E., Rubio-Ruiz, M. E., Manzano-Pech, L., & Guarner-Lans, V. (2021). Oxidative stress, plant natural an-

tioxidants, and obesity. International Journal of Molecular Sciences, 22(4), 1786.
Picó, C., Palou, M., Pomar, C. A., Rodríguez, A. M., & Palou, A. (2021). Leptin as a key regulator of the adipose organ. Reviews in Endocrine and Metabolic Disorders, 23(1), 13–30.
Prakash, J., Mittal, B., Awasthi, S., Agarwal, C. G., & Srivastava, N. (2012). Hypoadiponectinemia in obesity: Association with insulin resistance. Indian Journal of Clinical Biochemistry, 28(2), 158–163.
Ramakrishnan, N., Auger, K., Rahimi, N., & Jialal, I. (2023). Biochemistry, adiponectin. StatPearls Publishing, Treasure Island.
Sagar, R., & Gupta, T. (2017). Psychological aspects of obesity in children and adolescents. The Indian Journal of Pediatrics, 85(7), 554–559.
Senyigit, A., Durmus, S., Tabak, O., Oruc, A., Uzun, H., & Ekinci, I. (2024). The associations between asprosine, clusterin, zinc alpha-2-glycoprotein, nuclear factor kappa B, and peroxisome proliferator-activated receptor gamma in the development of complications in type 2 diabetes mellitus. Journal of Clinical Medicine, 13(20), 6126.
Shabir, K., Brown, J. E., Afzal, I., Gharanei, S., Weickert, M. O., Barber, T. M., Kyrou, I., & Randeva, H. S. (2021). Asprosin, a novel pleiotropic adipokine implicated in fasting and obesity-related cardio-metabolic disease: Comprehensive review of preclinical and clinical evidence. Cytokine and Growth Factor Reviews, 60, 120–132.
Shah, A., Hernandez, A., Mathur, D., Budoff, M. J., & Kanaya, A. M. (2011). Adipokines and body fat composition in South Asians: Results of the metabolic syndrome and atherosclerosis in South Asians living in America (MASALA) study. International Journal of Obesity, 36(6), 810–816.
Smith, J., Al-Amri, M., Sniderman, A., & Cianflone, K. (2006). Leptin and adiponectin in relation to body fat percentage, waist to hip ratio and the apoB/apoA1 ratio in Asian Indian and Caucasian men and women. Nutrition and Metabolism, 3(1), 18.
Tabatabaie, M., Soltani, S., Mozaffari-Khosravi, H., & Salehi-Abargouei, A. (2021). Zinc supplementation might not affect serum leptin and adiponectin levels in adults: A systematic review and meta-analysis of randomized controlled clinical trials. Iranian Journal of Public Health, 50(2), 5337.
Ugur, K., & Aydin, S. (2019). Saliva and blood asprosin hormone concentration associated with obesity. International Journal of Endocrinology, 2019, 2521096.
Wang, M., Yin, C., Wang, L., Liu, Y., Li, H., Li, M., Yi, X., & Xiao, Y. (2019). Serum asprosin concentrations are increased and associated with insulin resistance in children with obesity. Annals of Nutrition and Metabolism, 75(4), 205–212.
Wang, Y., Qu, H., Xiong, X., Qiu, Y., Liao, Y., Chen, Y., Zheng, Y., & Zheng, H. (2018). Plasma asprosin concentrations are increased in individuals with glucose dysregulation and correlated with insulin resistance and first-phase insulin secretion. Mediators of Inflammation, 2018, 9471583.
Wang, Z. V., & Scherer, P. E. (2016). Adiponectin, the past two decades. Journal of Molecular Cell Biology, 8(2), 93–100.
Woodward, L., Akoumianakis, I., & Antoniades, C. (2016). Unravelling the adiponectin paradox: Novel roles of adiponectin in the regulation of cardiovascular disease. British Journal of Pharmacology, 174(22), 4007–4020.
Zhang, L., Chen, C., Zhou, N., Fu, Y., & Cheng, X. (2019). Circulating asprosin concentrations are increased in type 2 diabetes mellitus and independently associated with fasting glucose and triglyceride. Clinica Chimica Acta, 489, 183–188.
Zhang, Y., Yang, P., Zhang, X., Liu, S., & Lou, K. (2024). Asprosin: Its function as a novel endocrine factor in metabolic-related diseases. Journal of Endocrinological Investigation, 47(8), 1839–1850.