



Review

Role of Adipokines Chemerin, Visfatin, and Omentin in Obesity and Their Inflammatory and Metabolic Implications

Wilson José S. Pedro ^{1,2}, Flávio V. Barbosa Júnior ^{1,2}, Fernanda N. B. R. Alves ^{1,2}, Lenita V. Braga ^{1,2}, Larissa R. Alves ^{1,2}, João Pedro R. Afonso ², Iranse O. Silva ² , Carlos Hassel M. Silva ², Sergio Vencio ^{2,3}, Paolo Capodaglio ^{4,5,6} , Luis V. F. Oliveira ^{1,2,*} and Wilson R. Freitas Júnior ¹

¹ Graduate Program in Health Sciences at the Faculty of Medical Sciences of Santa Casa de São Paulo (PPGCS), 01224-001 São Paulo, Brazil; wilsonpedrosena@gmail.com (W.J.S.P.); keyciflavio@gmail.com (F.V.B.J.); drafernandabueno@yahoo.com (F.N.B.R.A.); lenita.braga@aluno.fcmsantacasasp.edu.br (L.V.B.); lari.ralves@gmail.com (L.R.A.); wilsonrfreitasjunior@gmail.com (W.R.F.J.)

² Graduate Program in Human Movement and Rehabilitation (PPGMHR), Evangelical University of Goiás (UniEVANGELICA), 75083-515 Anápolis, Brazil; joaopedro180599@gmail.com (J.P.R.A.); iranseoliveira@hotmail.com (I.O.S.); carloshmendes@unievangelica.edu.br (C.H.M.S.); svencio@gmail.com (S.V.)

³ ICF–Institute of Pharmaceutical Sciences, 74935-530 Aparecida de Goiânia, Brazil

⁴ Orthopaedic Rehabilitation Unit and Research Lab for Biomechanics, Rehabilitation and Ergonomics, Ospedale San Giuseppe, Istituto Auxologico Italiano, IRCCS, 28824 Piancavallo di Oggebbio, Italy; p.capodaglio@auxologico.it

⁵ Department of Surgical Sciences, Physical Medicine and Rehabilitation, University of Torino, 10126 Torino, Italy

⁶ Physical and Rehabilitation Medicine Sector, Department of Biomedical, Surgical and Dental Sciences, Università Degli Studi di Milano (UNIMI), 20122 Milan, Italy

* Correspondence: oliveira.lvf@gmail.com; Tel.: +55-62-999052309

Abstract

Obesity is a multifactorial disease with endocrine, metabolic, and inflammatory underpinnings, leading to numerous comorbidities and increased mortality. This has driven research into adipose tissue's role as an endocrine organ that secretes adipokines. This review critically analyzes three of these adipokines: chemerin, omentin-1, and visfatin. Chemerin and omentin-1 have well-defined roles as pro- and anti-inflammatory mediators, respectively. However, the function of visfatin remains controversial, with conflicting data regarding its role in glucose metabolism and inflammation. This conflicting evidence highlights an urgent need for standardized assays and population-specific studies to clarify its true function. We conclude that while chemerin and omentin-1 represent promising targets, the ambiguity surrounding visfatin limits its current clinical utility, and resolving these knowledge gaps is essential for developing effective biomarkers and therapies for obesity and its comorbidities.

Keywords: obesity; adipokines; chemerin; omentin; visfatin; biomarkers; inflammation



Academic Editor: Jun Lu

Received: 27 August 2025

Revised: 12 September 2025

Accepted: 15 September 2025

Published: 23 September 2025

Citation: Pedro, W.J.S.; Barbosa Júnior, F.V.; Alves, F.N.B.R.; Braga, L.V.; Alves, L.R.; Afonso, J.P.R.; Silva, I.O.; Silva, C.H.M.; Vencio, S.; Capodaglio, P.; et al. Role of Adipokines Chemerin, Visfatin, and Omentin in Obesity and Their Inflammatory and Metabolic Implications. *Biomedicines* **2025**, *13*, 2321. <https://doi.org/10.3390/biomedicines13102321>

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

In its 2023 World Obesity Atlas, the World Obesity Federation presented a worrying obesity incidence in 2035 [1]. This trend is closely linked to global shifts in dietary patterns, where factors such as formal education and professional support are crucial in shaping healthy nutrition attitudes [2]. A global prevalence of overweight or obesity is projected at approximately 51% of the world's population, representing an increase of 13% when compared with the 2020 data [3,4]. As a result of this incidence, the economic impact

of obesity is estimated to reach a projected annual expenditure of approximately USD 4.32 trillion (approximately 3% of the global gross domestic product) if prevention and treatment measures are not effectively implemented [4,5]. In this context, obesity is a serious, chronic, and complex condition, directly related to several comorbidities such as cardiovascular disease, hypertension, type 2 diabetes (T2DM), and certain types of cancer [6–8]. Beyond these physiological consequences, obesity also presents significant social and healthcare challenges, including the prevalence of prejudice among health professionals, which can negatively impact patient care and treatment adherence [9].

A new understanding of obesity or excess fat has gained ground in recent decades, and body fat is being regarded as metabolically active, secretory, and responsive [10,11]. Adipose tissue is an endocrine organ that is dynamically involved in the regulation of cellular function and pathogenesis of diseases through a complex network of endocrine, paracrine, and autocrine signals that influence the response of many tissues, including the hypothalamus, pancreas, liver, skeletal muscle, kidneys, endothelium, and immune system [11,12]. These signals are mediated by proteins, such as hormones, growth factors, and cytokines, which are called adipokines [13]. Obesity alters the profile of these molecules, leading to an increase in pro-inflammatory adipokines such as leptin, chemerin, and visfatin, while levels of adiponectin and omentin, which exert counterbalancing anti-inflammatory effects, are typically reduced [11,13,14]. The secretion of these pro-inflammatory mediators is directly related to increase in M1 macrophages in adipose tissue, corroborating the idea of chronic inflammation related to obesity [15,16].

New inflammatory markers, such as omentin-1, visfatin, and chemerin, have demonstrated importance in the intricate regulatory network of obesity [17–19]. Chemerin is an adipokine that acts on autocrine and paracrine signals, thereby triggering adipocyte differentiation, modulating gene expression for glucose and lipid homeostasis, and stimulating lipolysis [20,21]. Studies have shown that circulating levels of chemerin are significantly higher in individuals with obesity [22]. In contrast, omentin, specifically its isoform 1, is an anti-inflammatory adipokine, expressed primarily in the vascular stroma of visceral adipose tissue (VAT) [23]. This protein plays a crucial role in the development of inflammatory diseases, a function supported by the observation that its circulating levels are typically decreased in these conditions. Its anti-inflammatory mechanisms include suppressing the expression of endothelial adhesion molecules such as VCAM-1 and ICAM-1 and promoting the polarization of macrophages toward an anti-inflammatory M2 phenotype, actions largely mediated by the inhibition of the NF- κ B signaling pathway. These protective actions contribute to its beneficial effects on energy homeostasis, glucose metabolism, and the cardiovascular system [24–26]. Finally, visfatin, an enzyme that activates insulin and has insulinotropic effects, is an adipokine produced primarily by VAT [27]. It is involved in glucose metabolism and systemic inflammation, although there are conflicting studies regarding its relationship with serum levels, diabetes, and insulin resistance [28,29].

Due to new studies highlighting the importance of adipokines, it is important to understand the actual role of these cytokines in the body and how we can use them to treat obesity. Therefore, this review aimed to critically analyze the role of chemerin, visfatin, and omentin in the pathophysiology of obesity, observing their functions in the inflammatory and metabolic processes, thereby elucidating gaps that require further scientific effort.

2. Adipose Tissue as an Endocrine Organ in Obesity

Besides its primary function in energy storage, white adipose tissue (WAT) is now recognized as a highly active endocrine organ [30]. It is currently known that WAT secretes several cytokines, chemokines, and hormonal factors (adipokines) that regulate several processes, including energy expenditure, insulin sensitivity, feeding behavior, inflammation,

and immunity [30]. WAT is organized into several depots in the body, including beneath the skin (subcutaneous), within a cavity (visceral), and in other small depots in organs. There are multiple physiological differences between VAT and subcutaneous adipose tissue. VAT adipocytes are more insulin-resistant, metabolically more active, and have greater lipolytic activity [30]. Furthermore, visceral fat accumulation is associated with an increased risk of developing T2DM and metabolic syndrome [31,32].

In the WAT of lean individuals, homeostasis occurs through the regulation between adipocytes and immune cells [33]. These cells are predominantly represented by regulatory and immunosuppressive cells: type 2 macrophages (M2), regulatory T lymphocytes, T helper cells, natural killer T lymphocytes, and eosinophils [34–38]. M2 macrophages are uniformly distributed within adipose tissues, and they perform several physiological functions, including clearance of dead adipocytes, inhibition of progenitor adipocyte proliferation, and secretion of anti-inflammatory adipokines such as interleukins [39–42] (Figure 1). Furthermore, this group exhibits increased adiponectin secretion, which improves insulin sensitivity [41].

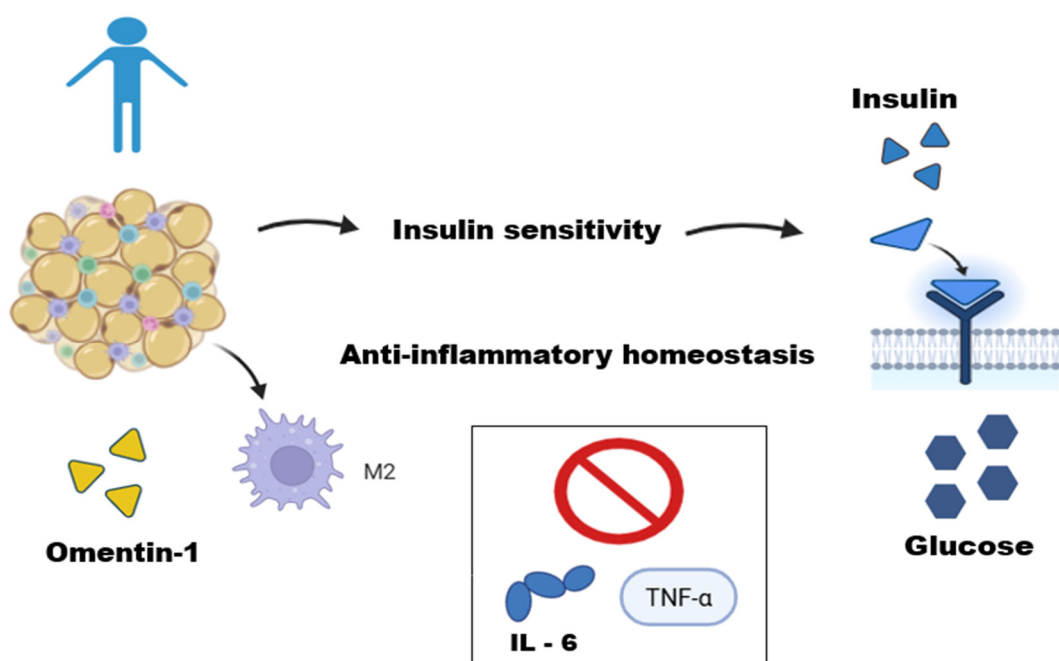


Figure 1. Adipose tissue function in a lean individual. This figure illustrates the role of adipose tissue in a lean individual as an active endocrine organ maintaining metabolic homeostasis. In these conditions, adipose tissue operates in equilibrium with immune cells, such as M2-type macrophages. The secretion of anti-inflammatory adipokines, like Omentin-1, helps regulate metabolism by improving insulin sensitivity, an effect mediated by potentiating the Akt signaling pathway in adipocytes and inhibiting inflammatory cytokines (IL-6 and TNF- α), thus contributing to anti-inflammatory homeostasis. This figure was made on Biorender.com.

Obesity is recognized as a multifactorial chronic disease in which qualitative and quantitative changes in the histological structure of adipose tissue leads to consequent functional alterations that explain disease severity and development of its complications [43,44]. The primary cause of obesity is likely an altered association between the environment and genetic makeup of control systems, which underlies the regulation of energy metabolism and influences the bidirectional pathways of energy transfer between the environment and body [45]. Positive energy balance results in adipocyte expansion with complex changes in this equilibrium environment. Increased lipid storage results in adipocyte hypertrophy, hypoxia, and increased cell apoptosis [45,46]. This dysfunctional microenvironment promotes

the secretion of pro-inflammatory cytokines by adipocytes, including tumor necrosis factor alpha (TNF- α), interleukins (IL)-6, and IL-8 [47–49] (Figure 2). Other chemokines produced by adipocytes or immune cells lead to infiltration and circulation of monocytes and other innate and adaptive immune cells within adipose tissue [46]. Increased monocytic infiltration results in a profound change in the adipose tissue environment, now with increased macrophage retention [33].

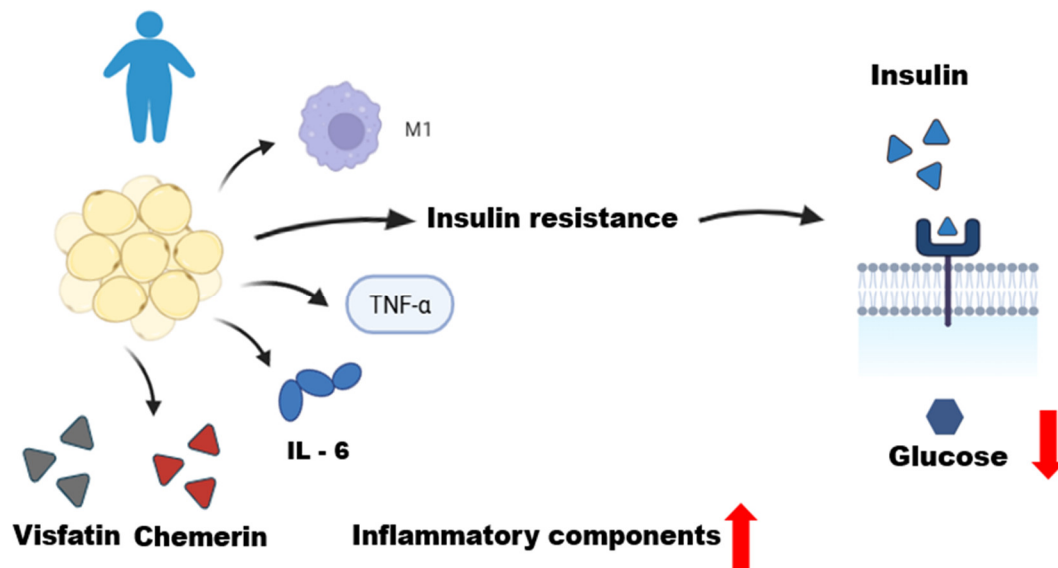


Figure 2. Dysfunctional adipose tissue in an obese individual. This figure illustrates the role of dysfunctional adipose tissue in an obese individual, characterized by a state of chronic low-grade inflammation. Qualitative and quantitative changes in adipose tissue, including adipocyte hypertrophy, lead to the infiltration of M1 macrophages and the production of inflammatory mediators. These include pro-inflammatory adipokines (chemerin and visfatin) and cytokines (TNF- α and IL-6). This inflammatory environment promotes systemic insulin resistance, resulting in decreased glucose uptake by the cells, as depicted by the reduced entry of glucose from the extracellular to the intracellular space. This figure was made on Biorender.com.

The distribution of cells is different in individuals with obesity. The observed inflammatory profile is characterized by the accumulation and infiltration of various immune cell populations in adipose tissue, with M1-type inflammatory macrophages predominating [50]. The adipose tissue of individuals with obesity releases pro-inflammatory adipokines such as TNF and IL-1 β [50,51]. TNF is considered one of the main factors driving low-grade systemic inflammation in obesity [51]. Furthermore, adipose tissues, especially VATs, produce excess IL-6 in obesity [52]. The production of these pro-inflammatory cytokines contributes to metabolic inflammation and promotes insulin resistance [53–55].

Given the above, it is clear how adipose tissue plays important roles in local and systemic metabolic modulation, establishing a strong link between obesity and its comorbidities. Due to this complexity, the study of different metabolic profiles is fundamental for studies in this area [56]. The understanding of different metabolic profiles is still evolving. For instance, the phenotype of metabolically healthy obesity is estimated to affect 19% of the global population, while metabolic abnormalities can be found in 22% of lean individuals. This complexity is compounded by the lack of a universal scientific consensus on the definition of ‘metabolic health’, which makes the analysis and interpretation of data challenging [56]. Table 1 shows the main findings of this review on the role of adipokines in the pathophysiology of obesity.

Table 1. Role of adipokines chemerin, visfatin, and omentin-1 in the pathophysiology of obesity.

Adipokine	Classification	Tissue Of Origin/Main Expression	Association With Obesity	Main Functions
Chemerin Refs. [20,21,57–61]	Pro-inflammatory	Liver and adipose tissue	Significantly higher circulating levels in obese individuals	It acts on adipocyte differentiation, modulates glucose and lipid homeostasis, and stimulates lipolysis. It recruits plasmacytoid dendritic cells, initiating an innate immune response.
Visfatin Refs. [62–65]	Complex profile	Visceral adipose tissue and adipose-derived macrophages	Variable and conflicting association with obesity. Expression in visceral adipose tissue (VAT) correlates with obesity, but not necessarily with circulating levels.	It activates insulin and has insulinotropic effects by binding to and activating the insulin receptor. Involved in glucose metabolism and systemic inflammation.
Omentin-1 Refs. [66–71]	Anti-inflammatory	Vascular stroma of visceral adipose tissue	Reduced circulating levels in obese individuals with poor glycemic regulation	Circulating levels of omentin-1 are reduced in obese individuals, suggesting a role in insulin resistance, diabetes, obesity, and metabolic syndrome. Omentin-1 inhibits pro-inflammatory cytokines (such as TNF, IL-6, and IL-1) and increases the secretion of anti-inflammatory adipokines (such as IL-10 and adiponectin).

This complexity is exemplified by the ongoing controversy surrounding the ‘metabolically healthy obesity’ (MHO) phenotype. Individuals with MHO are obese by BMI criteria, but they do not present a typical set of cardiometabolic abnormalities, such as insulin resistance, hypertension, and dyslipidemia [72]. The main point of debate is whether MHO is a stable, benign condition or merely a transient phase preceding the onset of metabolic disease. This controversy is compounded by the lack of standardization for MHO, making it difficult to compare results across studies [73].

Furthermore, longer-term studies suggest that individuals with MHO remain at higher risk of developing type 2 diabetes and cardiovascular events compared with lean, metabolically healthy individuals [74,75]. From an endocrine perspective, the adipokine profile in MHO is a key area of investigation, as these individuals often present intermediate levels of adipokines, such as adiponectin and leptin, compared with lean and metabolically unhealthy obese individuals. This profile suggests a less dysfunctional state of adipose tissue, which may explain their transiently protected phenotype [72,73,76].

This debate makes it clear that BMI alone cannot be considered a sufficient marker of cardiometabolic risk and highlights the need to understand underlying biological factors, such as adipokine secretion.

3. Chemerin: A Pro-Inflammatory Adipokine and Obesity

Chemerin, also known as tazarotene-induced gene 2 or retinoic acid receptor responder 2, is a chemotactic protein that is highly expressed in the liver and adipose tissues [57,58]. Most circulating chemerin is produced by the liver and found in an inactive form (pro-chemerin: 143 amino acids), which can be cleaved by extracellular proteases,

including plasmin, elastase, and cathepsin G, into its active isoforms [77]. Isoforms 1 and 2 mediate the direct biological effects of chemerin by binding to high-affinity receptors such as chemokine-like receptor 1 and G protein-coupled receptor 1 [77,78].

These adipokines play an important role in adipocyte differentiation and function regulation by controlling the expression of the glucose transporter GLUT4, synthesis of triglycerides, and expression of leptin and adiponectin [79,80]. Human studies have found a positive correlation between their circulating levels, obesity, and body mass index (BMI) [59,60]. Other studies establish an association between their serum elevation and adipose tissue with metabolic syndrome [81]. To better understand the role of chemerin, we must evaluate its intracellular signaling pathways, the main pathway being initiated by its binding to the G-protein-coupled receptor, CMKLR1 (Chemokine-Like Receptor 1), which is abundantly expressed in adipocytes and immune cells, such as macrophages [61]. This interaction triggers distinct cascades that govern inflammatory and metabolic processes.

In the context of inflammation, CMKLR1 activation is directly linked to the nuclear factor kappa B (NF- κ B) pathway. Chemerin signaling induces the phosphorylation and subsequent degradation of inhibitor of NF- κ B (I κ B), allowing NF- κ B to translocate to the cell nucleus [82,83]. Once in the nucleus, it acts as a potent transcription factor, increasing the expression of an arsenal of pro-inflammatory genes. These include cytokines crucial in the pathophysiology of obesity, such as tumor necrosis factor alpha (TNF- α), interleukin-6 (IL-6), and interleukin-1 β (IL-1 β), thus perpetuating the chronic low-grade inflammatory state [82,83].

From a metabolic perspective, chemerin influences the AMP-activated protein kinase (AMPK) pathway, a master sensor of cellular energy status that promotes catabolic processes. In metabolically active tissues, such as adipose tissue and vascular endothelium, studies indicate that chemerin exerts an inhibitory effect on AMPK activity [84,85]. AMPK suppression results in decreased fatty acid oxidation and reduced glucose uptake, mechanisms that directly contribute to the development of insulin resistance and lipid accumulation. Therefore, by modulating these two central pathways (NF- κ B and AMPK), chemerin functions as a crucial molecular bridge, connecting adipose tissue dysfunction with the systemic inflammation and metabolic dysregulation characteristic of obesity [61,84–86]. The chemokine-like receptor 1 expressed by macrophages, DCs, mast cells, neutrophils, and natural killer cells, also binds to chemerin, and its activation is involved in regulating immune cell recruitment to decrease an acute inflammatory response [86].

It is important to note, however, that while chemerin is predominantly pro-inflammatory in the chronic context of obesity, it can exhibit a dual role. In settings of acute inflammation, for instance, chemerin can contribute to the resolution phase by recruiting specific immune cell subsets that dampen the inflammatory response, highlighting the context-dependent nature of its biological function [58,61,80]. This complexity suggests that therapeutic interventions targeting the chemerin system must be highly specific to avoid unintended effects.

In vitro and in vivo studies have demonstrated chemerin involvement in energy balance and metabolism, with implications for obesity, diabetes, and metabolic syndrome [87,88]. According to one study, circulating chemerin levels were significantly higher in individuals with obesity individuals having a BMI > 25 kg/m² compared with those with a BMI < 25 kg/m². In humans, circulating chemerin levels have been strongly associated with multiple components of metabolic syndrome, including BMI, triglycerides, and high-density lipoprotein cholesterol, as well as with markers of systemic inflammation such as C-reactive protein, IL-6, and TNF- α [89].

Due to the strong association of chemerin with metabolic diseases, many studies are evaluating its receptor, CMKLR1, as a potential therapeutic target. A preclinical study with

obese diabetic mice has shown that the CMKLR1 antagonist, CCX832, yielded promising results [90]. Treatment with this antagonist led to improvements in important metabolic parameters, including a reduction in body weight, insulin, and glucose levels, as well as the restoration of vascular response to insulin [90]. Furthermore, blocking the chemerin receptor has also demonstrated benefits in related comorbidities, such as the attenuation of renal oxidative stress in diabetic mice [91]. Despite these interesting preclinical findings, the clinical development of chemerin-specific interventions for obesity and type 2 diabetes remains in its early stages. There is a notable lack of published data from late-stage clinical trials focusing on these specific conditions, indicating that more research is necessary to validate the safety and efficacy of this therapeutic approach in humans.

4. Visfatin: A Complex Profile in Obesity and Inflammation

Visfatin, a cytokine originating from VAT, has a complex profile in obesity and inflammation. It was initially identified as a lymphokine that acts as a growth and differentiation factor for B lymphocyte precursors [62]. Also known as pre-B cell colony-enhancing factor and later as nicotinamide phosphoribosyl transferase (NAMPT), visfatin has been associated with an insulin-mimetic effect by binding and activating the insulin receptor. Its tissue expression and secreted plasma levels increase parallel to obesity, making it an interesting area for future studies [62,92].

Studies related to visfatin have shown a relationship between bioenergetic metabolism and the nicotinamide-adenine dinucleotide oxidation (NAD⁺) pathway, suggesting a potential role for NAD-dependent enzymes in regulating the production of pro-inflammatory cytokines [92,93]. Visfatin/NAMPT is produced and released predominantly by adipose tissue-derived macrophages. Its association with inflammatory markers, such as the upregulation of IL-6, IL-1b, and TNF- α in human monocytes, suggests inflammatory properties [93]. The inflammatory response in adipose tissue is also linked to selective hypoxia in hypertrophied adipocytes, and studies indicate that circulating mononuclear cells in patients with obesity are in a pro-inflammatory state [94,95].

However, the relationship between visfatin and obesity is still unclear. The controversy surrounding visfatin was amplified by significant historical events. The seminal study by Fukuhara, which initially generated great enthusiasm by describing it as an adipokine with insulin-mimetic effects, was later retracted, fueling an intense debate in the scientific community that persists to this day [27]. Although visfatin mRNA expression in VAT correlates with obesity, its circulating levels show variable associations [93]. Recent evidence suggests that when the visfatin gene is expressed in adipose tissues, it does not necessarily correlate with its circulating levels, which may explain the inconsistent results. Furthermore, a positive correlation can be observed between plasma visfatin levels and visceral fat in humans [96]. Other studies reiterate this conflicting association of plasma levels with BMI and other anthropometric measurements [62,92]. Visfatin expression appears to be locally regulated in the VAT of individuals with obesity, where it is secreted by activated macrophages to act in an autocrine manner within a fat depot [96]. This increased local production, especially in cases of intra-abdominal obesity, may be a crucial factor in changing the properties of visfatin [96].

Furthermore, the relationship between visfatin with insulin resistance and T2DM also remains a topic of debate. The literature presents conflicting results regarding visfatin levels in different metabolic conditions. For example, some studies found that serum visfatin levels were similar in patients with T2DM, glucose intolerance, and those with normal glucose tolerance [63,64]. Furthermore, the relationship between visfatin with insulin resistance and T2DM also remains a topic of debate, with studies presenting conflicting results [65]. On one hand, a line of research demonstrates a positive correlation, where stud-

ies using the ELISA method have found significantly higher visfatin levels in populations with clear metabolic dysfunction—such as patients with obesity and metabolic syndrome or in psoriasis patients who also present with metabolic syndrome—when compared to healthy controls [62,66,97].

On the other hand, a substantial body of evidence points to a more complex association. For example, a systematic review and meta-analysis highlighted elevated visfatin levels in non-obese women with Polycystic Ovary Syndrome (PCOS). This finding, echoed in other studies on non-obese women with PCOS and patients with type 2 diabetes, suggests a link to the pathology that can be independent of obesity [98–100]. To systematically organize these divergent findings, Table 2 provides a comparative summary of these representative studies. These inconsistencies in the literature may be due to differences in study populations, including age, sex, and associated conditions [101,102].

Table 2. Summary of representative studies on the association between visfatin and obesity.

Category	Study	Population Characteristics	Test Method	SS
Positive Correlation	Ugur, K. et al., 2022 [62]	Patients with obesity and metabolic syndrome vs. healthy controls.	ELISA	Significantly higher visfatin levels in patients with obesity and metabolic syndrome, suggesting its role as a biomarker.
Positive Correlation	Sherly A A et al., 2025 [66]	Case-control study with patients with metabolic syndrome vs. healthy controls.	ELISA	Significantly altered visfatin levels in patients with metabolic syndrome, a condition strongly associated with obesity.
Positive Correlation	Dağdelen D et al., 2020 [97]	Patients with psoriasis, with and without Metabolic Syndrome.	ELISA	Higher visfatin levels in patients with Metabolic Syndrome, suggesting a link with metabolic dysfunction.
No correlation/Variable	Chen J et al., 2023 [98]	Meta-analysis of studies including non-obese women with Polycystic Ovary Syndrome (PCOS).	Meta-análise	Higher visfatin levels in non-obese women with PCOS compared with controls, indicating an association with pathology independent of obesity.
No correlation/Variable	Kärberg, K. et al., 2023 [99]	Patients with type 2 diabetes.	ELISA	No direct association found between visfatin and atherosclerosis; results were influenced by the use of cardiovascular medications.
No correlation/Variable	Ali and Nori, 2022 [100]	Non-obese women with polycystic ovary syndrome (PCOS) vs. healthy controls.	ELISA	No significant correlation was found between visfatin levels and BMI. Levels were elevated in PCOS, regardless of obesity.

The regulatory pattern of visfatin is complex. For instance, intravenous glucose infusion elevates its levels, a response that could be mechanistically linked to its role as the enzyme NAMPT (nicotinamide phosphoribosyltransferase). As NAMPT is the rate-limiting enzyme in the NAD⁺ salvage pathway, an acute glucose load increases the cellular demand for NAD⁺ to sustain glycolysis, potentially stimulating visfatin/NAMPT secretion to support this metabolic need [103]. Conversely, oral carbohydrate ingestion may reduce its levels, indicating that it may not follow the conventional adipokine profile [104,105]. An interesting hypothesis is that elevated visfatin levels could be a regulatory response to maintain glucose homeostasis, but an excessive increase may contribute to chronic inflammation, which in turn may lead to insulin resistance and T2DM [63,105,106].

Another factor that may be relevant to understanding this inconsistency in the literature is the variability in the assay methods used to measure visfatin levels and the fact that circulating levels may not reflect its local activity in visceral adipose tissue. For example, some studies that reported a positive correlation with obesity were conducted in specific populations with metabolic syndrome, while studies that found no significant association included more heterogeneous cohorts [23,29,30].

5. Omentin-1: An Anti-Inflammatory Adipokine and Its Role in Obesity

Omentin-1 is an adipokine, and the isoform 1 of omentin is its main circulating form in the body [107]. Its expression occurs in the vascular stroma of VAT, in greater quantity than in subcutaneous adipose tissue, and also shows high expression in epicardial adipose tissue [108]. Omentin-1 has emerged as an important key in the complex interaction between adipose tissues and the body's physiological processes [67]. Reduced circulating levels of omentin-1 have been consistently associated with obesity, insulin resistance, and cardiovascular dysfunction [68,109]. In fact, there is a negative correlation between serum concentrations of omentin-1 and BMI, the insulin resistance index, leptin, blood glucose, and Homa B, as well as pro-inflammatory cytokines such as TNF- α , L-1 β , and IL-6 [69,110,111]. Several factors, including obesity, insulin sensitivity, inflammation, genetic factors, and hormones, such as adiponectin and insulin, can affect the production and secretion of omentin-1 [25,112].

Omentin-1 may exert its metabolic and anti-inflammatory effects in a linked manner. This adipokine inhibits pro-inflammatory cytokines, such as TNF, IL-6, IL-1 β , and other cytokines, such as IL-8 and CCL2, while increasing the secretion of anti-inflammatory adipokines such as IL-10 and adiponectin [70,71,94]. Furthermore, omentin-1 inhibits oxidative stress in the endoplasmic reticulum and mitochondrial dysfunction [113]. Omentin-1 has gained attention due to its potential significance in vascular function and its role in glucose and lipid metabolism and insulin sensitivity [94]. Omentin-1 levels have been shown to decrease in dysmetabolic conditions, being downregulated according to glucose-insulin levels [114]. However, basal glucose transport is not stimulated independently, as it generates an improvement in insulin-mediated glucose uptake in adipose tissues, presenting a mode of action similar to that of adiponectin [70]. Some factors, such as physical exercise, aerobic exercise, and weight loss, are linked to high levels of omentin-1 [113].

Vascular function improves with positive effects due to omentin-1, making it an important target for studies. It promotes vasodilation, thereby exerting anti-inflammatory and potentially anti-atherosclerotic actions [115,116]. The mechanism of vasodilation involves stimulating nitric oxide production by endothelial cells, which relaxes vascular smooth muscle, thereby reducing vascular resistance and improving blood flow [116]. A recent study showed that omentin-1 plays important roles in endothelial cells through anti-inflammatory, antioxidant, and anti-apoptosis activities, preventing endothelial dysfunction and contributing to cardioprotection [116].

Omentin-1 may play an important role in fat breakdown (lipolysis) and lipid storage in adipose tissues [117]. The interactions between this adipokine and other hormones, such as insulin and adiponectin, contribute to the complex signaling network that controls lipid and glucose metabolism [118]. Given its important clinical roles, therapies targeting increased omentin-1 levels could be used for the treatment of conditions such as atherosclerosis, hypertension, and T2DM [119,120]. Omentin-1 should be explored as a potential biomarker for certain vascular and metabolic conditions. The potential of omentin-1 as a clinical biomarker has been proposed by several authors. Recent studies using ROC curve analysis have proposed specific diagnostic cut-off values. For example, in a study with obese patients, a cut-off value of ≤ 372.45 ng/mL was suggested to identify individuals with

metabolic syndrome [70]. In another study focused on patients with hypertension, a lower cut-off value of ≤ 62.20 ng/mL was identified to predict the development of the syndrome [121]. Notably, these proposed cut-off values vary considerably across studies. This variability is likely due to differences in the cohorts studied (e.g., ethnicity, underlying clinical conditions), the assay methods used, and the specific definition of the condition being diagnosed. Therefore, while several studies have established these cut-off points, further large-scale validation studies are necessary to establish standardized, clinically applicable cut-off values before omentin-1 can be widely adopted as a diagnostic biomarker.

6. Conclusions

Chemerin and omentin-1 have well-defined roles as pro- and anti-inflammatory adipokines, whereas visfatin remains controversial due to conflicting data. Based on this review, we reinforce that chemerin is a pro-inflammatory adipokine strongly associated with obesity, insulin resistance, and metabolic syndrome. However, visfatin has shown inconsistent results in the literature, indicating a complex systemic or local role in adipose tissues. Finally, omentin-1 stands out as an anti-inflammatory adipokine; some low circulating levels are associated with obesity and its comorbidities. Its beneficial role in insulin sensitivity and vascular function makes it a promising therapeutic target.

Despite the progress made, a complete understanding of adipokine mechanisms still requires further investigation. Future research should focus on elucidating specific downstream signaling pathways, such as the role of chemerin in activating the CMKLR1 receptor, which modulates inflammatory responses through the NF- κ B pathway, or how omentin-1 enhances insulin sensitivity via the Akt/eNOS signaling cascade. Furthermore, the complex role of visfatin as the enzyme NAMPT in regulating NAD⁺ metabolism offers a promising avenue for understanding its dual role in metabolic homeostasis and inflammation. Complementing this mechanistic focus, future studies should include genetic analyses and investigations in diverse populations and environments. This integrated approach is essential for fully uncovering the therapeutic potential of these molecules and validating their use as reliable biomarkers in the treatment of obesity and its associated diseases, such as T2DM and cardiovascular disease.

Author Contributions: Conceptualization, W.J.S.P., F.V.B.J., L.V.F.O. and W.R.F.J.; methodology, W.J.S.P., L.V.F.O., J.P.R.A. and W.R.F.J.; validation, W.J.S.P., F.V.B.J., L.V.F.O. and W.R.F.J.; formal analysis, W.J.S.P., F.V.B.J., L.V.F.O. and W.R.F.J., and investigation, W.J.S.P., F.V.B.J., L.V.F.O., W.R.F.J., F.N.B.R.A., L.V.B., L.R.A., I.O.S., C.H.M.S. and S.V.; resources, L.V.F.O. and W.J.S.P., data curation, S.V., P.C. and W.R.F.J.; writing—original draft preparation, L.V.F.O., W.J.S.P., J.P.R.A. and S.V.; writing—review and editing, W.J.S.P., F.V.B.J., J.P.R.A., L.V.F.O., W.R.F.J. and P.C., visualization, W.J.S.P., F.V.B.J., L.V.F.O. and W.R.F.J.; supervision, L.V.F.O., P.C. and W.R.F.J., project administration, L.V.F.O. and W.R.F.J.; funding acquisition, W.J.S.P. and L.V.F.O. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding. LVFO received grants from Research Productivity, modality PQII; process no. 310241/2022-7 of Conselho Nacional de Desenvolvimento Científico e Tecnológico (local acronym CNPq), Brazil, and, JPRA received a grant from the Fundação de Amparo a Pesquisa do Estado de Goiás (FAPEG), (GO), Brazil. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Institutional Review Board Statement: Does not apply to this study.

Informed Consent Statement: Does not apply to this study.

Data Availability Statement: The data presented in this study will be made available upon request to the corresponding author due to ethical restrictions.

Acknowledgments: The authors would like to thank Evangelical University of Goiás–UniEVANGELI CA and Fundação de Amparo a Pesquisa do Estado de Goiás–FAPEG who allowed this study to be conducted.

Conflicts of Interest: The authors declare that they have no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

T2DM	Type 2 diabetes mellitus
VAT	visceral adipose tissue
WAT	White adipose tissue
TNF- α	Tumor necrosis factor alpha
IL	Interleukin
NAD	Nicotinamide-adenine dinucleotide
NAMPT	Nicotinamide phosphoribosyl transferase
BMI	Body mass index

References

1. Lobstein, T.; Jackson-Leach, R.; Powis, J.; Brinsden, H.; Gray, M. *World Obesity Atlas 2023*; World Obesity Federation: London, UK, 2023; Available online: <https://www.worldobesity.org/resources/resource-library/world-obesity-atlas-2023> (accessed on 16 May 2025).
2. Özdemir, S.; Baltacı, F. Comparative determination of factors affecting attitude level towards healthy nutrition. *Sci. Rep.* **2025**, *15*, 5026. [CrossRef] [PubMed]
3. World Health Organization. *Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation*; WHO Technical Report Series; World Health Organization: Geneva, Switzerland, 2000; Volume 894, pp. i–xii+1–253.
4. Lam, T.M.; Aarestrup, J.; van den Akker, E.L.T.; Baker, J.L.; Banik, A.; Berntzen, B.J.; Bertoni, L.; Beulens, J.W.J.; Bjørnsbo, K.; Bryant, S.; et al. Advancing knowledge, maps and tools to address obesity and related socio-economic disparities in Europe: The OBCT project. *Glob. Health Action* **2025**, *18*, 2517492. [CrossRef]
5. Zhang, X.; Ha, S.; Lau, H.C.H.; Yu, J. Excess body weight: Novel insights into its roles in obesity comorbidities. *Semin. Cancer Biol.* **2023**, *89*, 10–18. [CrossRef]
6. Salama, M.; Balagopal, B.; Fennoy, I.; Kumar, S. Childhood Obesity, Diabetes, and Cardiovascular Disease Risk. *J. Clin. Endocrinol. Metab.* **2023**, *108*, e1112–e1118. [CrossRef] [PubMed]
7. Kloock, S.; Ziegler, C.G.; Dischinger, U. Obesity and its comorbidities, current treatment options and future perspectives: Challenging bariatric surgery? *Pharmacol. Ther.* **2023**, *254*, 108549. [CrossRef]
8. Avgerinos, K.I.; Spyrou, N.; Mantzoros, C.S.; Dalamaga, M. Obesity and cancer risk: Emerging biological mechanisms and perspectives. *Metabolism* **2019**, *92*, 121–135. [CrossRef] [PubMed]
9. Özdemir, S.; Parlak Özer, Z.; Türkoğlu, M.; Kardaş Kin, Ö. Determination of obesity prejudice levels of health professionals working in Gaziantep province. *J. Health Sci. Med.* **2025**, *8*, 469–475.
10. Coelho, M.; Oliveira, T.; Fernandes, R. Biochemistry of adipose tissue: An endocrine organ. *Arch. Med. Sci.* **2013**, *9*, 191–200. [CrossRef]
11. Felipe, L.A.; Bachi, A.L.L.; Oliveira, M.C.; Moreira, S.M.B.P.; Afonso, J.P.R.; Lino, M.E.M.; Paixão, V.; Silva, C.H.M.; Vieira, R.P.; Vencio, S.; et al. Effects of Roux-en-Y gastric bypass on the metabolic profile and systemic inflammatory status of women with metabolic syndrome: Randomized controlled clinical trial. *Diabetol. Metab. Syndr.* **2023**, *15*, 19. [CrossRef]
12. An, S.M.; Cho, S.H.; Yoon, J.C. Adipose Tissue and Metabolic Health. *Diabetes Metab. J.* **2023**, *47*, 595–611. [CrossRef]
13. Hagberg, C.E.; Spalding, K.L. White adipocyte dysfunction and obesity-associated pathologies in humans. *Nat. Rev. Mol. Cell Biol.* **2024**, *25*, 270–289. [CrossRef] [PubMed]
14. Ali, S.; Alam, R.; Ahsan, H.; Khan, S. Role of adipokines (omentin and visfatin) in coronary artery disease. *Nutr. Metab. Cardiovasc. Dis.* **2023**, *33*, 483–493. [CrossRef]
15. Sell, H.; Divoux, A.; Poitou, C.; Basdevant, A.A.; Bouilliot, J.L.; Bedossa, P.; Tordjman, J.; Eckel, J.; Clément, K. Chemerin correlates with markers for fatty liver in morbidly obese patients and strongly decreases after weight loss induced by bariatric surgery. *J. Clin. Endocrinol. Metab.* **2010**, *95*, 2892–2896. [CrossRef]
16. Ross, C.; Tschoner, A.; Engl, J.; Klaus, A.; Tilg, H.; Ebenbichler, C.F.; Patsch, J.R.; Kaser, S. Effect of bariatric surgery on circulating Chemerin levels. *Eur. J. Clin. Investig.* **2010**, *40*, 277–280. [CrossRef]

17. Huang, D.; Kidd, J.M.; Zou, Y.; Wu, X.; Gehr, T.W.B.; Li, P.L.; Li, G. Regulation of NLRP3 Inflammasome Activation and Inflammatory Exosome Release in Podocytes by Acid Sphingomyelinase During Obesity. *Inflammation* **2023**, *46*, 2037–2054. [[CrossRef](#)] [[PubMed](#)]
18. Arab, A.; Moosavian, S.P.; Hadi, A.; Karimi, E.; Nasirian, M. The association between serum omentin level and bodyweight: A systematic review and meta-analysis of observational studies. *Clin. Nutr. ESPEN* **2020**, *39*, 22–29. [[CrossRef](#)]
19. Askin, L.; Duman, H.; Ozyildiz, A.; Tanriverdi, O.; Turkmen, S. Association between omentin-1 and coronary artery disease: Pathogenesis and clinical research. *Curr. Cardiol. Rev.* **2020**, *16*, 198–201. [[CrossRef](#)]
20. Bozaoglu, K.; Bolton, K.; McMillan, J.; Zimmet, P.; Jowett, J.; Collier, G.; Walder, K.; Segal, D. Chemerin is a novel adipokine associated with obesity and metabolic syndrome. *Endocrinology* **2007**, *148*, 4687–4694. [[CrossRef](#)] [[PubMed](#)]
21. Goralski, K.B.; McCarthy, T.C.; Hanniman, E.A.; Zabel, B.A.; Butcher, E.C.; Parlee, S.D. Chemerin, a novel adipokine that regulates adipogenesis and adipocyte metabolism. *J. Biol. Chem.* **2007**, *282*, 28175–28188. [[CrossRef](#)]
22. Fatima, S.S.; Bozaoglu, K.; Rehman, R.; Alam, F.; Memon, A.S. Elevated chemerin levels in Pakistani men: An interrelation with metabolic syndrome phenotypes. *PLoS ONE* **2013**, *8*, e57113.
23. Jung, H.N.; Jung, C.H. The role of anti-inflammatory adipokines in cardiometabolic disorders: Moving beyond adiponectin. *Int. J. Mol. Sci.* **2021**, *22*, 13529. [[CrossRef](#)] [[PubMed](#)]
24. Kazama, K.; Usui, T.; Okada, M.; Hara, Y.; Yamawaki, H. Omentin plays an anti-inflammatory role through inhibition of TNF- α -induced superoxide production in vascular smooth muscle cells. *Eur. J. Pharmacol.* **2012**, *686*, 116–123. [[CrossRef](#)]
25. Watanabe, T.; Watanabe-Kominato, K.; Takahashi, Y.; Kojima, M.; Watanabe, R. Adipose tissue-derived omentin-1 function and regulation. *Compr. Physiol.* **2017**, *7*, 765–781. [[CrossRef](#)]
26. Landecho, M.F.; Tuero, C.; Valentí, V.; Bilbao, I.; de la Higuera, M.; Frühbeck, G. Relevance of leptin and other adipokines in obesity-associated cardiovascular risk. *Nutrients* **2019**, *11*, 2664. [[CrossRef](#)] [[PubMed](#)]
27. Fukuhara, A.; Matsuda, M.; Nishizawa, M.; Segawa, K.; Tanaka, M.; Kishimoto, K.; Matsuki, Y.; Murakami, M.; Ichisaka, T.; Murakami, H.; et al. Visfatin: A protein secreted by visceral fat that mimics the effects of insulin. *Science* **2005**, *307*, 426–430. [[CrossRef](#)]
28. Varma, V.; Yao-Borengasser, A.; Rasouli, N.; Bodles, A.M.; Phanavanh, B.; Lee, M.J.; Starks, T.; Kern, L.M.; Spencer, H.J., III.; McGehee, R.E., Jr. Human visfatin expression: Relationship to insulin sensitivity, intramyocellular lipids, and inflammation. *J. Clin. Endocrinol. Metab.* **2007**, *92*, 666–672. [[CrossRef](#)]
29. Haider, D.G.; Schindler, K.; Schaller, G.; Prager, G.; Wolzt, M.; Ludvik, B. Increased plasma visfatin concentrations in morbidly obese subjects are reduced after gastric banding. *J. Clin. Endocrinol. Metab.* **2006**, *91*, 1578–1581. [[CrossRef](#)]
30. Fantuzzi, G. Adipose tissue, adipokines, and inflammation. *J. Allergy Clin. Immunol.* **2005**, *115*, 911–999. [[CrossRef](#)] [[PubMed](#)]
31. Poirier, P. Adiposity and cardiovascular disease: Are we using the right definition of obesity? *Eur. Heart J.* **2007**, *28*, 2047–2048. [[CrossRef](#)]
32. Choe, S.S.; Huh, J.Y.; Hwang, I.J.; Kim, J.I.; Kim, J.B. Adipose tissue remodeling: Its role in energy metabolism and metabolic disorders. *Front. Endocrinol.* **2016**, *7*, 30. [[CrossRef](#)]
33. Tilg, H.; Ianiro, G.; Gasbarrini, A.; Adolph, T. Adipokines: Masterminds of metabolic inflammation. *Nat. Rev. Immunol.* **2025**, *25*, 250–265. [[CrossRef](#)]
34. Ohashi, K.; Parker, J.L.; Ouchi, N.; Higuchi, A.; Vita, J.A.; Gokce, N.; Pedersen, A.A.; Kalthoff, C.; Tullin, S.; Sams, A.; et al. Adiponectin promotes macrophage polarization toward an anti-inflammatory phenotype. *J. Biol. Chem.* **2010**, *285*, 6153–6160. [[CrossRef](#)]
35. Wolf, A.M.; Wolf, D.; Rumpold, H.; Enrich, B.; Tilg, H. Adiponectin induces the anti-inflammatory cytokines IL-10 and IL-1RA in human leukocytes. *Biochem. Biophys. Res. Commun.* **2004**, *323*, 630–635. [[CrossRef](#)]
36. Ramos-Ramirez, P.; Malmhall, C.; Tliba, O.; Radinger, M.; Bossios, A. Adiponectin/AdipoR1 axis promotes IL-10 release by human regulatory T cells. *Front. Immunol.* **2021**, *12*, 677550. [[CrossRef](#)]
37. Pang, T.T.; Narendran, P. The distribution of adiponectin receptors on human peripheral blood mononuclear cells. *Ann. N. Y. Acad. Sci.* **2008**, *1150*, 143–145. [[CrossRef](#)] [[PubMed](#)]
38. Zhang, K.; Guo, Y.; Ge, Z.; Zhang, Z.; Da, Y.; Li, W.; Zhang, Z.; Xue, Z.; Li, Y.; Ren, Y.; et al. Adiponectin suppresses T helper 17 cell differentiation and limits autoimmune CNS inflammation via the SIRT1/PPAR γ /ROR γ t pathway. *Mol. Neurobiol.* **2017**, *54*, 4908–4920.
39. Nawaz, A.; Aminuddin, A.; Kado, T.; Takikawa, A.; Yamamoto, S.; Tsuneyama, K.; Igarashi, Y.; Ikutani, M.; Nishida, Y.; Nagai, Y.; et al. CD206(+) M2-like macrophages regulate systemic glucose metabolism by inhibiting proliferation of adipocyte progenitors. *Nat. Commun.* **2017**, *8*, 286. [[CrossRef](#)] [[PubMed](#)]
40. Kim, E.Y.; Noh, H.M.; Choi, B.; Park, J.E.; Kim, J.E.; Jang, Y.; Lee, H.K.; Chang, E.-J. Interleukin-22 induces the infiltration of visceral fat tissue by a discrete subset of Duffy antigen receptor for chemokine-positive M2-like macrophages in response to a high fat diet. *Cells* **2019**, *8*, 1587. [[CrossRef](#)] [[PubMed](#)]

41. Li, X.; Ren, Y.; Chang, K.; Wu, W.; Griffiths, H.R.; Lu, S.; Gao, D. Adipose tissue macrophages as potential targets for obesity and metabolic diseases. *Front. Immunol.* **2023**, *14*, 1153915. [\[CrossRef\]](#)
42. Hu, Q.; Lyon, C.J.; Fletcher, J.K.; Tang, W.; Wan, M.; Hu, T.Y. Extracellular vesicle activities regulating macrophage- and tissue-mediated injury and repair responses. *Acta Pharm. Sin. B.* **2021**, *11*, 1493–1512. [\[CrossRef\]](#)
43. Vegiopoulos, A.; Rohm, M.; Herzig, S. Adipose tissue: Between the extremes. *EMBO J.* **2017**, *36*, 1999–2017. [\[CrossRef\]](#)
44. Kahn, C.R.; Wang, G.; Lee, K.Y. Altered adipose tissue and adipocyte function in the pathogenesis of metabolic syndrome. *J. Clin. Investig.* **2019**, *129*, 3990–4000. [\[CrossRef\]](#) [\[PubMed\]](#)
45. Pilon, N.J.; Loos, R.J.F.; Marshall, S.M.; Zierath, J.R. Metabolic consequences of obesity and type 2 diabetes: Balancing genes and environment for personalized care. *Cell* **2021**, *184*, 1530–1544. [\[CrossRef\]](#) [\[PubMed\]](#)
46. Lee, Y.S.; Wollam, J.; Olefsky, J.M. An integrated view of immunometabolism. *Cell* **2018**, *172*, 22–40. [\[CrossRef\]](#)
47. Liu, C.; Feng, X.; Li, Q.; Wang, Y.; Li, Q.; Hua, M. Adiponectin, TNF-Alpha and inflammatory cytokines and risk of Type 2 Diabetes: A systematic review and meta-analysis. *Cytokine* **2016**, *86*, 100–109. [\[CrossRef\]](#) [\[PubMed\]](#)
48. Nara, H.; Watanabe, R. Anti-Inflammatory Effect of Muscle-Derived Interleukin-6 and Its Involvement in Lipid Metabolism. *Int. J. Mol. Sci.* **2021**, *22*, 9889–9903. [\[CrossRef\]](#)
49. Alizadeh Pahlavani, H. Exercise Therapy for People With Sarcopenic Obesity: Myokines and Adipokines as Effective Actors. *Front. Endocrinol.* **2022**, *13*, 811751. [\[CrossRef\]](#)
50. Vieira-Potter, V.J. Inflammation and macrophage modulation in adipose tissues. *Cell. Microbiol.* **2014**, *16*, 1484–1492. [\[CrossRef\]](#)
51. Pestel, J.; Blangero, F.; Watson, J.; Pirola, L.; Eljaafari, A. Adipokines in obesity and metabolic-related-diseases. *Biochimie* **2023**, *212*, 48–59. [\[CrossRef\]](#)
52. Al-Ibraheem, A.M.T.; Hameed, A.A.Z.; Marsool, M.D.M.; Jain, H.; Prajwal, P.; Khazmi, I.; Nazzal, R.S.; Al-Najati, H.M.H.; Al-Zuhairi, B.H.Y.K.; Razzaq, M.; et al. Exercise-Induced cytokines, diet, and inflammation and their role in adipose tissue metabolism. *Health Sci. Rep.* **2024**, *7*, e70034. [\[CrossRef\]](#)
53. Soták, M.; Clark, M.; Suur, B.E.; Börgeson, E. Inflammation and resolution in obesity. *Nat. Rev. Endocrinol.* **2025**, *21*, 45–61. [\[CrossRef\]](#)
54. Shaikh, S.R.; Beck, M.A.; Alwarawrah, Y.; MacIver, N.J. Emerging mechanisms of obesity-associated immune dysfunction. *Nat. Rev. Endocrinol.* **2024**, *20*, 136–148. [\[PubMed\]](#)
55. Bradley, D.; Deng, T.; Shantaram, D.; Hsueh, W.A. Orchestration of the adipose tissue immune landscape by adipocytes. *Annu. Rev. Physiol.* **2024**, *86*, 199–223. [\[CrossRef\]](#) [\[PubMed\]](#)
56. Zenas-Trujillo, G.; Trujillo-Ramirez, I.; Carhuavilca-Torres, J.; Ayala-Mendivil, R.; Vera-Ponce, V. Prevalence of Metabolically-Obese Normal-Weight Worldwide: Systematic Review and Meta-Analysis. *J. Endocrinol. Metab.* **2023**, *13*, 104–113. [\[CrossRef\]](#)
57. Zhang, Q.; Ye, J.; Wang, X. Progress in the contrary effects of glucagon-like peptide-1 and chemerin on obesity development. *Exp. Biol. Med.* **2023**, *248*, 2020–2029. [\[CrossRef\]](#)
58. Fischer, T.; Beck-Sicking, A. Chemerin—Exploring a versatile adipokine. *Biol. Chem.* **2022**, *403*, 625–642. [\[CrossRef\]](#)
59. Chou, H.H.; Teng, M.S.; Hsu, L.A.; Er, L.K.; Wu, S.; Ko, Y.L. Circulating chemerin level is associated with metabolic, biochemical and haematological parameters-A population-based study. *Clin. Endocrinol.* **2021**, *94*, 927–939. [\[CrossRef\]](#)
60. Lara-Guzmán, Ó.J.; Arango-González, Á.M.; Álvarez-Quintero, R.; Escobar, J.S.; Muñoz-Durango, K.; Sierra, J.A. Circulating hs-CRP, IL-18, Chemerin, Leptin, and Adiponectin Levels Reflect Cardiometabolic Dysfunction in Adults with Excess Weight. *Int. J. Mol. Sci.* **2025**, *26*, 1176. [\[CrossRef\]](#)
61. Laffranchi, M.; Schioppa, T.; Sozio, F.; Piserà, A.; Tiberio, L.; Salvi, V.; Bosisio, D.; Musso, T.; Sozzani, S.; Del Prete, A. Chemerin in immunity. *J. Leukoc. Biol.* **2025**, *117*, qiae181. [\[CrossRef\]](#) [\[PubMed\]](#)
62. Ugur, K.; Erman, F.; Turkoglu, S.; Aydin, Y.; Aksoy, A.; Lale, A.; Karagöz, Z.K.; Ugur, I.; Akkoc, R.F.; Yalniz, M. Asprosin, visfatin and subfatin as new biomarkers of obesity and metabolic syndrome. *Eur. Rev. Med. Pharmacol. Sci.* **2022**, *26*, 2124–2133. [\[CrossRef\]](#)
63. Jerusha, F.R.; Raghunath, V. Assessment of serum and salivary visfatin levels in newly diagnosed patients of type-II DM. *J. Oral. Maxillofac. Pathol.* **2023**, *27*, 663–667. [\[CrossRef\]](#)
64. Gunduz, F.O.; Yildirmak, S.T.; Temizel, M.; Faki, Y.; Cakmak, M.; Durmuscan, M.; Sezgin, F. Serum visfatin and fetuin-a levels and glycemic control in patients with obese type 2 diabetes mellitus. *Diabetes Metab. J.* **2011**, *35*, 523–528. [\[CrossRef\]](#)
65. Al Doghaither, H.A.; Alshaikh, E.M.; Omar, U.M.; Alsufiani, H.M.; Mansouri, R.A.; Tarbiah, N.I.; Alshaikh, A.A.; Alshaikh, A.M. Insulin resistance and its correlation with chemerin and visfatin in Saudi patients with hyperthyroidism. *Int. J. Health Sci.* **2019**, *13*, 18–21.
66. Sherly, A.A.; Rukmini, M.S.; Hegde, A.; Arun, S.; Kotian, H. Serum levels of omentin and visfatin in patients with metabolic syndrome. *Arch. Physiol. Biochem.* **2025**, *131*, 683–690. [\[CrossRef\]](#)
67. Zhao, A.; Xiao, H.; Zhu, Y.; Liu, S.; Zhang, S.; Yang, Z.; Du, L.; Li, X.; Niu, X.; Wang, C.; et al. Omentin-1: A newly discovered warrior against metabolic related diseases. *Expert. Opin. Ther. Targets.* **2022**, *26*, 275–289. [\[CrossRef\]](#)
68. Dooxa Nongrum, A.; Guru, S.R.; Nisha, J.K.; Aghanashini, S. Analysing adipokine Omentin-1 in periodontal disease and type-2 diabetes mellitus: An interventional comparative study. *J. Oral Biol. Craniofac. Res.* **2022**, *12*, 273–278. [\[CrossRef\]](#)

69. Ko, C.Y.; Lin, Y.Y.; Achudhan, D.; Chang, J.W.; Liu, S.C.; Lai, C.Y.; Huang, Y.L.; Tsai, C.H.; Fong, Y.C.; Chen, H.T.; et al. Omentin-1 ameliorates the progress of osteoarthritis by promoting IL-4-dependent anti-inflammatory responses and M2 macrophage polarization. *Int. J. Biol. Sci.* **2023**, *19*, 5275–5289. [\[CrossRef\]](#)
70. de Luis Román, D.; Izaola Jáuregui, O.; Primo, D. Relationship between serum omentin-1 levels and nascent metabolic syndrome in Caucasian patients with obesity. *Nutr. Hosp.* **2024**, *41*, 1231–1237. [\[CrossRef\]](#) [\[PubMed\]](#)
71. Cabral, V.L.F.; Wang, F.; Peng, X.; Gao, J.; Zhou, Z.; Sun, R.; Bao, J.; Wu, X. Omentin-1 promoted proliferation and ameliorated inflammation, apoptosis, and degeneration in human nucleus pulposus cells. *Arch. Gerontol. Geriatr.* **2022**, *102*, 104748. [\[CrossRef\]](#)
72. Schulze, M.B.; Stefan, N. Metabolically Healthy Obesity: From Epidemiology and Mechanisms to Clinical Implications. *Nat. Rev. Endocrinol.* **2024**, *20*, 633–646. [\[CrossRef\]](#) [\[PubMed\]](#)
73. Abiri, B.; Koochi, F.; Ebadinejad, A.; Valizadeh, M.; Hosseinpanah, F. Transition from Metabolically Healthy to Unhealthy Overweight/Obesity and Risk of Cardiovascular Disease Incidence: A Systematic Review and Meta-Analysis. *Nutr. Metab. Cardiovasc. Dis.* **2022**, *32*, 2041–2051. [\[CrossRef\]](#) [\[PubMed\]](#)
74. Opio, J.; Croker, E.; Odongo, G.S.; Attia, J.; Wynne, K.; McEvoy, M. Metabolically Healthy Overweight/Obesity Are Associated with Increased Risk of Cardiovascular Disease in Adults, Even in the Absence of Metabolic Risk Factors: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. *Obes. Rev.* **2020**, *21*, e13127. [\[CrossRef\]](#)
75. Huang, M.Y.; Wang, M.Y.; Lin, Y.S.; Lin, C.J.; Lo, K.; Chang, I.J.; Cheng, T.Y.; Tsai, S.Y.; Chen, H.H.; Lin, C.Y.; et al. The Association between Metabolically Healthy Obesity, Cardiovascular Disease, and All-Cause Mortality Risk in Asia: A Systematic Review and Meta-Analysis. *Int. J. Environ. Res. Public Health* **2020**, *17*, 1320. [\[CrossRef\]](#) [\[PubMed\]](#)
76. Li, Q.; Wang, P.; Ma, R.; Guo, X.; Sun, Y.; Zhang, X. A Novel Criterion of Metabolically Healthy Obesity Could Effectively Identify Individuals with Low Cardiovascular Risk Among Chinese Cohort. *Front. Endocrinol.* **2023**, *14*, 1140472. [\[CrossRef\]](#) [\[PubMed\]](#)
77. Zhao, L.; Leung, L.L.; Morser, J. Chemerin Forms: Their Generation and Activity. *Biomedicines* **2022**, *10*, 2018. [\[CrossRef\]](#)
78. Kennedy, A.J.; Davenport, A.P. International Union of Basic and Clinical Pharmacology CIII: Chemerin Receptors CMKLR1 (Chemerin1) and GPR1 (Chemerin2) Nomenclature, Pharmacology, and Function. *Pharmacol. Rev.* **2018**, *70*, 174–196. [\[CrossRef\]](#)
79. Van Gerwen, J.; Shun-Shion, A.S.; Fazakerley, D.J. Insulin signalling and GLUT4 trafficking in insulin resistance. *Biochem. Soc. Trans.* **2023**, *51*, 1057–1069. [\[CrossRef\]](#)
80. Kim, J.E.; Kim, J.S.; Jo, M.J.; Cho, E.; Ahn, S.Y.; Kwon, Y.J.; Ko, G.J. The Roles and Associated Mechanisms of Adipokines in Development of Metabolic Syndrome. *Molecules* **2022**, *27*, 334. [\[CrossRef\]](#)
81. Bastard, J.P.; Dridi-Brahimi, I.; Vatiér, C.; Fellahi, S.; Fève, B. Biological markers of adipose tissue: Adipokines. *Ann. Endocrinol.* **2024**, *85*, 171–172. [\[CrossRef\]](#)
82. Hu, S.; Shao, Z.; Zhang, C.; Chen, L.; Mamun, A.A.; Zhao, N.; Cai, J.; Lou, Z.; Wang, X.; Chen, J. Chemerin facilitates intervertebral disc degeneration via TLR4 and CMKLR1 and activation of NF- κ B signaling pathway. *Aging* **2020**, *12*, 11732–11753. [\[CrossRef\]](#)
83. Tian, J.; Mu, Y.; Ma, L. Chemerin/CMKLR1 pathway exacerbates cisplatin-induced spiral ganglion neuron injury. *Toxicol. Res.* **2023**, *40*, 73–81. [\[CrossRef\]](#)
84. Pezzino, S.; Puleo, S.; Luca, T.; Castorina, M.; Castorina, S. Adipokine and Hepatokines in Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): Current and Developing Trends. *Biomedicines* **2025**, *13*, 1854. [\[CrossRef\]](#)
85. Becker, M.; Rabe, K.; Lebherz, C.; Zugwurst, J.; Göke, B.; Parhofer, K.G.; Lehrke, M.; Broedl, U.C. Expression of human chemerin induces insulin resistance in the skeletal muscle but does not affect weight, lipid levels, and atherosclerosis in LDL receptor knockout mice on high-fat diet. *Diabetes* **2010**, *59*, 2898–2903. [\[CrossRef\]](#)
86. De Henau, O.; Degroot, G.N.; Imbault, V.; Robert, V.; De Poorter, C.; Mcheik, S.; Galés, C.; Parmentier, M.; Springael, J.Y. Signaling Properties of Chemerin Receptors CMKLR1, GPR1 and CCRL2. *PLoS ONE* **2016**, *11*, e0164179. [\[CrossRef\]](#) [\[PubMed\]](#)
87. Zhu, L.; Huang, J.; Wang, Y.; Yang, Z.; Chen, X. Chemerin causes lipid metabolic imbalance and induces passive lipid accumulation in human hepatoma cell line via the receptor GPR1. *Life Sci.* **2021**, *278*, 119530. [\[CrossRef\]](#)
88. Zhou, X.; Jiang, Y.; Wang, Z.; Wei, L.; Zhang, H.; Fang, C.; Zhu, S.; Du, Y.; Su, R.; Li, W.; et al. Chemerin alleviates the placental oxidative stress and improves fetal overgrowth of gestational diabetes mellitus mice induced by high fat diet. *Mol. Med.* **2024**, *30*, 239. [\[CrossRef\]](#)
89. Aravindraj, R.; Renuka, P.; Vinodhini, V.M.; Meenakshi Sundari, S.N. Circulating Chemerin Levels in Obese and Non-obese Individuals and Its Association With Obesity in Metabolic Dysfunction-Associated Fatty Liver Disease. *Cureus* **2024**, *16*, e68105. [\[CrossRef\]](#)
90. Neves, K.B.; Nguyen Dinh Cat, A.; Alves-Lopes, R.; Harvey, K.Y.; Costa, R.M.D.; Lobato, N.S.; Montezano, A.C.; Oliveira, A.M.; Touyz, R.M.; Tostes, R.C. Chemerin receptor blockade improves vascular function in diabetic obese mice via redox-sensitive and Akt-dependent pathways. *Am. J. Physiol. Heart Circ. Physiol.* **2018**, *315*, H1851–H1860. [\[CrossRef\]](#) [\[PubMed\]](#)
91. Neves, K.B.; Montezano, A.C.; Alves-Lopes, R.; Bruder-Nascimento, T.; Costa, R.M.; Costa, R.S.; Touyz, R.M.; Tostes, R.C. Upregulation of Nrf2 and Decreased Redox Signaling Contribute to Renoprotective Effects of Chemerin Receptor Blockade in Diabetic Mice. *Int. J. Mol. Sci.* **2018**, *19*, 2454. [\[CrossRef\]](#)

92. Chen, S.; Wu, K.; Ke, Y.; Chen, S.; He, R.; Zhang, Q.; Shen, C.; Li, Q.; Ruan, Y.; Zhu, Y.; et al. Association of circulating visfatin level and metabolic fatty liver disease: An updated meta-analysis and systematic review. *Medicine* **2024**, *103*, e39613. [[CrossRef](#)] [[PubMed](#)]
93. Heo, Y.J.; Choi, S.E.; Jeon, J.Y.; Han, S.J.; Kim, D.J.; Kang, Y.; Lee, K.W.; Kim, H.J. Visfatin Induces Inflammation and Insulin Resistance via the NF- κ B and STAT3 Signaling Pathways in Hepatocytes. *J. Diabetes Res.* **2019**, *2019*, 4021623. [[CrossRef](#)]
94. Ren, Y.; Zhao, H.; Yin, C.; Lan, X.; Wu, L.; Du, X.; Griffiths, H.R.; Gao, D. Adipokines, Hepatokines and Myokines: Focus on Their Role and Molecular Mechanisms in Adipose Tissue Inflammation. *Front. Endocrinol.* **2022**, *13*, 873699. [[CrossRef](#)]
95. de A Boleti, A.P.; de O Cardoso, P.H.; Frihling, B.E.F.; Silva, P.S.E.; de Moraes, L.F.R.N.; Migliolo, L. Adipose tissue, systematic inflammation, and neurodegenerative diseases. *Neural Regen. Res.* **2023**, *18*, 38–46. [[CrossRef](#)]
96. Zaidi, H.; Aksnes, T.; Åkra, S.; Eggesbø, H.B.; Byrkjeland, R.; Seljeflot, I.; Opstad, T.B. Abdominal Adipose Tissue Associates With Adiponectin and TNF α in Middle-Aged Healthy Men. *Front. Endocrinol.* **2022**, *13*, 874977. [[CrossRef](#)]
97. Dağdelen, D.; Karadag, A.S.; Kasapoglu, E.; Wang, J.V.; Erman, H. Correlation of metabolic syndrome with serum omentin-1 and visfatin levels and disease severity in psoriasis and psoriatic arthritis. *Dermatol. Ther.* **2020**, *33*, e14378. [[CrossRef](#)] [[PubMed](#)]
98. Chen, J.; Hu, L.; Ling, Y.; Xu, Y.; Yu, X.; Ma, L.; Shou, M. Risk Correlation Analysis between Polycystic Ovary Syndrome (PCOS) and Serum Visfatin Levels in Middle-Aged Women: Systematic Review and Meta-Analysis. *Discov. Med.* **2023**, *35*, 168–177. [[CrossRef](#)] [[PubMed](#)]
99. Kärberg, K.; Forbes, A.; Lember, M. Visfatin and Subclinical Atherosclerosis in Type 2 Diabetes: Impact of Cardiovascular Drugs. *Medicina* **2023**, *59*, 1324. [[CrossRef](#)] [[PubMed](#)]
100. Ali, A.I.; Nori, W. Correlation of Serum Visfatin Level in Non-obese Women with Polycystic Ovary Syndrome and Matched Control. *Reprod. Sci.* **2022**, *29*, 3285–3293. [[CrossRef](#)]
101. Huang, Y.L.; Chen, Y.L.; Lin, J.D.; Pei, D.; Pitrone, P.; Chen, J.S.; Wu, C.Z. Visfatin and Retinol Binding Protein-4 in Young-Onset Type 2 Diabetes Mellitus. *Medicina* **2023**, *59*, 1278. [[CrossRef](#)]
102. Mir, M.M.; Mir, R.; Alghamdi, M.A.A.; Wani, J.I.; Sabah, Z.U.; Jeelani, M.; Marakala, V.; Sohail, S.K.; O'haj, M.; Alharthi, M.H.; et al. Differential Association of Selected Adipocytokines, Adiponectin, Leptin, Resistin, Visfatin and Chemerin, with the Pathogenesis and Progression of Type 2 Diabetes Mellitus (T2DM) in the Asir Region of Saudi Arabia: A Case Control Study. *J. Pers. Med.* **2022**, *12*, 735. [[CrossRef](#)]
103. Garten, A.; Schuster, S.; Penke, M.; Gorski, T.; de Giorgis, T.; Kiess, W. Physiological and pathophysiological roles of NAMPT and NAD metabolism. *Nat. Rev. Endocrinol.* **2015**, *11*, 535–546. [[CrossRef](#)] [[PubMed](#)]
104. Haider, D.G.; Schaller, G.; Kapiotis, S.; Maier, C.; Luger, A.; Wolzt, M. The release of the adipocytokine visfatin is regulated by glucose and insulin. *Diabetologia* **2006**, *49*, 1909–1914. [[CrossRef](#)]
105. Yang, L.; Qiu, Y.; Ling, W.; Liu, Z.; Yang, L.; Wang, C.; Peng, X.; Wang, L.; Chen, J. Anthocyanins regulate serum adipsin and visfatin in patients with prediabetes or newly diagnosed diabetes: A randomized controlled trial. *Eur. J. Nutr.* **2021**, *60*, 1935–1944. [[CrossRef](#)]
106. Abdalla, M.M.I. Role of visfatin in obesity-induced insulin resistance. *World J. Clin. Cases* **2022**, *10*, 10840–10851. [[CrossRef](#)]
107. De Souza Batista, C.M.; Yang, R.-Z.; Lee, M.-J.; Glynn, N.M.; Yu, D.-Z.; Pray, J.; Ndubuizu, K.; Patil, S.; Schwartz, A.; Kligman, M.; et al. Omentin Plasma Levels and Gene Expression Are Decreased in Obesity. *Diabetes* **2007**, *56*, 1655–1661. [[CrossRef](#)]
108. Miroshnikova, V.V.; Polyakova, E.A.; Pobozheva, I.A.; Panteleeva, A.A.; Razgildina, N.D.; Kolodina, D.A.; Belyaeva, O.D.; Berkovich, O.A.; Pchelina, S.N.; Baranova, E.I. FABP4 and omentin-1 gene expression in epicardial adipose tissue from coronary artery disease patients. *Genet. Mol. Biol.* **2021**, *44*, e20200441. [[CrossRef](#)]
109. Atashak, S.; Stannard, S.R.; Daraei, A.; Soltani, M.; Saeidi, A.; Moradi, F.; Laher, I.; Hackney, A.C.; Zouhal, H. High-intensity Interval Training Improves Lipocalin-2 and Omentin-1 Levels in Men with Obesity. *Int. J. Sports Med.* **2022**, *43*, 328–335. [[CrossRef](#)] [[PubMed](#)]
110. Lin, Y.Y.; Huang, C.C.; Ko, C.Y.; Tsai, C.H.; Chang, J.W.; Achudhan, D.; Tang, C.H. Omentin-1 modulates interleukin expression and macrophage polarization: Implications for rheumatoid arthritis therapy. *Int. Immunopharmacol.* **2025**, *149*, 114205. [[CrossRef](#)]
111. Özkan, E.A.; Sadigov, A.; Öztürk, O. Evaluation of Serum Omentin-1, Vaspin, Leptin, Adiponectin Levels in Obese/Overweight Children and Their Relationship With Non-Alcoholic Fatty Liver Disease. *Clin. Nutr. Res.* **2022**, *11*, 194–203. [[CrossRef](#)]
112. Sperling, M.; Grzelak, T.; Pelczyńska, M.; Bogdański, P.; Formanowicz, D.; Czyżewska, K. Association of Serum Omentin-1 Concentration with the Content of Adipose Tissue and Glucose Tolerance in Subjects with Central Obesity. *Biomedicines* **2023**, *11*, 331. [[CrossRef](#)] [[PubMed](#)]
113. Mousavi, S.M.; Heidarianpour, A.; Tavassoli, H. Aerobic Exercise Training Effects on Omentin-1, Insulin Resistance, and Lipid Profile Among Male Smokers. *Res. Q. Exerc. Sport.* **2023**, *94*, 880–885. [[CrossRef](#)] [[PubMed](#)]
114. Sena, C.M. Omentin: A Key Player in Glucose Homeostasis, Atheroprotection, and Anti-Inflammatory Potential for Cardiovascular Health in Obesity and Diabetes. *Biomedicines* **2024**, *12*, 284. [[CrossRef](#)] [[PubMed](#)]
115. Song, M.; Jiao, B.; Tian, X.J.; Qi, B.R. Therapeutic potential of omentin-1 in preeclampsia: Enhancing fetal outcomes, vascular function, and reducing inflammation. *Exp. Anim.* **2025**, *74*, 216–228. [[CrossRef](#)] [[PubMed](#)]

116. Okamura, Y.; Adachi, K.; Nijima, R.; Kodama, T.; Otani, K.; Okada, M.; Yamawaki, H. Human omentin-1 reduces vascular insulin resistance and hypertension in Otsuka Long-Evans Tokushima Fatty rats. *Naunyn-Schmiedeberg's Arch. Pharmacol.* **2024**, *397*, 3379–3387. [[CrossRef](#)]
117. Michalczyk, K.; Niklas, N.; Rychlicka, M.; Cymbaluk-Płoska, A. The Influence of Biologically Active Substances Secreted by the Adipose Tissue on Endometrial Cancer. *Diagnostics* **2021**, *11*, 494. [[CrossRef](#)]
118. Biegański, H.M.; Dąbrowski, K.M.; Różańska-Wałędziak, A. Omentin-General Overview of Its Role in Obesity, Metabolic Syndrome and Other Diseases; Problem of Current Research State. *Biomedicines* **2025**, *13*, 632. [[CrossRef](#)]
119. Xu, J.; Li, M.; Jiang, X.; Wang, Y.; Ma, H.; Zhou, Y.; Tian, M.; Liu, Y. Omentin-1 and diabetes: More evidence but far from enough. *Arch. Physiol. Biochem.* **2024**, *130*, 599–605. [[CrossRef](#)]
120. Zamanian, M.Y.; Maleki, S.; Oghenemaro, E.F.; Singh, M.; Mohammadi, M.; Alkhayyat, A.H.; Sapaev, I.B.; Kaur, P.; Shirsalimi, N.; Nagarwal, A. Omentin-1 as a promising biomarker and therapeutic target in hypertension and heart failure: A comprehensive review. *Naunyn-Schmiedeberg's Arch. Pharmacol.* **2025**, *ahead of print*. [[CrossRef](#)]
121. Yilmaz, M.F.; Kalkan, Z.; Cander, B.; Gul, M.; Isik, M.; Ilhan, M. Relationship between circulating serum omentin-1 levels and nascent metabolic syndrome in patients with hypertension. *J. Investig. Med.* **2022**, *70*, 385–390. [[CrossRef](#)]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.