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Natural Product-Based Modulation of Adipokines and Myokines: Implications for Obesity-Driven Diabetes

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ABSTRACT

Obesity-driven type 2 diabetes is a multifactorial metabolic disorder in which dysfunctional inter-organ communication particularly between adipose tissue and skeletal muscle plays a pivotal role. Adipokines and myokines are hormone-like factors produced by adipocytes and myocytes, respectively, that regulate energy homeostasis, insulin sensitivity, inflammation, and substrate metabolism. In obesity, adipose tissue secretes a proinflammatory adipokine profile (e.g., increased leptin resistance, resistin, visfatin, and decreased adiponectin) while skeletal muscle myokine tone shifts in ways that can exacerbate or ameliorate insulin resistance (e.g., irisin, IL-6, myostatin). Natural products plant polyphenols, flavonoids, terpenoids, alkaloids, and bioactive peptides exert pleiotropic effects on these signaling molecules and their downstream pathways. This review synthesizes mechanistic and translational evidence for natural product modulation of adipokines and myokines, examining molecular targets, preclinical efficacy, human trial data where available, and the pharmacological and safety challenges of translating nutraceutical interventions into clinical practice. We highlight how select natural molecules restore adipokine balance, enhance myokine-mediated insulin-sensitizing effects, and attenuate chronic inflammation, thereby offering adjunctive therapeutic potential for obesity-associated diabetes. Finally, gaps in evidence, methodological limitations in current studies, and priorities for future research standardization, dosing, bioavailability improvement, and rigorous clinical trials are discussed. The goal is to provide a coherent, mechanistic, and pragmatic framework for researchers and clinicians exploring natural product strategies to rebalance adipose-muscle cross-talk and mitigate metabolic disease progression.
Keywords: adipokines, myokines, natural products, obesity, type 2 diabetes

INTRODUCTION

Inter-organ communication is central to metabolic homeostasis, and the dialogue between adipose tissue and skeletal muscle is particularly important in the pathogenesis of obesity-driven type 2 diabetes[1–3]. Adipose tissue and skeletal muscle are not passive storage or locomotor organs; rather, they are endocrine organs that secrete adipokines and myokines respectively peptides and proteins that act locally and systemically to regulate appetite, energy expenditure, lipid handling, insulin sensitivity, and inflammatory responses[1, 4–6]. In healthy physiology, this cytokine-like signaling maintains metabolic flexibility: adiponectin promotes insulin sensitivity and fatty acid oxidation, leptin regulates appetite and energy expenditure, and muscle-derived myokines such as irisin and IL-6 contribute to substrate switching and anti-inflammatory signaling during physical activity. However, with positive energy balance leading to adipocyte hypertrophy and adipose tissue inflammation, the secretory profile becomes maladaptive[7, 8]. Proinflammatory adipokines and reduced beneficial adipokines create a milieu of chronic low-grade inflammation, lipotoxicity, and insulin resistance. Concurrently, skeletal muscle in sedentary, obese individuals exhibits altered myokine secretion and reduced capacity for glucose uptake and oxidative metabolism, further amplifying metabolic deterioration[9, 10].

Given the multifactorial and systemic nature of obesity-driven diabetes, single-target pharmacological strategies have limited long-term success for many patients. This has fueled interest in pleiotropic interventions that act across multiple tissues and signaling nodes an area where natural products and nutraceuticals are particularly promising[11, 12]. Natural compounds often have multiple molecular targets, modulate oxidative stress and inflammation, and influence transcriptional networks governing metabolism, including AMP-activated protein kinase (AMPK), peroxisome proliferator–activated receptors (PPARs), nuclear factor kappa B (NF-κB), and the

insulin signaling cascade. Importantly, many natural products have been shown in preclinical models to modify adipokine and myokine expression or secretion, thereby directly affecting the adipose–muscle axis[13, 14].

The biological plausibility for natural product interventions arises from a large and growing literature: flavonoids and polyphenols can increase adiponectin and reduce proinflammatory adipokine expression in adipocytes; plant-derived alkaloids and terpenoids modulate myostatin and irisin expression in muscle cells; and certain bioactive peptides enhance insulin receptor signaling and mitochondrial function[15, 16]. These effects translate into improved glucose tolerance, reduced adipose inflammation, and favorable lipid profiles in animal models. However, translation to humans remains uneven. Clinical trials are heterogeneous in dosage, formulation, and endpoints; bioavailability constraints and metabolic transformation of natural compounds create additional complexity; and safety evaluation is sometimes limited or inconsistent[17]. This review aims to synthesize mechanistic insights and translational evidence on how natural products modulate adipokines and myokines and the implications for obesity-driven diabetes. We will first summarize the roles of key adipokines and myokines in metabolic regulation and disease. We then review classes of natural products that influence these mediators, describe molecular mechanisms and signaling pathways involved, and appraise preclinical and clinical evidence for metabolic benefit. Finally, we discuss challenges for clinical translation, including standardization, bioavailability, safety, and the need for well-powered, mechanism-informed clinical trials. By focusing on the adipose–muscle endocrine axis, we propose an integrated framework for future research that may enable targeted nutraceutical strategies to prevent or ameliorate obesity-associated diabetes.

2. Adipokines in Obesity-Driven Diabetes

Adipokines encompass a diverse set of bioactive molecules secreted by adipose tissue that influence systemic metabolism, immune responses, and vascular function[18–23]. In the context of obesity, adipose tissue undergoes cellular and extracellular remodeling, marked by adipocyte hypertrophy, hypoxia, immune cell infiltration, and altered extracellular matrix dynamics. These changes dysregulate adipokine secretion, shifting the balance from insulin-sensitizing and anti-inflammatory factors to proinflammatory and insulin-antagonistic mediators [24]. Adiponectin, a key insulin-sensitizing adipokine, is consistently reduced in obesity and correlates inversely with insulin resistance; its decrease impairs fatty acid oxidation in muscle and liver, reduces AMPK activation, and promotes ectopic lipid accumulation[9, 25, 26]. Leptin, which normally signals satiety and promotes energy expenditure, often rises in obesity but is accompanied by leptin resistance that negates central and peripheral effects[7, 27–29]. Concurrently, adipose tissue secretes increased levels of resistin, chemerin, visfatin, and proinflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6; these factors interfere with insulin receptor signaling via serine phosphorylation of insulin receptor substrates and activation of stress kinases like JNK and IKKβ[30].

The proinflammatory milieu fosters macrophage polarization toward a proinflammatory M1 phenotype, creating a feed-forward loop that sustains cytokine production and tissue dysfunction[31–33]. Moreover, adipokines influence pancreatic β-cell function, endothelial health, and appetite-regulatory circuits, extending their effects beyond classical metabolic tissues. For example, elevated resistin has been associated with impaired glucose uptake and hepatic glucose output, while decreased adiponectin compromises pancreatic β-cell survival and amplifies oxidative stress[34–36]. At the molecular level, adipokines modulate critical nodes such as AMPK, PPARs, and NF-κB, thereby controlling gene programs for lipid metabolism, mitochondrial biogenesis, and inflammatory responses.

Importantly, adipokine dysregulation is heterogeneous across adipose depots. Visceral fat displays a more deleterious secretory profile than subcutaneous fat, contributing disproportionately to cardiometabolic risk[37, 38]. This depot-specificity is relevant for interventions targeting adipokine balance: strategies that reduce visceral adiposity or selectively modulate its secretome may yield greater metabolic improvements. Natural products that upregulate adiponectin or downregulate proinflammatory adipokines can re-establish metabolic signaling that favors insulin sensitivity, improved lipid handling, and reduced systemic inflammation, making adipokine modulation a promising therapeutic axis for obesity-driven diabetes.

3. Myokines and Skeletal Muscle Signaling in Metabolic Health

Skeletal muscle is the largest organ for glucose disposal and a dynamic endocrine organ that secretes myokines peptides and proteins released into circulation in response to contraction, metabolic state, and muscle remodeling[39]. Myokines orchestrate autocrine, paracrine, and endocrine effects that regulate muscle metabolism, inter-organ substrate flux, and systemic inflammation. Exercise-induced myokines such as irisin and IL-6 at physiological levels promote browning of adipose tissue, increase lipolysis, and improve insulin sensitivity through AMPK activation and enhanced mitochondrial biogenesis[40]. Conversely, myostatin, a negative regulator of muscle growth belonging to the TGF-β family, promotes muscle atrophy and has been linked to insulin resistance when elevated. Other myokines, including fibroblast growth factor 21, brain-derived neurotrophic factor, and decorin, play roles in lipid oxidation, neuromuscular health, and modulation of adipose tissue phenotype[41].

In obesity and sedentary states, altered myokine profiles contribute to metabolic dysfunction. Reduced exercise-induced myokine release and increased expression of negative regulators like myostatin impair muscle insulin

responsiveness and reduce glucose uptake. Insulin resistance in muscle is often accompanied by mitochondrial dysfunction, oxidative stress, and alterations in substrate preference toward lipid accumulation[42, 43]. The crosstalk between myokines and adipokines is bidirectional: beneficial myokines can counteract adipose inflammation and promote a healthier adipokine profile, while adipose-derived proinflammatory factors can blunt myokine production and muscle metabolic capacity.

Molecular pathways common to myokine action include AMPK signaling, PGC-1α-mediated mitochondrial biogenesis, and modulation of the PI3K–Akt insulin signaling cascade. Natural products that mimic exercise-like stimuli or enhance myokine production may therefore restore muscle metabolic function and systemic insulin sensitivity[44]. For instance, compounds that increase PGC-1α expression, promote mitochondrial turnover, or suppress myostatin can shift muscle phenotype toward oxidative, insulin-responsive tissue. Additionally, interventions that facilitate muscle contractile activity either pharmacologically or via combination with structured exercise can potentiate myokine-mediated benefits[45]. Therefore, understanding how natural products influence myokine secretion and signaling is essential for designing integrated strategies that leverage muscle-endocrine function to combat obesity-driven diabetes.

4. Natural Products Targeting Adipokine Signaling

A diverse array of plant-derived compounds modulate adipokine secretion and signaling pathways relevant to metabolic health. Polyphenols, including resveratrol, quercetin, and epigallocatechin gallate, exert insulin-sensitizing effects in part by elevating adiponectin expression and suppressing proinflammatory adipokines[46]. These molecules activate AMPK and SIRT1, improve mitochondrial function, and reduce NF-κB–mediated cytokine production in adipocytes. Terpenoids and saponins found in medicinal plants modulate PPARγ activity and adipogenesis, thereby influencing the adipose secretome. For example, certain triterpenoids restore adiponectin levels while inhibiting expression of MCP-1 and TNF-α, which are central to macrophage recruitment and adipose inflammation[47].

Flavonoids can also attenuate endoplasmic reticulum stress in adipocytes, a contributor to dysregulated adipokine secretion, and improve insulin receptor signaling by reducing serine phosphorylation of IRS proteins[48–50]. Alkaloids such as berberine reduce hepatic glucose output and indirectly improve adipokine balance by decreasing visceral fat and systemic inflammation[51–53]. Marine-derived peptides and omega-3 polyunsaturated fatty acids modulate adipose tissue macrophage polarization toward anti-inflammatory phenotypes and increase adiponectin synthesis, while reducing resistin and chemerin expression[54].

Mechanistically, natural compounds influence transcriptional regulators (PPARs, C/EBP, SREBP), kinases (AMPK, JNK), and redox-sensitive transcription factors to shift adipose tissue toward a less inflammatory, more metabolically active state. Several botanical extracts combine multiple active constituents that act synergistically on adipokine networks. Nevertheless, variability in extract composition, bioavailability of active molecules, and metabolic conversion in humans complicate extrapolation from preclinical models[55, 56]. Rigorous standardization, metabolomic profiling, and pharmacokinetic characterization are therefore necessary to translate adipokine-modulating natural products into clinically useful therapies.

5. Natural Products Influencing Myokine Biology

Natural products can modulate skeletal muscle function and myokine secretion through mechanisms that parallel exercise adaptations. Polyphenols like resveratrol and green tea catechins upregulate PGC-1α and mitochondrial biogenesis in muscle cells, processes associated with increased secretion of beneficial myokines such as irisin and FGF21[57]. Compounds that enhance mitochondrial function and reduce oxidative stress facilitate greater contractile efficiency and endurance capacity, both of which potentiate exercise-induced myokine release. Additionally, small molecules that inhibit myostatin signaling or its downstream SMAD effectors can prevent muscle atrophy and improve insulin sensitivity; several plant-derived triterpenes and peptides have shown myostatin-inhibitory activity in preclinical studies[58].

Amino acid–derived nutraceuticals and bioactive peptides derived from food proteins stimulate anabolic signaling and can increase muscle-derived IGF-1 and related growth factors. Certain polyunsaturated fatty acids and specialized lipids influence membrane composition and signaling microdomains in myocytes, modulating secretion of cytokines and myokines that affect systemic metabolism[59]. Moreover, some natural compounds indirectly enhance myokine profiles by improving overall metabolic milieu—reducing systemic inflammation and insulin resistance thereby restoring muscle's capacity to produce and secrete beneficial endocrine factors.

Crucially, natural products often act synergistically with physical activity. When combined with exercise, nutraceuticals that improve mitochondrial function, reduce inflammation, or enhance muscle protein synthesis amplify myokine responses and the consequent cross-talk with adipose tissue[60, 61]. Translationally, interventions that combine well-characterized natural compounds with structured exercise programs may present a pragmatic strategy for leveraging myokine biology to reduce obesity-driven metabolic risk. However, precise dosing, timing relative to exercise, and long-term safety require systematic investigation in controlled human trials[60].

6. Integrated Adipokine–Myokine Cross-talk and Nutraceutical Strategies

The interplay between adipokines and myokines forms a regulatory network that determines systemic metabolic outcomes. Beneficial myokines can promote adipose browning, enhance fatty acid oxidation, and suppress adipose inflammation, while a healthier adipokine profile supports muscle insulin sensitivity and mitochondrial function[60]. Natural products that simultaneously shift adipose secretome toward higher adiponectin and lower proinflammatory cytokines while promoting muscle PGC-1α and irisin expression are therefore especially attractive as multimodal interventions. Polyphenol-rich diets and whole-food interventions exemplify this integrative approach: they reduce visceral adiposity, decrease systemic inflammatory mediators, and improve muscle oxidative capacity, producing a coordinated improvement in adipose–muscle cross-talk[62].

Systems-level mechanisms include modulation of AMPK as a metabolic master switch, enhancement of mitochondrial biogenesis via PGC-1α, attenuation of NF-κB–driven inflammation, and regulation of insulin signaling through PI3K–Akt pathways. Natural products often target several of these nodes simultaneously, leading to synergistic effects on tissue crosstalk[63]. Nutraceutical formulations that combine compounds with complementary pharmacodynamics such as a mitochondrial enhancer with an anti-inflammatory polyphenol may offer superior outcomes compared with single-agent approaches. Importantly, such strategies must account for pharmacokinetic interactions and metabolite activity, since gut metabolism and host microbiota can transform parent compounds into bioactive or inactive derivatives, altering systemic effects on adipokines and myokines[64].

Precision nutraceutical approaches may tailor interventions based on adipose depot distribution, baseline inflammatory status, muscle mass and function, and even genetic polymorphisms that affect metabolism of active compounds[65]. Combining nutraceutical therapy with lifestyle interventions, particularly resistance and aerobic exercise, can maximize myokine release and potentiate adipokine normalization. Ultimately, the integrated modulation of adipokines and myokines by natural products represents a holistic, tissue-network-focused therapeutic paradigm for obesity-associated diabetes, but its clinical realization depends on mechanistic clarity, optimized formulations, and outcome-driven clinical research[66].

7. Clinical Evidence, Challenges, and Future Directions

Clinical translation of adipokine- and myokine-targeted natural products has met with mixed results. Several small randomized trials and observational studies report improvements in insulin sensitivity, modest reductions in inflammatory biomarkers, and favorable shifts in adipokine levels with interventions such as omega-3 supplementation, green tea extracts, and resveratrol. However, heterogeneity in formulations, small sample sizes, and short durations limit generalizability[67]. Bioavailability remains a persistent challenge: many polyphenols are extensively metabolized by gut microbiota and liver, producing metabolites with distinct bioactivity, which complicates dose–response relationships [68]. Safety profiling is often incomplete, particularly for concentrated extracts and chronic administration. Interactions with prescription medications, effects on micronutrient absorption, and idiosyncratic adverse events require rigorous pharmacovigilance[69].

To advance the field, standardized extract characterization, robust pharmacokinetic-pharmacodynamic mapping, and integration of biomarker-driven endpoints (adipokine/myokine panels, insulin sensitivity indices, tissue-specific imaging) are needed in clinical trials[70, 71]. Precision approaches that stratify participants by baseline inflammation, visceral fat burden, or muscle function may reveal subgroups most likely to respond. Formulation science—nanoparticle encapsulation, prodrugs, and co-administration with adjuvants that improve absorption—offers avenues to enhance efficacy [72]. Mechanistic human studies that pair tissue biopsies with systemic biomarkers will clarify causal pathways and validate targets. Regulatory pathways for nutraceuticals and botanical drugs require adherence to quality standards and evidence thresholds commensurate with therapeutic claims.

CONCLUSION

In conclusion, natural products provide a biologically plausible and multifaceted means to rebalance adipokine and myokine signaling in obesity-driven diabetes. The path forward demands multidisciplinary collaboration among natural product chemists, molecular physiologists, clinical trialists, and formulation scientists to translate preclinical promise into safe, effective, and evidence-based interventions.

REFERENCES

1. Kahn, B.B.: Adipose Tissue, Inter-Organ Communication, and the Path to Type 2 Diabetes: The 2016 Banting Medal for Scientific Achievement Lecture. Diabetes. 68, 3–14 (2019). https://doi.org/10.2337/dbi18-0035
2. Tokizane, K., Imai, S.: Inter-organ communication is a critical machinery to regulate metabolism and aging. Trends in Endocrinology & Metabolism. 36, 756–766 (2025). https://doi.org/10.1016/j.tem.2024.11.013
3. Blackwell, J.A., Stanford, K.I.: Exercise-induced intertissue communication: adipose tissue and the heart. Current Opinion in Physiology. 31, 100626 (2023). https://doi.org/10.1016/j.cophys.2022.100626

4. Alzaid, F., Fagherazzi, G., Riveline, J.-P., Bahman, F., Al-Rashed, F., Al-Mulla, F., Ahmad, R.: Immune cell–adipose tissue crosstalk in metabolic diseases with a focus on type 1 diabetes. Diabetologia. 68, 1616–1631 (2025). https://doi.org/10.1007/s00125-025-06437-z
5. Anguita-Ruiz, A., Bustos-Aibar, M., Plaza-Díaz, J., Mendez-Gutierrez, A., Alcalá-Fdez, J., Aguilera, C.M., Ruiz-Ojeda, F.J.: Omics Approaches in Adipose Tissue and Skeletal Muscle Addressing the Role of Extracellular Matrix in Obesity and Metabolic Dysfunction. International Journal of Molecular Sciences. 22, 2756 (2021). https://doi.org/10.3390/ijms22052756
6. Obasi, D.C., Abba, J.N., Aniokete, U.C., Okoroh, P.N., Akwari, A.Ak.: Evolving Paradigms in Nutrition Therapy for Diabetes: From Carbohydrate Counting to Precision Diets. Obesity Medicine. 100622 (2025). https://doi.org/10.1016/j.obmed.2025.100622
7. Stern, J.H., Rutkowski, J.M., Scherer, P.E.: Adiponectin, Leptin, and Fatty Acids in the Maintenance of Metabolic Homeostasis Through Adipose Tissue Crosstalk. Cell metabolism. 23, 770 (2016). https://doi.org/10.1016/j.cmet.2016.04.011
8. Matar, D.B., Zhra, M., Nassar, W.K., Altemyatt, H., Naureen, A., Abotouk, N., Elahi, M.A., Aljada, A.: Adipose tissue dysfunction disrupts metabolic homeostasis: mechanisms linking fat dysregulation to disease. Frontiers in Endocrinology. 16, 1592683 (2025). https://doi.org/10.3389/fendo.2025.1592683
9. Babaei, P., Hoseini, R.: Exercise training modulates adipokine dysregulations in metabolic syndrome. Sports Medicine and Health Science. 4, 18–28 (2022). https://doi.org/10.1016/j.smhs.2022.01.001
10. Pollak, N., Janežič, E.G., Šink, Ž., Ugwoke, C.K.: Crosstalk Between Skeletal Muscle and Proximal Connective Tissues in Lipid Dysregulation in Obesity and Type 2 Diabetes. Metabolites. 15, 581 (2025). https://doi.org/10.3390/metabo15090581
11. Guerra, J.V.S., Dias, M.M.G., Brilhante, A.J.V.C., Terra, M.F., García-Arévalo, M., Figueira, A.C.M.: Multifactorial Basis and Therapeutic Strategies in Metabolism-Related Diseases. Nutrients. 13, 2830 (2021). https://doi.org/10.3390/nu13082830
12. Ullah, M.I., Tamanna, S.: Obesity: Clinical Impact, Pathophysiology, Complications, and Modern Innovations in Therapeutic Strategies. Medicines. 12, 19 (2025). https://doi.org/10.3390/medicines12030019
13. Liu, H., Wang, S., Wang, J., Guo, X., Song, Y., Fu, K., Gao, Z., Liu, D., He, W., Yang, L.-L.: Energy metabolism in health and diseases. Sig Transduct Target Ther. 10, 69 (2025). https://doi.org/10.1038/s41392-025-02141-x
14. Smith, R.L., Soeters, M.R., Wüst, R.C.I., Houtkooper, R.H.: Metabolic Flexibility as an Adaptation to Energy Resources and Requirements in Health and Disease. Endocr Rev. 39, 489–517 (2018). https://doi.org/10.1210/er.2017-00211
15. Khalilpourfarshbafi, M., Gholami, K., Murugan, D.D., Abdul Sattar, M.Z., Abdullah, N.A.: Differential effects of dietary flavonoids on adipogenesis. Eur J Nutr. 58, 5–25 (2019). https://doi.org/10.1007/s00394-018-1663-8
16. Uti, D.E., Atangwho, I.J., Alum, E.U., Egba, S.I., Ugwu, O.P.-C., Ikechukwu, G.C.: Natural Antidiabetic Agents: Current Evidence and Development Pathways from Medicinal Plants to Clinical use. Natural Product Communications. 20, 1934578X251323393 (2025). https://doi.org/10.1177/1934578X251323393
17. Rendine, M., Marino, M., Martini, D., Riso, P., Møller, P., Bo', C.D.: Effect of (Poly)phenols on Lipid and Glucose Metabolisms in 3T3-L1 Adipocytes: an Integrated Analysis of Mechanistic Approaches. Current Obesity Reports. 14, 64 (2025). https://doi.org/10.1007/s13679-025-00656-6
18. Al-Mansoori, L., Al-Jaber, H., Prince, M.S., Elrayess, M.A.: Role of Inflammatory Cytokines, Growth Factors and Adipokines in Adipogenesis and Insulin Resistance. Inflammation. 45, 31–44 (2022). https://doi.org/10.1007/s10753-021-01559-z
19. Datta, S., Koka, S., Boini, K.M.: Understanding the Role of Adipokines in Cardiometabolic Dysfunction: A Review of Current Knowledge. Biomolecules. 15, 612 (2025). https://doi.org/10.3390/biom15050612
20. Hemat Jouy, S., Mohan, S., Scichilone, G., Mostafa, A., Mahmoud, A.M.: Adipokines in the Crosstalk between Adipose Tissues and Other Organs: Implications in Cardiometabolic Diseases. Biomedicines. 12, 2129 (2024). https://doi.org/10.3390/biomedicines12092129
21. Kirichenko, T.V., Markina, Y.V., Bogatyreva, A.I., Tolstik, T.V., Varaeva, Y.R., Starodubova, A.V.: The Role of Adipokines in Inflammatory Mechanisms of Obesity. Int J Mol Sci. 23, 14982 (2022). https://doi.org/10.3390/ijms232314982
22. Ouchi, N., Parker, J.L., Lugus, J.J., Walsh, K.: Adipokines in inflammation and metabolic disease. Nat Rev Immunol. 11, 85–97 (2011). https://doi.org/10.1038/nri2921
23. Uti, D.E., Atangwho, I.J., Omang, W.A., Alum, E.U., Obeten, U.N., Udeozor, P.A., Agada, S.A., Bawa, I., Ogbu, C.O.: Cytokines as key players in obesity low grade inflammation and related complications. Obesity Medicine. 54, 100585 (2025). https://doi.org/10.1016/j.obmed.2025.100585

24. Izah, S.C., Betiang, P.A., Paul-Chima Ugwu, O., Ainebyoona, C., Uti, D.E., Echegu, D.A.: The Ketogenic Diet in Obesity Management: Friend or Foe? Cell Biochem Biophys. (2025). https://doi.org/10.1007/s12013-025-01878-0
25. Roy, P.K., Islam, J., Lalhlenmawia, H.: Prospects of potential adipokines as therapeutic agents in obesity-linked atherogenic dyslipidemia and insulin resistance. The Egyptian Heart Journal. 75, 24 (2023). https://doi.org/10.1186/s43044-023-00352-7
26. Alum, E.U.: Metabolic memory in obesity: Can early-life interventions reverse lifelong risks? Obesity Medicine. 55, 100610 (2025). https://doi.org/10.1016/j.obmed.2025.100610
27. Andò, S., Gelsomino, L., Panza, S., Giordano, C., Bonofiglio, D., Barone, I., Catalano, S.: Obesity, Leptin and Breast Cancer: Epidemiological Evidence and Proposed Mechanisms. Cancers (Basel). 11, 62 (2019). https://doi.org/10.3390/cancers11010062
28. Bocian-Jastrzębska, A., Malczewska-Herman, A., Kos-Kudła, B.: Role of Leptin and Adiponectin in Carcinogenesis. Cancers (Basel). 15, 4250 (2023). https://doi.org/10.3390/cancers15174250
29. de Candia, P., Prattichizzo, F., Garavelli, S., Alviggi, C., La Cava, A., Matarese, G.: The pleiotropic roles of leptin in metabolism, immunity, and cancer. J Exp Med. 218, e20191593 (2021). https://doi.org/10.1084/jem.20191593
30. Hemat Jouy, S., Mohan, S., Scichilone, G., Mostafa, A., Mahmoud, A.M.: Adipokines in the Crosstalk between Adipose Tissues and Other Organs: Implications in Cardiometabolic Diseases. Biomedicines. 12, 2129 (2024). https://doi.org/10.3390/biomedicines12092129
31. Cavallucci, V., Palucci, I., Fidaleo, M., Mercuri, A., Masi, L., Emoli, V., Bianchetti, G., Fiori, M.E., Bachrach, G., Scaldaferri, F., Maulucci, G., Delogu, G., Pani, G.: Proinflammatory and Cancer-Promoting Pathobiont Fusobacterium nucleatum Directly Targets Colorectal Cancer Stem Cells. Biomolecules. 12, 1256 (2022). https://doi.org/10.3390/biom12091256
32. Veilleux, C., Roy, M.-È., Zgheib, A., Desjarlais, M., Annabi, B.: Evidence for a JAK2/STAT3 proinflammatory and vasculogenic mimicry interrelated molecular signature in adipocyte-derived mesenchymal stromal/stem cells. Cell Communication and Signaling. 23, 291 (2025). https://doi.org/10.1186/s12964-025-02298-6
33. Zhang, Q., Han, X., Chen, J., Xie, X., Xu, J., Zhao, Y., Shen, J., Hu, L., Xu, P., Song, H., Zhang, L., Zhao, B., Wang, Y., Xia, Z.: Yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ) mediate cell density–dependent proinflammatory responses. J Biol Chem. 293, 18071–18085 (2018). https://doi.org/10.1074/jbc.RA118.004251
34. AL-Suhaimi, E.A., Shehzad, A.: Leptin, resistin and visfatin: the missing link between endocrine metabolic disorders and immunity. Eur J Med Res. 18, 12 (2013). https://doi.org/10.1186/2047-783X-18-12
35. Parafiniuk, K., Skiba, W., Pawłowska, A., Suszczyk, D., Maciejczyk, A., Wertel, I.: The Role of the Adipokine Resistin in the Pathogenesis and Progression of Epithelial Ovarian Cancer. Biomedicines. 10, 920 (2022). https://doi.org/10.3390/biomedicines10040920
36. Üstünsoy, S.: Resistin as a Biomarker and Applications to Prediabetes. In: Biomarkers in Diabetes. pp. 67–82. Springer, Cham (2023)
37. Ziegler, A.K., Scheele, C.: Human adipose depots' diverse functions and dysregulations during cardiometabolic disease. NPJ Metab Health Dis. 2, 34 (2024). https://doi.org/10.1038/s44324-024-00036-z
38. Korac, A., Srdic-Galic, B., Stancic, A., Otasevic, V., Korac, B., Jankovic, A.: Adipokine signatures of subcutaneous and visceral abdominal fat in normal-weight and obese women with different metabolic profiles. https://doi.org/10.5114/aoms/92118
39. Hoffmann, C., Weigert, C.: Skeletal Muscle as an Endocrine Organ: The Role of Myokines in Exercise Adaptations. Cold Spring Harb Perspect Med. 7, a029793 (2017). https://doi.org/10.1101/cshperspect.a029793
40. Severinsen, M.C.K., Pedersen, B.K.: Muscle–Organ Crosstalk: The Emerging Roles of Myokines. Endocr Rev. 41, 594–609 (2020). https://doi.org/10.1210/endrev/bnaa016
41. Baig, M.H., Ahmad, K., Moon, J.S., Park, S.-Y., Ho Lim, J., Chun, H.J., Qadri, A.F., Hwang, Y.C., Jan, A.T., Ahmad, S.S., Ali, S., Shaikh, S., Lee, E.J., Choi, I.: Myostatin and its Regulation: A Comprehensive Review of Myostatin Inhibiting Strategies. Front Physiol. 13, 876078 (2022). https://doi.org/10.3389/fphys.2022.876078
42. Chen, Z.-T., Weng, Z.-X., Lin, J.D., Meng, Z.-X.: Myokines: metabolic regulation in obesity and type 2 diabetes. Life Metab. 3, loae006 (2024). https://doi.org/10.1093/lifemeta/loae006
43. Alum, E.U.: Optimizing patient education for sustainable self-management in type 2 diabetes. Discov Public Health. 22, 44 (2025). https://doi.org/10.1186/s12982-025-00445-5
44. Rodríguez, A., Becerril, S., Ezquerro, S., Méndez-Giménez, L., Frühbeck, G.: Crosstalk between adipokines and myokines in fat browning. Acta Physiol (Oxf). 219, 362–381 (2017). https://doi.org/10.1111/apha.12686

45. Tero-Vescan, A., Degens, H., Matsakas, A., Ştefănescu, R., Ősz, B.E., Slevin, M.: Exercise-Induced Muscle–Fat Crosstalk: Molecular Mediators and Their Pharmacological Modulation for the Maintenance of Metabolic Flexibility in Aging. Pharmaceuticals. 18, 1222 (2025). https://doi.org/10.3390/ph18081222
46. Derdemezis, C.S., Kiortsis, D.N., Tsimihodimos, V., Petraki, M.P., Vezyraki, P., Elisaf, M.S., Tselepis, A.D.: Effect of Plant Polyphenols on Adipokine Secretion from Human SGBS Adipocytes. Biochem Res Int. 2011, 285618 (2011). https://doi.org/10.1155/2011/285618
47. Xu, Y., Bai, L., Yang, X., Huang, J., Wang, J., Wu, X., Shi, J.: Recent advances in anti-inflammation via AMPK activation. Heliyon. 10, e33670 (2024). https://doi.org/10.1016/j.heliyon.2024.e33670
48. Chen, S., Wang, X., Cheng, Y., Gao, H., Chen, X.: A Review of Classification, Biosynthesis, Biological Activities and Potential Applications of Flavonoids. Molecules. 28, 4982 (2023). https://doi.org/10.3390/molecules28134982
49. Gajender, Mazumder, A., Sharma, A., Azad, Md.A.K.: A Comprehensive Review of the Pharmacological Importance of Dietary Flavonoids as Hepatoprotective Agents. Evidence-Based Complementary and Alternative Medicine. 2023, 4139117 (2023). https://doi.org/10.1155/2023/4139117
50. Hu, L., Luo, Y., Yang, J., Cheng, C.: Botanical Flavonoids: Efficacy, Absorption, Metabolism and Advanced Pharmaceutical Technology for Improving Bioavailability. Molecules. 30, 1184 (2025). https://doi.org/10.3390/molecules30051184
51. Adhikari, B.: Roles of Alkaloids from Medicinal Plants in the Management of Diabetes Mellitus. Journal of Chemistry. 2021, 2691525 (2021). https://doi.org/10.1155/2021/2691525
52. Dey, P., Kundu, A., Kumar, A., Gupta, M., Lee, B.M., Bhakta, T., Dash, S., Kim, H.S.: Analysis of alkaloids (indole alkaloids, isoquinoline alkaloids, tropane alkaloids). Recent Advances in Natural Products Analysis. 505–567 (2020). https://doi.org/10.1016/B978-0-12-816455-6.00015-9
53. Kasimir, M., Wolbeck, A., Behrens, M., Humpf, H.-U.: Intestinal Metabolism of Selected Steroidal Glycoalkaloids in the Pig Cecum Model. ACS Omega. 8, 18266–18274 (2023). https://doi.org/10.1021/acsomega.3c01990
54. Shahidi, F., Saeid, A.: Bioactivity of Marine-Derived Peptides and Proteins: A Review. Mar Drugs. 23, 157 (2025). https://doi.org/10.3390/md23040157
55. Umoru, G.U., Atangwho, I.J., David-Oku, E., Uti, D.E., De Campos, O.C., Udeozor, P.A., Nfona, S.O., Lawal, B., Alum, E.U.: Modulation of Lipogenesis by Tetracarpidium conophorum Nuts via SREBP-1/ACCA-1/FASN Inhibition in Monosodium-Glutamate-Induced Obesity in Rats. Natural Product Communications. 20, 1934578X251344035 (2025). https://doi.org/10.1177/1934578X251344035
56. Umoru, G.U., Atangwho, I.J., David-Oku, E., Uti, D.E., Agwupuye, E.I., Obeten, U.N., Maitra, S., Subramaniyan, V., Wong, L.S., Aljarba, N.H., Kumarasamy, V.: Tetracarpidium conophorum nuts (African walnuts) up-regulated adiponectin and PPAR-γ expressions with reciprocal suppression of TNF-α gene in obesity. J Cell Mol Med. 28, e70086 (2024). https://doi.org/10.1111/jcmm.70086
57. Wood dos Santos, T., Cristina Pereira, Q., Teixeira, L., Gambero, A., A. Villena, J., Lima Ribeiro, M.: Effects of Polyphenols on Thermogenesis and Mitochondrial Biogenesis. Int J Mol Sci. 19, 2757 (2018). https://doi.org/10.3390/ijms19092757
58. Mthembu, S.X.H., Dludla, P.V., Ziqubu, K., Nyambuya, T.M., Kappo, A.P., Madoroba, E., Nyawo, T.A., Nkambule, B.B., Silvestri, S., Muller, C.J.F., Mazibuko-Mbeje, S.E.: The Potential Role of Polyphenols in Modulating Mitochondrial Bioenergetics within the Skeletal Muscle: A Systematic Review of Preclinical Models. Molecules. 26, 2791 (2021). https://doi.org/10.3390/molecules26092791
59. Barclay, R.D., Burd, N.A., Tyler, C., Tillin, N.A., Mackenzie, R.W.: The Role of the IGF-1 Signaling Cascade in Muscle Protein Synthesis and Anabolic Resistance in Aging Skeletal Muscle. Front Nutr. 6, 146 (2019). https://doi.org/10.3389/fnut.2019.00146
60. Chen, X., Ji, Y., Liu, R., Zhu, X., Wang, K., Yang, X., Liu, B., Gao, Z., Huang, Y., Shen, Y., Liu, H., Sun, H.: Mitochondrial dysfunction: roles in skeletal muscle atrophy. Journal of Translational Medicine. 21, 503 (2023). https://doi.org/10.1186/s12967-023-04369-z
61. Alum, E.U.: Unlocking the Secrets of Nature: Phytochemicals as Key Players in Longevity and Healthy Aging. Cell Biochem Biophys. (2025). https://doi.org/10.1007/s12013-025-01872-6
62. Vannuchi, N., Pisani, L.: PGC-1α Activation by Polyphenols: A Pathway to Thermogenesis. Mol Nutr Food Res. 69, e70072 (2025). https://doi.org/10.1002/mnfr.70072
63. Xu, Y., Bai, L., Yang, X., Huang, J., Wang, J., Wu, X., Shi, J.: Recent advances in anti-inflammation via AMPK activation. Heliyon. 10, e33670 (2024). https://doi.org/10.1016/j.heliyon.2024.e33670
64. Davì, F., Iaconis, A., Cordaro, M., Di Paola, R., Fusco, R.: Nutraceutical Strategies for Targeting Mitochondrial Dysfunction in Neurodegenerative Diseases. Foods. 14, 2193 (2025). https://doi.org/10.3390/foods14132193
65. Reguero, M., Gómez de Cedrón, M., Wagner, S., Reglero, G., Quintela, J.C., Ramírez de Molina, A.: Precision Nutrition to Activate Thermogenesis as a Complementary Approach to Target Obesity and

Associated-Metabolic-Disorders. Cancers (Basel). 13, 866 (2021). https://doi.org/10.3390/cancers13040866
66. Senesi, P., Luzi, L., Terruzzi, I.: Adipokines, Myokines, and Cardiokines: The Role of Nutritional Interventions. Int J Mol Sci. 21, 8372 (2020). https://doi.org/10.3390/ijms21218372
67. 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.: The Role of Adipokines in Health and Disease. Biomedicines. 11, 1290 (2023). https://doi.org/10.3390/biomedicines11051290
68. Alum, E.U.: Climate change and its impact on the bioactive compound profile of medicinal plants: implications for global health. Plant Signal Behav. 19, 2419683 (2024). https://doi.org/10.1080/15592324.2024.2419683
69. Würfel, M., Blüher, M., Stumvoll, M., Ebert, T., Kovacs, P., Tönjes, A., Breitfeld, J.: Adipokines as Clinically Relevant Therapeutic Targets in Obesity. Biomedicines. 11, 1427 (2023). https://doi.org/10.3390/biomedicines11051427
70. Alum, E.U., Ejemot-Nwadiaro, R.I., Betiang, P.A., Basajja, M., Uti, D.E.: Obesity and Climate Change: A Two-way Street with Global Health Implications. Obesity Medicine. 56, 100623 (2025). https://doi.org/10.1016/j.obmed.2025.100623
71. Fegade, B.S., Chaudhari, S.Y., Likhar, R.V., Bhole, R.P., Uttekar, P.S., Pathare, S.S., Maitra, S., Uti, D.E., Zaki, M.E.A., Alum, E.U.: Design, synthesis, molecular docking and molecular dynamics studies of some 3-methoxy flavone derivatives as an anti-breast cancer agent. Discov Onc. 16, 773 (2025). https://doi.org/10.1007/s12672-025-02491-6
72. Nwuruku, O.A., Ugwu, O.P.-C., Uti, D.E., Edwin, N.: Harnessing nature: plant-derived nanocarriers for targeted drug delivery in cancer therapy. Phytomedicine Plus. 5, 100828 (2025). https://doi.org/10.1016/j.phyplu.2025.100828

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