https://rijournals.com/scientific-and-experimental-sciences/

RESEARCH INVENTION JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES 5(2):68-75, 2025

©RIJSES Publications ONLINE ISSN: 1115-618X

PRINT ISSN: 1597-2917

https://doi.org/10.59298/RIJSES/2025/526875

The Endocrine-Modulating Effects of Phytochemicals in Obesity and Diabetes: Targeting Leptin, Adiponectin, and Insulin Resistance

Kibibi Wairimu H.

School of Natural and Applied Sciences Kampala International University Uganda

ABSTRACT

Obesity and diabetes are globally prevalent metabolic disorders, leading to significant morbidity and mortality. The pathophysiology of these conditions is often driven by dysregulated endocrine signaling pathways, including the dysfunction of adipokines such as leptin and adiponectin, as well as insulin resistance. Recent advances have demonstrated that plant-derived compounds, also known as phytochemicals, possess potential endocrine-modulating properties that can restore balance to these disrupted metabolic processes. This review aims to explore the regulatory effects of phytochemicals on key adipokines and insulin signaling pathways, with a focus on leptin, adiponectin, and insulin resistance. Various phytochemicals, including polyphenols, flavonoids, terpenoids, alkaloids, and saponins, have been shown to influence these pathways through mechanisms such as anti-inflammatory activity, antioxidant effects, and modulation of gene expression. The review also highlights the mechanisms through which specific phytochemicals exert their beneficial effects, including their ability to promote insulin sensitivity, reduce leptin resistance, and enhance adiponectin levels. By examining both preclinical and clinical studies, this review provides a comprehensive overview of the potential for phytochemicals to serve as therapeutic agents in managing obesity and diabetes. Further research is needed to establish the clinical efficacy and safety of these compounds for metabolic health.

Keywords: Phytochemicals, obesity, diabetes, endocrine modulation, leptin, adiponectin, insulin resistance, adipokines, metabolic dysfunction

INTRODUCTION

Obesity and diabetes are two of the most prevalent and concerning health issues of the 21st century, with both conditions often coexisting in individuals[1–5]. These metabolic disorders not only contribute significantly to the global health burden but also serve as major risk factors for a wide range of comorbidities, including cardiovascular diseases, metabolic syndrome, and even certain types of cancer[6, 7]. Central to the pathophysiology of obesity and diabetes is the dysfunction of key endocrine signaling pathways that regulate physiological processes such as energy balance, glucose metabolism, and inflammation[8–10]. Among these, adipokines, such as leptin, adiponectin, and insulin, play critical roles in maintaining metabolic homeostasis. In individuals with obesity and type 2 diabetes, the dysregulation of these pathways exacerbates disease progression, leading to a vicious cycle of impaired metabolic functions and worsening health outcomes[11, 12]. Adipokines are bioactive molecules secreted by adipose tissue, and they regulate various physiological processes, including appetite regulation, insulin sensitivity, and energy metabolism[13]. Leptin, the most well-known adipokine, is primarily involved in energy homeostasis and appetite regulation[14]. It signals the brain to reduce food intake and increase energy expenditure when fat stores are sufficient. However, in individuals with obesity, leptin resistance can develop, wherein the body fails to respond to leptin signals despite elevated leptin levels[15]. This resistance contributes to hyperphagia (increased hunger) and reduced energy expenditure, thereby promoting further weight gain and metabolic dysfunction. Adiponectin, another key adipokine, has anti-inflammatory and insulin-sensitizing effects. Lower levels of adiponectin are associated with obesity, insulin resistance, and an increased risk of cardiovascular disease[16, 17]. Insulin, the hormone responsible for regulating blood glucose levels, plays an equally pivotal role in the development of type 2 diabetes. Insulin resistance, a hallmark of type 2 diabetes, occurs when the body's cells become less responsive to insulin, leading to higher blood glucose levels and compensatory insulin production by the pancreas[18].

The interplay between these hormones and their dysregulation is crucial in the development of obesity and diabetes[19]. Disruptions in adipokine signaling, especially leptin and adiponectin, contribute to the onset and progression of insulin resistance, which is the primary feature of type 2 diabetes. The failure of insulin to effectively regulate glucose metabolism leads to chronically elevated blood glucose levels, causing further complications such as diabetic retinopathy, nephropathy, and neuropathy[20]. Moreover, the inflammatory environment created by dysfunctional adipokines, particularly leptin, amplifies the risk of cardiovascular diseases and other complications associated with obesity and diabetes. Phytochemicals, naturally occurring compounds in plants, have recently garnered significant interest for their potential to modulate these endocrine pathways and offer a therapeutic approach to managing obesity and diabetes[21]. Numerous studies have highlighted the ability of specific phytochemicals to influence the secretion and activity of adipokines, thereby improving insulin sensitivity and reducing the complications associated with metabolic disorders. For example, certain flavonoids, polyphenols, and alkaloids have been shown to increase adiponectin levels, thereby enhancing insulin sensitivity and exerting anti-inflammatory effects[10]. Additionally, several plant-based compounds have demonstrated the ability to improve leptin sensitivity, potentially reversing leptin resistance and helping to regulate appetite and energy balance. In particular, phytochemicals found in common foods such as curcumin (from turmeric), resveratrol (from grapes), and catechins (from green tea) have been shown to exert beneficial effects on metabolic health. These compounds work by modulating key signaling pathways involved in adipokine secretion, including the AMP-activated protein kinase (AMPK) pathway, the peroxisome proliferator-activated receptor gamma (PPAR-γ) pathway, and the sirtuin pathway[4, 10]. By influencing these pathways, phytochemicals help to restore the balance of adipokines, improving glucose metabolism, reducing inflammation, and enhancing insulin sensitivity. This review aims to critically examine the current evidence on the endocrine-modulating effects of phytochemicals, focusing on their interactions with leptin, adiponectin, and insulin resistance. We will explore the molecular mechanisms by which these compounds influence adipokine signaling and their potential therapeutic applications for managing obesity and diabetes. Given the growing interest in plant-based therapies for metabolic disorders, phytochemicals may offer a promising avenue for future research and therapeutic development in the fight against obesity and type 2 diabetes. Further clinical studies and trials are necessary to confirm the efficacy and safety of these natural compounds and to establish their role in clinical practice.

Leptin and Obesity: The Role of Phytochemicals

Leptin, a hormone primarily secreted by adipocytes (fat cells), plays a crucial role in regulating energy balance and body weight[22]. It communicates with the hypothalamus in the brain to signal satiety, decrease food intake, and promote energy expenditure[22]. When body fat stores increase, leptin levels rise, signaling the brain to reduce appetite and enhance energy use. However, in obesity, a phenomenon known as leptin resistance can develop. In this condition, the brain becomes less responsive to leptin's signals, despite elevated levels of the hormone[23]. This impaired response to leptin contributes to an increased appetite, reduced energy expenditure, and a tendency to gain more weight, thus exacerbating obesity. Leptin resistance is considered one of the key drivers of obesity and related metabolic disorders, including insulin resistance, hypertension, and dyslipidemia[24, 25]. It is largely caused by a combination of factors, including chronic inflammation, oxidative stress, and alterations in the signaling pathways that mediate leptin's effects. Given the central role leptin resistance plays in the pathophysiology of obesity, strategies to restore leptin sensitivity have garnered considerable interest in the scientific community[26].

One promising approach to address leptin resistance is the use of phytochemicals, which are bioactive compounds found in plants. Many phytochemicals have been shown to influence various aspects of leptin signaling, offering potential therapeutic benefits for obesity and related metabolic disorders[27]. Polyphenols, a group of naturally occurring compounds found in fruits, vegetables, tea, and wine, have received significant attention due to their ability to modulate leptin sensitivity. Resveratrol, a polyphenol found in grapes, red wine, and some berries, is one such compound that has demonstrated the ability to enhance leptin sensitivity[28, 29]. Studies have shown that resveratrol reduces inflammation and oxidative stress, two major contributors to leptin resistance. Chronic low-grade inflammation is often present in obesity and disrupts normal leptin signaling[10]. Resveratrol has anti-inflammatory and antioxidant properties that can mitigate these conditions, thereby restoring leptin's effectiveness in regulating appetite and energy expenditure. In addition, resveratrol has been found to modulate various signaling pathways that affect leptin's actions, further supporting its potential as a therapeutic agent for obesity.

Another promising compound is curcumin, the active ingredient in turmeric. Curcumin has been widely studied for its anti-inflammatory, antioxidant, and anti-obesity properties. It has been shown to influence leptin expression and improve leptin sensitivity[30]. Curcumin modulates several molecular pathways, including those involved in inflammation and oxidative stress, which are known to impair leptin signaling in obese individuals. By reducing the pro-inflammatory cytokines and reactive oxygen species (ROS) that contribute to leptin resistance, curcumin can help restore normal leptin function, promoting weight loss and improved metabolic health[31]. Additionally, other phytochemicals such as epigallocatechin gallate (EGCG) from green tea, quercetin from apples and onions, and catechins found in various fruits, have all shown potential in modulating leptin signaling and promoting weight management. These compounds exert their effects through antioxidant, anti-inflammatory, and gene expression-modulating mechanisms, which could provide effective complementary treatments for obesity[32]. In sum, leptin resistance is a central issue in the development of obesity, and phytochemicals represent a promising avenue for restoring leptin sensitivity. Compounds like resveratrol and curcumin have demonstrated significant potential in enhancing leptin signaling by reducing inflammation and oxidative stress, addressing key factors contributing to leptin resistance[32]. As research continues, these natural compounds may offer valuable therapeutic options for individuals struggling with obesity and its related metabolic disorders.

Adiponectin and Metabolic Health: The Therapeutic Potential of Phytochemicals

Adiponectin is a crucial adipokine that plays an essential role in regulating glucose and lipid metabolism. It is secreted primarily by adipocytes (fat cells) and is involved in maintaining metabolic homeostasis by enhancing insulin sensitivity, promoting fatty acid oxidation, and reducing inflammation[33]. Unlike leptin, which is typically elevated in individuals with obesity, adiponectin levels are usually reduced in individuals with obesity and type 2 diabetes. This reduction in adiponectin is believed to contribute to the development of insulin resistance[34], dyslipidemia (abnormal lipid profiles), and other metabolic disorders. As a result, increasing adiponectin levels has been proposed as a potential therapeutic strategy for improving metabolic health and managing conditions like obesity, type 2 diabetes, and cardiovascular diseases. One of the key features of adiponectin is its ability to improve insulin sensitivity[34]. It enhances the action of insulin in peripheral tissues, such as muscle and liver, and reduces hepatic glucose production. Moreover, adiponectin helps regulate lipid metabolism by increasing the breakdown of fatty acids and preventing the accumulation of triglycerides in tissues such as the liver and skeletal muscles[35]. These actions of adiponectin help reduce the risk of metabolic diseases, including type 2 diabetes and cardiovascular disease. However, in obesity and type 2 diabetes, adiponectin levels are typically low, leading to impaired glucose and lipid metabolism. The reduction in adiponectin secretion in these conditions is often associated with the presence of chronic low-grade inflammation, oxidative stress, and increased fat accumulation in visceral fat depots[35]. These factors contribute to the development of insulin resistance, which is a hallmark of metabolic diseases. To address this issue, researchers have explored various approaches to increase adiponectin levels. One promising avenue is the use of phytochemicals, which are naturally occurring compounds found in plants. Numerous studies have examined the effects of phytochemicals on adiponectin expression, as they are believed to have the potential to enhance adiponectin secretion and improve metabolic health[36–38].

Epigallocatechin gallate (EGCG), a major polyphenol found in green tea, is one such phytochemical that has shown promising effects on adiponectin levels[39, 40]. EGCG activates AMP-activated protein kinase (AMPK), a key regulator of energy metabolism. AMPK activation leads to the phosphorylation of various downstream targets that promote the breakdown of fatty acids and improve insulin sensitivity. As a result, EGCG has been shown to increase adiponectin secretion and improve metabolic parameters such as blood glucose levels and lipid profiles in both animal and human studies[41]. Additionally, EGCG has antioxidant and anti-inflammatory properties, which further contribute to its beneficial effects on metabolic health. Another phytochemical with potential adiponectin-enhancing effects is berberine, an alkaloid found in various plants such as *Berberis* species[42]. Berberine has been extensively studied for its beneficial effects on metabolic health, particularly in relation to insulin resistance and dyslipidemia. It has been shown to increase adiponectin levels by activating AMPK, similar to EGCG. In animal models, berberine supplementation has led to improvements in insulin sensitivity, lipid profiles, and body weight[43]. Berberine's effects on adiponectin are thought to be partly responsible for its ability to improve metabolic parameters, making it a promising candidate for managing metabolic disorders such as type 2 diabetes and obesity[43]. Summarily, adiponectin plays a central role in regulating glucose and lipid metabolism, and its reduced levels in obesity and type 2 diabetes contribute to insulin resistance and dyslipidemia. Increasing adiponectin levels is a promising therapeutic strategy for improving metabolic health. Phytochemicals like EGCG from green tea and berberine from plants have shown potential in enhancing adiponectin secretion and improving metabolic parameters. Further research into the mechanisms by which these phytochemicals regulate adiponectin levels could lead to the development of novel treatments for metabolic diseases.

Insulin Resistance and Phytochemical Interventions

Insulin resistance, a condition where the body's cells become less responsive to insulin, is a key feature of obesity and type 2 diabetes[44, 45]. It leads to impaired glucose metabolism, elevated blood glucose levels, and an increased risk of developing metabolic disorders. As a result, managing insulin resistance is a crucial therapeutic goal for individuals with these conditions. While conventional treatments like insulin sensitizers and lifestyle

modifications remain foundational, the potential of phytochemicals in improving insulin sensitivity has garnered considerable attention in recent years [46,47,48].
Phytochemicals, natural bioactive compounds found in plants, have shown promise in ameliorating insulin resistance through various mechanisms[49,50,51,52,53]. These include the activation of AMP-activated protein kinase (AMPK), a key regulator of cellular energy metabolism, inhibition of pro-inflammatory pathways, and modulation of gene expression related to glucose and lipid metabolism. One of the most well-studied phytochemicals is berberine, an alkaloid derived from plants like *Berberis* species [54,55,56,57,58,59,60]. Berberine has been shown to enhance insulin sensitivity by regulating metabolic enzymes involved in glucose uptake, lipid metabolism, and energy expenditure. It has also been found to improve mitochondrial function and reduce the accumulation of fat in tissues, both of which contribute to insulin resistance. Curcumin, the active compound in turmeric, is another promising phytochemical. Its anti-inflammatory properties help reduce the chronic low-grade inflammation that often accompanies insulin resistance. Curcumin has also been shown to activate AMPK and modulate signaling pathways that improve glucose uptake and insulin sensitivity [61,62,63,64,65,66,67,68]. Additionally, flavonoids such as quercetin have demonstrated insulin-sensitizing effects through their antioxidant and anti-inflammatory properties, which help reduce oxidative stress and inflammation, both of which exacerbate insulin resistance [69,70,71,72,73,74,75]. Overall, the emerging evidence highlights the potential of phytochemicals like berberine, curcumin, and flavonoids as natural adjuncts to conventional therapies for managing insulin resistance and preventing the progression of obesity and type 2 diabetes.

Mechanisms of Action

The mechanisms through which phytochemicals regulate leptin, adiponectin, and insulin resistance are multifaceted, involving various biochemical pathways and cellular processes[27, 51]. Phytochemicals are bioactive compounds found in plants that can influence metabolic functions through the modulation of inflammation, oxidative stress, and cellular signaling networks. Many of these compounds target specific pathways to improve insulin sensitivity and adipokine production, thus contributing to the regulation of body weight and metabolic health. A key mechanism through which phytochemicals exert their effects is the activation of AMP-activated protein kinase (AMPK). AMPK is a critical enzyme that serves as an energy sensor within the cell, regulating glucose uptake, fatty acid oxidation, and mitochondrial biogenesis. The activation of AMPK enhances insulin sensitivity and promotes the utilization of stored fat, contributing to a reduction in insulin resistance[52, 53]. By stimulating AMPK, phytochemicals can help correct metabolic imbalances and improve glucose homeostasis. Moreover, many phytochemicals help mitigate the inflammatory processes that drive insulin resistance and leptin resistance. Pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), are major contributors to the development of insulin resistance, and their inhibition is an important therapeutic strategy. Phytochemicals like flavonoids, polyphenols, and alkaloids can reduce the levels of these cytokines, thus improving insulin sensitivity and restoring normal leptin signaling. In addition to their anti-inflammatory effects, certain phytochemicals also influence key transcription factors involved in lipid metabolism and insulin sensitivity. For instance, the peroxisome proliferator-activated receptor gamma (PPAR-γ) and sterol regulatory element-binding protein 1c (SREBP-1c) are pivotal in regulating adipogenesis, lipid accumulation, and insulin action[54, 55]. Phytochemicals modulate the expression of these transcription factors, enhancing lipid metabolism and improving the overall insulin response. Through these combined mechanisms, phytochemicals offer promising therapeutic potential for managing insulin resistance, obesity, and related metabolic disorders.

Clinical Evidence and Future Directions

While numerous preclinical studies have demonstrated the potential of phytochemicals in modulating leptin, adiponectin, and insulin resistance, clinical evidence remains limited. Some clinical trials have reported positive outcomes, such as improvements in insulin sensitivity and adiponectin levels following the consumption of phytochemical-rich diets or supplements[56, 57]. However, the results are often inconsistent, and more rigorous, large-scale studies are needed to confirm the clinical efficacy and safety of these compounds. Future research should focus on identifying the most effective phytochemicals, determining optimal dosages, and understanding their interactions with other metabolic pathways. Additionally, investigating the synergistic effects of combining different phytochemicals or using them in conjunction with existing pharmacological therapies could provide new avenues for treating obesity and diabetes.

CONCLUSION

Phytochemicals offer a promising approach to modulating endocrine signaling pathways involved in obesity and diabetes. Through their effects on leptin sensitivity, adiponectin levels, and insulin resistance, these plant-derived compounds have the potential to alleviate the metabolic dysfunctions associated with these diseases. Although further research is needed to establish their clinical applicability, phytochemicals may one day serve as valuable adjuncts or alternatives to conventional therapies for managing obesity and diabetes.

REFERENCES

1. Alahmari, L.A.: Dietary fiber influence on overall health, with an emphasis on CVD, diabetes, obesity, colon cancer, and inflammation. Front. Nutr. 11, (2024). https://doi.org/10.3389/fnut.2024.1510564
2. 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
3. Alum, E.U., Krishnamoorthy, R., Gatasheh, M.K., Subbarayan, S., Vijayalakshmi, P., Uti, D.E.: Protective Role of Jimson Weed in Mitigating Dyslipidemia, Cardiovascular, and Renal Dysfunction in Diabetic Rat Models: In Vivo and in Silico Evidence. Nat. Prod. Commun. 19, 1934578X241299279 (2024). https://doi.org/10.1177/1934578X241299279
4. Uti, D.E., Atangwho, I.J., Eyong, E.U., Umoru, G.U., Egbung, G.E., Rotimi, S.O., Nna, V.U.: African walnuts (Tetracarpidium conophorum) modulate hepatic lipid accumulation in obesity via reciprocal actions on HMG-CoA reductase and paraoxonase. Endocr. Metab. Immune Disord.-Drug Targets Former. Curr. Drug Targets-Immune Endocr. Metab. Disord. 20, 365–379 (2020)
5. 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. Obes. Med. 54, 100585 (2025). https://doi.org/10.1016/j.obmed.2025.100585
6. Alahmari, L.A.: Dietary fiber influence on overall health, with an emphasis on CVD, diabetes, obesity, colon cancer, and inflammation. Front. Nutr. 11, 1510564 (2024). https://doi.org/10.3389/fnut.2024.1510564
7. Boccellino, M., D'Angelo, S.: Anti-Obesity Effects of Polyphenol Intake: Current Status and Future Possibilities. Int. J. Mol. Sci. 21, 5642 (2020). https://doi.org/10.3390/ijms21165642
8. Reynolds, A., Mitri, J.: Dietary Advice For Individuals with Diabetes. In: Feingold, K.R., Ahmed, S.F., Anawalt, B., Blackman, M.R., Boyce, A., Chrousos, G., Corpas, E., de Herder, W.W., Dhatariya, K., Dungan, K., Hofland, J., Kalra, S., Kaltsas, G., Kapoor, N., Koch, C., Kopp, P., Korbonits, M., Kovacs, C.S., Kuohung, W., Laferrère, B., Levy, M., McGee, E.A., McLachlan, R., Muzumdar, R., Purnell, J., Rey, R., Sahay, R., Shah, A.S., Singer, F., Sperling, M.A., Stratakis, C.A., Trence, D.L., and Wilson, D.P. (eds.) Endotext. MDText.com, Inc., South Dartmouth (MA) (2000)
9. Ugwu, O.P.-C., Alum, E.U., Okon, M.B., Aja, P.M., Obeagu, E.I., Onyeneke, E.C.: Ethanol root extract and fractions of Sphenocentrum jollyanum abrogate hyperglycaemia and low body weight in streptozotocin-induced diabetic Wistar albino rats. RPS Pharm. Pharmacol. Rep. 2, rqad010 (2023). https://doi.org/10.1093/rpsppr/rqad010
10. 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. Nat. Prod. Commun. 20, 1934578X251323393 (2025). https://doi.org/10.1177/1934578X251323393
11. Aja, P.M., Chiadikaobi, C.D., Agu, P.C., Ale, B.A., Ani, O.G., Ekpono, E.U., Ogwoni, H.A., Awoke, J.N., Ogbu, P.N., Aja, L., Nwite, F.E., Ukachi, O.U., Orji, O.U., Nweke, P.C., Egwu, C.O., Ekpono, E.U., Ewa, G.O., Igwenyi, I.O., Tusubira, D., Offor, C.E., Maduagwuna, E.K., Alum, E.U., Uti, D.E., Njoku, A., Atoki, V.A., Awuchi, C.G.: Cucumeropsis mannii seed oil ameliorates Bisphenol-A-induced adipokines dysfunctions and dyslipidemia. Food Sci. Nutr. 11, 2642–2653 (2023). https://doi.org/10.1002/fsn3.3271
12. Roy, P.K., Islam, J., Lalhlenmawia, H.: Prospects of potential adipokines as therapeutic agents in obesity-linked atherogenic dyslipidemia and insulin resistance. Egypt. Heart J. 75, 24 (2023). https://doi.org/10.1186/s43044-023-00352-7
13. Liu, Y., Qian, S.-W., Tang, Y., Tang, Q.-Q.: The secretory function of adipose tissues in metabolic regulation. Life Metab. 3, loae003 (2024). https://doi.org/10.1093/lifemeta/loae003
14. Ahima, R.S., Park, H.-K.: Adipokines and Metabolism. In: Ahima, R.S. (ed.) Metabolic Syndrome: A Comprehensive Textbook. pp. 1–22. Springer International Publishing, Cham (2020)
15. Freitas Lima, L.C., Braga, V. de A., do Socorro de França Silva, M., Cruz, J. de C., Sousa Santos, S.H., de Oliveira Monteiro, M.M., Balarini, C. de M.: Adipokines, diabetes and atherosclerosis: an inflammatory association. Front. Physiol. 6, (2015). https://doi.org/10.3389/fphys.2015.00304
16. 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
17. Luo, L., Liu, M.: Adiponectin: friend or foe in obesity and inflammation. Med. Rev. 2, 349–362. https://doi.org/10.1515/mr-2022-0002
18. Alum, E.U., Umoru, G.U., Uti, D.E., Aja, P.M., Ugwu, O.P., Orji, O.U., Nwali, B.U., Ezeani, N.N., Edwin, N., Orinya, F.O.: Hepato-Protective Effect Of Ethanol Leaf Extract Of Datura Stramonium In Alloxan-Induced Diabetic Albino Rats. J. Chem. Soc. Niger. 47, (2022). https://doi.org/10.46602/jcsn.v47i5.819

19. Ylli, D., Sidhu, S., Parikh, T., Burman, K.D.: Endocrine Changes in Obesity. In: Feingold, K.R., Ahmed, S.F., Anawalt, B., Blackman, M.R., Boyce, A., Chrousos, G., Corpas, E., de Herder, W.W., Dhatariya, K., Dungan, K., Hofland, J., Kalra, S., Kaltsas, G., Kapoor, N., Koch, C., Kopp, P., Korbonits, M., Kovacs, C.S., Kuohung, W., Laferrère, B., Levy, M., McGee, E.A., McLachlan, R., Muzumdar, R., Purnell, J., Rey, R., Sahay, R., Shah, A.S., Singer, F., Sperling, M.A., Stratakis, C.A., Trence, D.L., and Wilson, D.P. (eds.) Endotext. MDText.com, Inc., South Dartmouth (MA) (2000)
20. Cao, H.: Adipocytokines in Obesity and Metabolic Disease. J. Endocrinol. 220, T47–T59 (2014). https://doi.org/10.1530/JOE-13-0339
21. Dilworth, L., Facey, A., Omoruyi, F.: Diabetes Mellitus and Its Metabolic Complications: The Role of Adipose Tissues. Int. J. Mol. Sci. 22, 7644 (2021). https://doi.org/10.3390/ijms22147644
22. Stefanakis, K., Upadhyay, J., Ramirez-Cisneros, A., Patel, N., Sahai, A., Mantzoros, C.S.: Leptin physiology and pathophysiology in energy homeostasis, immune function, neuroendocrine regulation and bone health. Metabolism. 161, 156056 (2024). https://doi.org/10.1016/j.metabol.2024.156056
23. Kumar, V., Singh, D.D., Lakhawat, S.S., Yasmeen, N., Pandey, A., Singla, R.K.: Biogenic Phytochemicals Modulating Obesity: From Molecular Mechanism to Preventive and Therapeutic Approaches. Evid.-Based Complement. Altern. Med. ECAM. 2022, 6852276 (2022). https://doi.org/10.1155/2022/6852276
24. Obradovic, M., Sudar-Milovanovic, E., Soskic, S., Essack, M., Arya, S., Stewart, A.J., Gojobori, T., Isenovic, E.R.: Leptin and Obesity: Role and Clinical Implication. Front. Endocrinol. 12, 585887 (2021). https://doi.org/10.3389/fendo.2021.585887
25. Vilariño-García, T., Polonio-González, M.L., Pérez-Pérez, A., Ribalta, J., Arrieta, F., Aguilar, M., Obaya, J.C., Gimeno-Orna, J.A., Iglesias, P., Navarro, J., Durán, S., Pedro-Botet, J., Sánchez-Margalet, V.: Role of Leptin in Obesity, Cardiovascular Disease, and Type 2 Diabetes. Int. J. Mol. Sci. 25, 2338 (2024). https://doi.org/10.3390/ijms25042338
26. Kotsis, V., Antza, C., Doundoulakis, G., Stabouli, S.: Obesity, Hypertension, and Dyslipidemia. In: Sbraccia, P. and Finer, N. (eds.) Obesity: Pathogenesis, Diagnosis, and Treatment. pp. 227–241. Springer International Publishing, Cham (2019)
27. Rao, P.P.: Phytochemicals in Obesity Management: Mechanisms and Clinical Perspectives. Curr. Nutr. Rep. 14, 17 (2025). https://doi.org/10.1007/s13668-025-00611-w
28. Li, Z., Zhang, Z., Ke, L., Sun, Y., Li, W., Feng, X., Zhu, W., Chen, S.: Resveratrol promotes white adipocytes browning and improves metabolic disorders in Sirt1-dependent manner in mice. FASEB J. Off. Publ. Fed. Am. Soc. Exp. Biol. 34, 4527–4539 (2020). https://doi.org/10.1096/fj.201902222R
29. Zhu, X., Wu, C., Qiu, S., Yuan, X., Li, L.: Effects of resveratrol on glucose control and insulin sensitivity in subjects with type 2 diabetes: systematic review and meta-analysis. Nutr. Metab. 14, 60 (2017). https://doi.org/10.1186/s12986-017-0217-z
30. Islam, Md.R., Rauf, A., Akash, S., Trisha, S.I., Nasim, A.H., Akter, M., Dhar, P.S., Ogaly, H.A., Hemeg, H.A., Wilairatana, P., Thiruvengadam, M.: Targeted therapies of curcumin focus on its therapeutic benefits in cancers and human health: Molecular signaling pathway-based approaches and future perspectives. Biomed. Pharmacother. 170, 116034 (2024). https://doi.org/10.1016/j.biopha.2023.116034
31. Sharifi-Rad, J., Rayess, Y.E., Rizk, A.A., Sadaka, C., Zgheib, R., Zam, W., Sestito, S., Rapposelli, S., Neffe-Skocińska, K., Zielińska, D., Salehi, B., Setzer, W.N., Dosoky, N.S., Taheri, Y., El Beyrouthy, M., Martorell, M., Ostrander, E.A., Suleria, H.A.R., Cho, W.C., Maroyi, A., Martins, N.: Turmeric and Its Major Compound Curcumin on Health: Bioactive Effects and Safety Profiles for Food, Pharmaceutical, Biotechnological and Medicinal Applications. Front. Pharmacol. 11, 01021 (2020). https://doi.org/10.3389/fphar.2020.01021
32. Singh, B.N., Shankar, S., Srivastava, R.K.: Green tea catechin, epigallocatechin-3-gallate (EGCG): mechanisms, perspectives and clinical applications. Biochem. Pharmacol. 82, 1807–1821 (2011). https://doi.org/10.1016/j.bcp.2011.07.093
33. Nguyen, T.M.D.: Adiponectin: Role in Physiology and Pathophysiology. Int. J. Prev. Med. 11, 136 (2020). https://doi.org/10.4103/ijpvm.IJPVM_193_20
34. Wang, X., Zhang ,Siwen, and Li, Z.: Adipokines in glucose and lipid metabolism. Adipocyte. 12, 2202976 (2023). https://doi.org/10.1080/21623945.2023.2202976
35. Mallick, R., Basak, S., Das, R.K., Banerjee, A., Paul, S., Pathak, S., Duttaroy, A.K.: Fatty Acids and their Proteins in Adipose Tissue Inflammation. Cell Biochem. Biophys. 82, 35–51 (2024). https://doi.org/10.1007/s12013-023-01185-6
36. Liu, Y., Vu, V., Sweeney, G.: Examining the Potential of Developing and Implementing Use of Adiponectin-Targeted Therapeutics for Metabolic and Cardiovascular Diseases. Front. Endocrinol. 10, 842 (2019). https://doi.org/10.3389/fendo.2019.00842
37. Shabalala, S.C., Dludla, P.V., Mabasa, L., Kappo, A.P., Basson, A.K., Pheiffer, C., Johnson, R.: The effect of adiponectin in the pathogenesis of non-alcoholic fatty liver disease (NAFLD) and the potential role of

polyphenols in the modulation of adiponectin signaling. Biomed. Pharmacother. 131, 110785 (2020). https://doi.org/10.1016/j.biopha.2020.110785
38. Achari, A.E., Jain, S.K.: Adiponectin, a Therapeutic Target for Obesity, Diabetes, and Endothelial Dysfunction. Int. J. Mol. Sci. 18, 1321 (2017). https://doi.org/10.3390/ijms18061321
39. James, A., Wang, K., Wang, Y.: Therapeutic Activity of Green Tea Epigallocatechin-3-Gallate on Metabolic Diseases and Non-Alcoholic Fatty Liver Diseases: The Current Updates. Nutrients. 15, 3022 (2023). https://doi.org/10.3390/nu15133022
40. Legeay, S., Rodier, M., Fillon, L., Faure, S., Clere, N.: Epigallocatechin Gallate: A Review of Its Beneficial Properties to Prevent Metabolic Syndrome. Nutrients. 7, 5443–5468 (2015). https://doi.org/10.3390/nu7075230
41. Mokra, D., Joskova, M., Mokry, J.: Therapeutic Effects of Green Tea Polyphenol (–)-Epigallocatechin-3-Gallate (EGCG) in Relation to Molecular Pathways Controlling Inflammation, Oxidative Stress, and Apoptosis. Int. J. Mol. Sci. 24, 340 (2022). https://doi.org/10.3390/ijms24010340
42. Neag, M.A., Mocan, A., Echeverría, J., Pop, R.M., Bocsan, C.I., Crişan, G., Buzoianu, A.D.: Berberine: Botanical Occurrence, Traditional Uses, Extraction Methods, and Relevance in Cardiovascular, Metabolic, Hepatic, and Renal Disorders. Front. Pharmacol. 9, 557 (2018). https://doi.org/10.3389/fphar.2018.00557
43. Cao, C., Su, M.: Effects of berberine on glucose-lipid metabolism, inflammatory factors and insulin resistance in patients with metabolic syndrome. Exp. Ther. Med. 17, 3009–3014 (2019). https://doi.org/10.3892/etm.2019.7295
44. Alum, E., P.C., U., Obeagu, E., Extension, K.P.: Beyond Pregnancy: Understanding the Long-Term Implications of Gestational Diabetes Mellitus. INOSR Sci. Res. 11, 63–71 (2024). https://doi.org/10.59298/INOSRSR/2024/1.1.16371
45. Alum, E., P.C., U., Obeagu, E., Aja, P., Ugwu, C., Okon, M.: Nutritional Care In Diabetes Mellitus: A Comprehensive Guide. 11, 16–15 (2023). https://doi.org/10.58538/IJIAR/2057
46. Alam, S., Sarker, Md.M.R., Sultana, T.N., Chowdhury, Md.N.R., Rashid, M.A., Chaity, N.I., Zhao, C., Xiao, J., Hafez, E.E., Khan, S.A., Mohamed, I.N.: Antidiabetic Phytochemicals From Medicinal Plants: Prospective Candidates for New Drug Discovery and Development. Front. Endocrinol. 13, 800714 (2022). https://doi.org/10.3389/fendo.2022.800714
47. Hu, X., Zhang, Y., Xue, Y., Zhang, Z., Wang, J.: Berberine is a potential therapeutic agent for metabolic syndrome via brown adipose tissue activation and metabolism regulation. Am. J. Transl. Res. 10, 3322–3329 (2018)
48. Ai, X., Yu, P., Peng, L., Luo, L., Liu, J., Li, S., Lai, X., Luan, F., Meng, X.: Berberine: A Review of its Pharmacokinetics Properties and Therapeutic Potentials in Diverse Vascular Diseases. Front. Pharmacol. 12, (2021). https://doi.org/10.3389/fphar.2021.762654
49. Bertoncini-Silva, C., Vlad, A., Ricciarelli, R., Giacomo Fassini, P., Suen, V.M.M., Zingg, J.-M.: Enhancing the Bioavailability and Bioactivity of Curcumin for Disease Prevention and Treatment. Antioxidants. 13, 331 (2024). https://doi.org/10.3390/antiox13030331
50. Karthikeyan, A., Senthil, N., Min, T.: Nanocurcumin: A Promising Candidate for Therapeutic Applications. Front. Pharmacol. 11, (2020). https://doi.org/10.3389/fphar.2020.00487
51. Aqil, F., Munagala, R., Jeyabalan, J., Vadhanam, M.V.: Bioavailability of phytochemicals and its enhancement by drug delivery systems. Cancer Lett. 334, 133–141 (2013). https://doi.org/10.1016/j.canlet.2013.02.032
52. Piccialli, I., Tedeschi, V., Caputo, L., D'Errico, S., Ciccone, R., De Feo, V., Secondo, A., Pannaccione, A.: Exploring the Therapeutic Potential of Phytochemicals in Alzheimer's Disease: Focus on Polyphenols and Monoterpenes. Front. Pharmacol. 13, (2022). https://doi.org/10.3389/fphar.2022.876614
53. Sayem, A.S.M., Arya, A., Karimian, H., Krishnasamy, N., Ashok Hasamnis, A., Hossain, C.F.: Action of Phytochemicals on Insulin Signaling Pathways Accelerating Glucose Transporter (GLUT4) Protein Translocation. Molecules. 23, 258 (2018). https://doi.org/10.3390/molecules23020258
54. Enayati, A., Ghojoghnejad, M., Roufogalis, B.D., Maollem, S.A., Sahebkar, A.: Impact of Phytochemicals on PPAR Receptors: Implications for Disease Treatments. PPAR Res. 2022, 4714914 (2022). https://doi.org/10.1155/2022/4714914
55. Woonnoi, W., Suttithumsatid, W., Muneerungsee, N., Saetan, J., Tanasawet, S., Sukketsiri, W.: Sangyod rice extract inhibits adipocyte growth and differentiation via mTOR, Akt, and AMPK pathways. J. Funct. Foods. 111, 105913 (2023). https://doi.org/10.1016/j.jff.2023.105913
56. Begum, M., Choubey, M., Tirumalasetty, M.B., Arbee, S., Mohib, M.M., Wahiduzzaman, M., Mamun, M.A., Uddin, M.B., Mohiuddin, M.S.: Adiponectin: A Promising Target for the Treatment of Diabetes and Its Complications. Life. 13, 2213 (2023). https://doi.org/10.3390/life13112213

57. 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 Metab. 23, 770–784 (2016). https://doi.org/10.1016/j.cmet.2016.04.011
58. Orji OU, Ibiam UA, Aja PM, Ugwu P, Uraku AJ, Aloke C, Obasi OD, Nwali BU. Evaluation of the phytochemical and nutritional profiles of Cnidoscolus aconitifolius leaf collected in Abakaliki South East Nigeria. World J Med Sci. 2016;13(3):213-217.
59. Enechi OC, Okpe CC, Ibe GN, Omeje KO, Ugwu Okechukwu PC. Effect of Buchholzia coriacea methanol extract on haematological indices and liver function parameters in *Plasmodium berghei*-infected mice. Glob Veterinaria. 2016;16(1):57-66.
60. Alum EU, Uti DE, Ugwu Okechukwu PC, Alum BN. Toward a cure–Advancing HIV/AIDS treatment modalities beyond antiretroviral therapy: A review. Med. 2024;103(27):e38768.
61. Obeagu EI, Bot YS, Obeagu GU, Alum EU, Ugwu Okechukwu PC. Anaemia and risk factors in lactating mothers: A concern in Africa. Int J Innov Appl Res. 2024;11(2):15-17.
62. Alum EU, Ibiam UA, Ugwuja EI, Aja PM, Igwenyi IO, Offor CE, Orji UO, Ezeani NN, Ugwu OP, Aloke C, Egwu CO. Antioxidant effect of Buchholzia coriacea ethanol leaf extract and fractions on Freund's adjuvant-induced arthritis in albino rats: A comparative study. 2022;59(1):31-45.
63. Offor CE, Ugwu Okechukwu PC, Alum EU. Determination of ascorbic acid contents of fruits and vegetables. Int J Pharm Med Sci. 2015;5:1-3.
64. Amusa MO, Adepoju AO, Ugwu Okechukwu PC, Alum EU, Obeagu EI, Okon MB, Aja PM, Samson AOS. Effect of ethanol leaf extract of *Chromolaena odorata* on lipid profile of streptozotocin-induced diabetic Wistar albino rats. IAA J Biol Sci. 2024;10(1):109-117.
65. Amusa MO, Adepoju AO, Ugwu Okechukwu PC, Alum EU, Obeagu EI, Okon MB, Aja PM, Samson AOS. Effect of ethanol leaf extract of *Chromolaena odorata* on lipid profile of streptozotocin-induced diabetic Wistar albino rats. IAA J Biol Sci. 2024;10(1):109-117.
66. Enechi YS, Ugwu OC, Ugwu Okechukwu PC, Omeh K. Evaluation of the antinutrient levels of *Ceiba pentandra* leaves. IJRRPAS. 2013;3(3):394-400.
67. Ugwu Okechukwu PC, Nwodo OFC, Joshua EP, Odo CE, Ossai EC. Effect of ethanol leaf extract of *Moringa oleifera* on lipid profile of malaria-infected mice. Res J Pharm Biol Chem Sci. 2014;4(1):1324-1332.
68. Ugwu OPC, Alum EU, Uhama KC. Dual burden of diabetes mellitus and malaria: Exploring the role of phytochemicals and vitamins in disease management. Res Inven J Res Med Sci. 2024;3(2):38-49.
69. Alum EU, Ugwu Okechukwu PC, Aja PM, Obeagu EI, Inya JE, Onyeije AP, Agu E, Awuchi CG. Restorative effects of ethanolic leaf extract of *Datura stramonium* against methotrexate-induced hematological impairments. Cogent Food Agric. 2013;9(1):2258774.
70. Offor CE, Nwankwegu FC, Joshua EP, Ugwu Okechukwu PC. Acute toxicity investigation and anti-diarrhoeal effect of the chloroform-methanol extract of the leaves of *Persea americana*. Iran J Pharm Res. 2014;13(2):651-658. PMID: 25237361; PMCID: PMC4157041.
71. Afiukwa CA, Oko AO, Afiukwa JN, Ugwu Okechukwu PC, Ali FU, Ossai EC. Proximate and mineral element compositions of five edible wild grown mushroom species in Abakaliki, southeast Nigeria. Res J Pharm Biol Chem Sci. 2013;4:1056-1064.
72. Ugwu OP, Alum EU, Ugwu JN, Eze VH, Ugwu CN, Ogenyi FC, Okon MB. Harnessing technology for infectious disease response in conflict zones: Challenges, innovations, and policy implications. Med. 2024;103(28):e38834.
73. Obeagu EI, Ugwu OPC, Alum EU. Poor glycaemic control among diabetic patients; A review on associated factors. Newport Int J Res Med Sci (NIJRMS). 2023;3(1):30-33.
74. Nwaka AC, Ikechi-Agba MC, Okechukwu PU, Igwenyi IO, Agbafor KN, Orji OU, Ezugwu AL. The effects of ethanol extracts of *Jatropha curcas* on some hematological parameters of chloroform intoxicated rats. Am-Eur J Sci Res. 2015;10(1):45-49.
75. Ezeani NN, Ibiam UA, Orji OU, Igwenyi IO, Aloke C, Alum E, Aja PM, Ugwu OP. Effects of aqueous and ethanol root extracts of *Olax subscopioidea* on inflammatory parameters in complete Freund's adjuvant-collagen type II induced arthritic albino rats. Pharmacogn J. 2019;11(1)

CITE AS: Kibibi Wairimu H. (2025). The Endocrine-Modulating Effects of Phytochemicals in Obesity and Diabetes: Targeting Leptin, Adiponectin, and Insulin Resistance. RESEARCH INVENTION JOURNAL OF SCIENTIFIC AND EXPERIMENTAL SCIENCES 5(2):68-75. https://doi.org/10.59298/RIJSES/2025/526875