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# Phytochemicals as Dual Modulators of Gut Microbiota and Metabolic Disorders: Potential in Obesity-Linked Diabetes

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## ABSTRACT

Obesity and type 2 diabetes mellitus (T2DM) are complex metabolic disorders with a strong interplay between gut microbiota and host metabolism. Emerging evidence suggests that phytochemicals bioactive compounds derived from plants can modulate gut microbiota composition and function, thereby influencing metabolic health. This review explores the potential of phytochemicals as dual modulators that regulate gut microbiota and mitigate obesity-induced insulin resistance. Key phytochemicals, including polyphenols, flavonoids, alkaloids, and terpenoids, are examined for their ability to enhance gut microbial diversity, promote beneficial bacterial growth, and suppress pro-inflammatory pathways implicated in metabolic dysfunction. Furthermore, the mechanisms through which these compounds improve glucose homeostasis and lipid metabolism are discussed. The therapeutic implications of integrating phytochemicals into dietary and pharmaceutical strategies for managing obesity-linked diabetes are also highlighted. Future research directions should focus on clinical validation and the identification of specific microbial signatures influenced by phytochemicals to tailor precision nutrition approaches.

**Keywords:** Phytochemicals, Gut Microbiota, Obesity, Insulin Resistance, Type 2 Diabetes, Metabolic Disorders, Polyphenols, Flavonoids

## INTRODUCTION

Obesity and type 2 diabetes mellitus (T2DM) have emerged as significant public health concerns due to their increasing global prevalence and associated comorbidities[1–5]. These metabolic disorders are strongly influenced by multiple factors, including genetic predisposition, lifestyle choices, and environmental influences. Among the emerging contributors, recent research has highlighted the gut microbiota as a crucial regulator of metabolic homeostasis[6, 7]. The gut microbiota, comprising trillions of microorganisms, plays a fundamental role in modulating various physiological processes, including glucose metabolism, lipid homeostasis, and immune function[8–10]. An imbalance in gut microbial composition, known as dysbiosis, is closely associated with metabolic disorders, particularly obesity-linked diabetes[11, 12]. Dysbiosis leads to altered microbial diversity, impaired production of short-chain fatty acids, increased gut permeability, and heightened systemic inflammation, all of which contribute to insulin resistance and metabolic dysfunction[12]. Consequently, therapeutic strategies targeting the gut microbiota have gained traction as potential interventions for preventing and managing obesity-induced metabolic disorders. Among these strategies, dietary modulation through bioactive compounds, particularly phytochemicals, has drawn considerable interest due to its natural, non-invasive approach to restoring microbial balance and improving metabolic health.

Phytochemicals, naturally occurring bioactive compounds derived from plants, have been extensively studied for their beneficial effects on gut microbiota composition and function[13–15]. These compounds, including polyphenols, flavonoids, alkaloids, and terpenoids, exhibit diverse mechanisms of action that promote gut microbial diversity and modulate metabolic pathways[14–16]. Polyphenols, abundant in fruits, vegetables, and tea, serve as prebiotic-like molecules, selectively enhancing the growth of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus* while suppressing pathogenic microbes[17, 18]. Flavonoids, found in citrus fruits and berries, exert anti-inflammatory and antioxidant effects, reducing systemic inflammation associated

with obesity and insulin resistance[19, 20]. Alkaloids and terpenoids, present in various medicinal plants, have been shown to influence gut microbiota composition, enhance gut barrier integrity, and regulate glucose metabolism[21–23]. Through these mechanisms, phytochemicals contribute to improving insulin sensitivity, reducing lipid accumulation, and mitigating chronic low-grade inflammation, which are hallmarks of obesity-linked T2DM. Given their multifaceted roles, phytochemicals represent a promising avenue for developing functional foods and nutraceuticals aimed at modulating gut microbiota to prevent and manage metabolic dysfunction. This review delves into the intricate relationship between phytochemicals and gut microbiota, elucidating their potential in mitigating obesity-induced insulin resistance and offering insights into future therapeutic strategies.



## Gut Microbiota and Metabolic Disorders

The gut microbiota, comprising trillions of microorganisms, plays a crucial role in regulating host metabolism through multiple mechanisms[8, 12, 24]. These include the fermentation of dietary fibers, which leads to the production of short-chain fatty acids (SCFAs) that influence energy metabolism, immune modulation, and gut barrier integrity[25]. Additionally, the gut microbiota interacts with the immune system, helping to maintain a balanced inflammatory response. However, in conditions such as obesity and type 2 diabetes mellitus (T2DM), gut microbial dysbiosis occurs, disrupting these essential metabolic functions[26].

In obesity and T2DM, gut dysbiosis is characterized by a reduction in microbial diversity, particularly in beneficial bacteria like *Bifidobacterium* and *Lactobacillus*[27]. These microbes play key roles in maintaining gut health and metabolic homeostasis. Conversely, there is an increase in pro-inflammatory bacteria, such as *Firmicutes* and *Proteobacteria*, which contribute to systemic inflammation and metabolic dysfunction. Moreover, dysbiosis leads to diminished SCFA production, which negatively impacts glucose metabolism and insulin sensitivity, thereby exacerbating insulin resistance and increasing the risk of metabolic complications[28].

Restoring gut microbial balance offers a promising approach to managing obesity and its associated metabolic disorders. Dietary interventions, including increased fiber intake, can promote the growth of beneficial microbes and enhance SCFA production. Probiotics, which introduce beneficial bacterial strains, and phytochemicals, derived from plant-based sources, have shown potential in modulating gut microbiota composition. These strategies help to improve metabolic health by reducing inflammation, enhancing insulin sensitivity, and supporting overall gut homeostasis.

## Phytochemicals and Gut Microbiota Modulation

**Polyphenols**: Polyphenols, a diverse group of plant-derived compounds, are abundant in dietary sources such as fruits, vegetables, tea, and cocoa[29]. These bioactive compounds exhibit prebiotic-like effects by selectively promoting beneficial gut bacteria while suppressing the growth of pathogenic microbes. One of the primary mechanisms by which polyphenols influence gut microbiota is through the enhancement of short-chain fatty acid (SCFA) production. SCFAs, particularly butyrate and propionate, improve insulin sensitivity and regulate energy metabolism, thereby mitigating obesity-related metabolic dysfunctions. Additionally, polyphenols regulate inflammatory pathways by reducing the production of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which are implicated in chronic metabolic diseases[29]. Furthermore, polyphenols strengthen gut barrier integrity by modulating tight junction proteins, preventing endotoxemia-induced systemic inflammation. Specific polyphenols have been shown to influence gut microbiota composition beneficially. For example, green tea catechins selectively increase the populations of Bifidobacterium and Akkermansia muciniphila, bacterial strains known to enhance glucose metabolism and reduce obesity risk. Similarly, resveratrol, a polyphenol found in red wine and grapes, has been reported to promote Lactobacillus and Bacteroidetes while reducing Firmicutes, a microbial shift associated with improved weight control and metabolic balance[30].

**Flavonoids**: Flavonoids, a subclass of polyphenols found in citrus fruits, berries, legumes, and tea, exhibit potent anti-obesity and anti-diabetic properties through multiple metabolic pathways[31]. One significant mechanism involves the inhibition of digestive enzymes such as α-glucosidase and α-amylase, which delays carbohydrate absorption and reduces postprandial hyperglycemia. Flavonoids also contribute to metabolic homeostasis by selectively enhancing beneficial gut bacteria while suppressing pathogenic strains[31]. This modulation of the gut microbiome results in improved glucose utilization and insulin sensitivity. Furthermore, flavonoids inhibit lipogenesis and adipogenesis while simultaneously promoting fat oxidation, thereby reducing overall adiposity. Specific flavonoids have demonstrated profound effects on gut microbiota composition and metabolic health. For instance, quercetin, a flavonoid found in apples, onions, and capers, has been shown to enhance Bifidobacterium populations, leading to improved insulin sensitivity and reduced inflammation. Similarly, naringenin, a citrus-derived flavonoid, not only suppresses lipogenesis but also significantly increases Akkermansia muciniphila, a bacterial species associated with improved gut barrier function and reduced obesity risk[32]. These findings highlight the critical role of flavonoids in modulating gut microbiota and regulating metabolic processes, making them promising candidates for dietary interventions aimed at preventing and managing metabolic disorders such as obesity and type 2 diabetes.

**Alkaloids**: Alkaloids, naturally occurring nitrogen-containing compounds found in tea, coffee, and various medicinal plants, exert profound effects on gut microbiota and metabolic health. These bioactive compounds play a crucial role in reducing inflammatory responses, which in turn improves insulin signaling and glucose homeostasis[33, 34]. By modulating inflammatory pathways, alkaloids help to suppress chronic low-grade inflammation commonly observed in metabolic disorders. Additionally, alkaloids promote the growth of SCFA-producing bacteria, which aids in energy homeostasis and enhances metabolic flexibility[35]. The beneficial effects of alkaloids on gut microbiota composition are exemplified by berberine, a plant-derived alkaloid widely studied for its anti-diabetic and anti-obesity properties. Berberine has been shown to increase the abundance of Bacteroidetes while reducing Firmicutes, a microbial shift associated with improved glycemic control and weight loss. Furthermore, caffeine, a well-known alkaloid present in coffee and tea, significantly alters gut microbiota composition, promoting the growth of beneficial bacteria while reducing pathogenic strains[35]. These microbial alterations contribute to improved metabolic flexibility, allowing for better adaptation to fluctuating energy demands. The regulatory effects of alkaloids on gut microbiota and metabolic processes underscore their potential therapeutic applications in the management of obesity, insulin resistance, and other metabolic disorders. As research continues to unravel the intricate interactions between alkaloids and gut microbiota, these compounds may pave the way for novel dietary and pharmacological interventions aimed at improving metabolic health and reducing the global burden of obesity-related diseases.



**Terpenoids:** Terpenoids, a diverse class of bioactive compounds found abundantly in herbs and spices, have demonstrated significant anti-obesity and anti-diabetic properties through multiple mechanisms[23]. One of their primary actions involves modulating gut microbiota composition, effectively reducing obesity-associated dysbiosis and fostering a healthier microbial environment[36]. By promoting beneficial bacteria, terpenoids contribute to improved metabolic health. Additionally, these compounds enhance mitochondrial function, leading to increased energy expenditure and improved cellular metabolism, which are crucial for combating obesity and insulin resistance[37]. Notable examples of terpenoids with such effects include curcumin and ginsenosides. Curcumin, a major bioactive component of turmeric, has been shown to increase the abundance of Akkermansia muciniphila, a bacterium known for its beneficial effects on gut barrier integrity and metabolic regulation. This microbial modulation helps reduce systemic inflammation and enhance insulin sensitivity, thereby mitigating metabolic disorders. Similarly, ginsenosides, the active terpenoid compounds found in ginseng, have been observed to promote the proliferation of Bifidobacterium, a key probiotic genus associated with improved glucose metabolism. By enhancing the presence of these beneficial microbes, ginsenosides contribute to better glycemic control, making them valuable candidates for managing obesity and diabetes. Collectively, terpenoids act through multiple metabolic pathways to exert their therapeutic effects, making them promising natural agents in the prevention and treatment of metabolic disorders.

## Mechanistic Insights: How Phytochemicals Influence Insulin Resistance

Phytochemicals influence insulin sensitivity through multiple mechanisms. One key pathway is the modulation of gut microbiota composition[38]. These bioactive compounds enhance the abundance of short-chain fatty acid (SCFA)-producing bacteria, which play a crucial role in maintaining metabolic homeostasis. SCFAs, such as butyrate and propionate, contribute to improved insulin sensitivity by promoting glucose metabolism and reducing inflammation[38]. Another important mechanism is the regulation of intestinal barrier function. Phytochemicals help strengthen the gut lining, preventing the translocation of endotoxins into the bloodstream. This process reduces endotoxemia, which is a major contributor to chronic inflammation and insulin resistance. By preserving gut integrity, these compounds support overall metabolic health and improve insulin signaling[39, 40]. Phytochemicals also activate the AMP-activated protein kinase (AMPK) pathway, a central regulator of energy balance. Activation of AMPK enhances glucose uptake by cells and promotes lipid oxidation, reducing excess fat accumulation that can impair insulin sensitivity. This metabolic shift supports better glycemic control and lowers the risk of insulin resistance-related disorders [39, 40, 41, 42, 43, 44]. Furthermore, phytochemicals exert anti-inflammatory effects by suppressing nuclear factor-kappa B (NF-κB) and cytokine-mediated pathways associated with insulin resistance[41, 45, 46, 47]. Chronic inflammation is a key driver of metabolic dysfunction, and by inhibiting pro-inflammatory signaling, these compounds help maintain insulin sensitivity. Their ability to reduce oxidative stress and inflammatory mediators contributes to improved metabolic function and overall health.

## Clinical and Translational Perspectives

Although preclinical studies support the role of phytochemicals in modulating gut microbiota and metabolic disorders, clinical evidence remains limited. Several challenges hinder their translation into therapeutic applications. One major challenge is bioavailability and metabolism. Many phytochemicals have low bioavailability, meaning they are poorly absorbed, metabolized, or rapidly excreted, limiting their therapeutic potential. To overcome this, novel delivery systems, such as nanoparticle formulations and encapsulation techniques, are being explored to enhance their stability and absorption[48,49,50,51,52]. Another significant issue is the variability in individual microbiota responses. The composition of gut microbiota varies greatly

among individuals, influencing how phytochemicals are metabolized and their subsequent effects on health. Personalized approaches, including microbiome-based interventions, are essential to optimize therapeutic outcomes and ensure efficacy across diverse populations [48,49,50,51,52]. Lastly, the long-term safety and efficacy of phytochemicals in metabolic health require further investigation[44]. While short-term studies suggest promising benefits, more extensive clinical trials are necessary to confirm their long-term impact, potential side effects, and appropriate dosages. Addressing these challenges will be crucial for advancing phytochemical-based strategies in the management of metabolic disorders.



## Future Directions

Future research should prioritize identifying microbial signatures linked to phytochemical intake to better understand how these bioactive compounds influence gut microbiota composition and function. By characterizing specific microbial taxa associated with different phytochemicals, researchers can elucidate their role in modulating metabolic pathways, particularly in conditions such as diabetes. Additionally, developing microbiome-targeted dietary interventions tailored to individual gut microbiota profiles could optimize diabetes management. Personalized nutrition strategies leveraging probiotics, prebiotics, and phytochemicals could enhance glycemic control and metabolic health by fostering a beneficial gut microbial environment. Another crucial avenue for research is exploring the synergistic effects of multiple phytochemicals on gut microbiota. Since different phytochemicals may work in concert to enhance microbial diversity and metabolic activity, understanding their combined effects could lead to more effective dietary interventions. Moreover, improving phytochemical bioavailability through advanced delivery systems, such as nanotechnology and encapsulation, can enhance their stability, absorption, and therapeutic potential. Encapsulation techniques can protect phytochemicals from degradation in the digestive tract, ensuring targeted release and increased efficacy. These advancements will pave the way for innovative dietary strategies that harness the gut microbiome's role in disease prevention and management.

## CONCLUSION

Phytochemicals serve as promising modulators of gut microbiota, offering potential therapeutic benefits in obesity-linked diabetes. Their ability to enhance microbial diversity, regulate inflammatory pathways, and improve insulin sensitivity underscores their role as dual modulators of metabolic health. Integrating phytochemical-rich diets with microbiome-targeted interventions may pave the way for precision nutrition strategies in managing metabolic disorders.

## REFERENCES


1. Annett, S., Moore, G., Robson, T.: Obesity and Cancer Metastasis: Molecular and Translational Perspectives. Cancers. 12, 3798 (2020). https://doi.org/10.3390/cancers12123798
2. Ashour, M.M., Mabrouk, M., Aboelnasr, M.A., Beherei, H.H., Tohamy, K.M., Das, D.B.: Anti-Obesity Drug Delivery Systems: Recent Progress and Challenges. Pharmaceutics. 15, 2635 (2023). https://doi.org/10.3390/pharmaceutics15112635
3. Basu, T., Selman, A., Reddy, A.P., Reddy, P.H.: Current Status of Obesity: Protective Role of Catechins. Antioxidants. 12, 474 (2023). https://doi.org/10.3390/antiox12020474
4. 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
5. 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)
6. 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
7. Aloo, S.O., Barathikannan, K., Oh, D.-H.: Polyphenol-rich fermented hempseed ethanol extracts improve obesity, oxidative stress, and neural health in high-glucose diet-induced *Caenorhabditis elegans*. Food Chem. X. 21, 101233 (2024). https://doi.org/10.1016/j.fochx.2024.101233
8. Bemark, M., Pitcher, M.J., Dionisi, C., Spencer, J.: Gut-associated lymphoid tissue: a microbiota-driven hub of B cell immunity. Trends Immunol. 45, 211 (2024). https://doi.org/10.1016/j.it.2024.01.006
9. Cronin, P., Joyce, S.A., O'Toole, P.W., O'Connor, E.M.: Dietary Fibre Modulates the Gut Microbiota. Nutrients. 13, 1655 (2021). https://doi.org/10.3390/nu13051655
10. Ugwu, O.P.-C., Alum, E.U., Okon, M.B., Obeagu, E.I.: Mechanisms of microbiota modulation: Implications for health, disease, and therapeutic interventions. Medicine (Baltimore). 103, e38088 (2024). https://doi.org/10.1097/MD.0000000000038088
11. Fakharian, F., Thirugnanam, S., Welsh, D.A., Kim, W.-K., Rappaport, J., Bittinger, K., Rout, N.: The Role of Gut Dysbiosis in the Loss of Intestinal Immune Cell Functions and Viral Pathogenesis. Microorganisms. 11, 1849 (2023). https://doi.org/10.3390/microorganisms11071849

12. Hrncir, T.: Gut Microbiota Dysbiosis: Triggers, Consequences, Diagnostic and Therapeutic Options. Microorganisms. 10, 578 (2022). https://doi.org/10.3390/microorganisms10030578
13. 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
14. Ansari, P., Khan, J.T., Chowdhury, S., Reberio, A.D., Kumar, S., Seidel, V., Abdel-Wahab, Y.H.A., Flatt, P.R.: Plant-Based Diets and Phytochemicals in the Management of Diabetes Mellitus and Prevention of Its Complications: A Review. Nutrients. 16, 3709 (2024). https://doi.org/10.3390/nu16213709
15. Iside, C., Scafuro, M., Nebbioso, A., Altucci, L.: SIRT1 Activation by Natural Phytochemicals: An Overview. Front. Pharmacol. 11, (2020). https://doi.org/10.3389/fphar.2020.01225
16. Kawish, S.M., Sharma, S., Gupta, P., Ahmad, F.J., Iqbal, M., Alshabrmi, F.M., Anwer, Md.K., Fathi-karkan, S., Rahdar, A., Aboudzadeh, M.A.: Nanoparticle-Based Drug Delivery Platform for Simultaneous Administration of Phytochemicals and Chemotherapeutics: Emerging Trends in Cancer Management. Part. Part. Syst. Charact. 41, 2400049 (2024). https://doi.org/10.1002/ppsc.202400049
17. Bešlo, D., Golubić, N., Rastija, V., Agić, D., Karnaš, M., Šubarić, D., Lučić, B.: Antioxidant Activity, Metabolism, and Bioavailability of Polyphenols in the Diet of Animals. Antioxidants. 12, 1141 (2023). https://doi.org/10.3390/antiox12061141
18. Callizot, N., Campanari, M.L., Rouvière, L., Jacquemot, G., Henriques, A., Garayev, E., Poindron, P.: Huperzia serrata Extract 'NSP01' With Neuroprotective Effects-Potential Synergies of Huperzine A and Polyphenols. Front. Pharmacol. 12, (2021). https://doi.org/10.3389/fphar.2021.681532
19. Alum, E.U., Ugwu, O.P.C.: Beyond Nutrients: Exploring the Potential of Phytochemicals for Human Health. IAA J. Appl. Sci. 10, 1–7 (2023). https://doi.org/10.59298/IAAJAS/2023/4.1.3211
20. Alum, E. U.: Phytochemicals in malaria treatment: Mechanisms of action and clinical efficacy. KIU J. Health Sci. 4, 71–84 (2024). https://doi.org/10.59568/KJHS-2024-4-2-06
21. Adhikari, B.: Roles of Alkaloids from Medicinal Plants in the Management of Diabetes Mellitus. J. Chem. 2021, 2691525 (2021). https://doi.org/10.1155/2021/2691525
22. Heinrich, M., Mah, J., Amirkia, V.: Alkaloids Used as Medicines: Structural Phytochemistry Meets Biodiversity—An Update and Forward Look. Molecules. 26, 1836 (2021). https://doi.org/10.3390/molecules26071836
23. Kim, T., Song, B., Cho, K.S., Lee, I.-S.: Therapeutic Potential of Volatile Terpenes and Terpenoids from Forests for Inflammatory Diseases. Int. J. Mol. Sci. 21, 2187 (2020). https://doi.org/10.3390/ijms21062187
24. Chen, J., Chen, B., Lin, B., Huang, Y., Li, J., Li, J., Chen, Z., Wang, P., Ran, B., Yang, J., Huang, H., Liu, L., Wei, Q., Ai, J., Cao, D.: The role of gut microbiota in prostate inflammation and benign prostatic hyperplasia and its therapeutic implications. Heliyon. 10, e38302 (2024). https://doi.org/10.1016/j.heliyon.2024.e38302
25. Xu, H., Zhang, Y., Zhang, Y., Shen, C., Zhang, Z., Wang, J., Zhou, D., Wu, Z., Qie, Y., Liu, S., Tian, D., Hu, H., Wu, C.: Causal associations between gut microbiota and chronic prostatitis/chronic pelvic pain syndrome: a two-sample Mendelian randomization study. Egypt. J. Med. Hum. Genet. 25, 68 (2024). https://doi.org/10.1186/s43042-024-00540-3
26. Cunningham, A.L., Stephens, J.W., Harris, D.A.: Gut microbiota influence in type 2 diabetes mellitus (T2DM). Gut Pathog. 13, 50 (2021). https://doi.org/10.1186/s13099-021-00446-0
27. Patra, D., Banerjee, D., Ramprasad, P., Roy, S., Pal, D., Dasgupta, S.: Recent insights of obesity-induced gut and adipose tissue dysbiosis in type 2 diabetes. Front. Mol. Biosci. 10, 1224982 (2023). https://doi.org/10.3389/fmolb.2023.1224982
28. Zaky, A., Glastras, S.J., Wong, M.Y.W., Pollock, C.A., Saad, S.: The Role of the Gut Microbiome in Diabetes and Obesity-Related Kidney Disease. Int. J. Mol. Sci. 22, 9641 (2021). https://doi.org/10.3390/ijms22179641
29. Luo, B., Wen, Y., Ye, F., Wu, Y., Li, N., Farid, M.S., Chen, Z., El-Seedi, H.R., Zhao, C.: Bioactive phytochemicals and their potential roles in modulating gut microbiota. J. Agric. Food Res. 12, 100583 (2023). https://doi.org/10.1016/j.jafr.2023.100583
30. Santhiravel, S., Bekhit, A.E.-D.A., Mendis, E., Jacobs, J.L., Dunshea, F.R., Rajapakse, N., Ponnampalam, E.N.: The Impact of Plant Phytochemicals on the Gut Microbiota of Humans for a Balanced Life. Int. J. Mol. Sci. 23, 8124 (2022). https://doi.org/10.3390/ijms23158124
31. Ciupei, D., Colişar, A., Leopold, L., Stănilă, A., Diaconeasa, Z.M.: Polyphenols: From Classification to Therapeutic Potential and Bioavailability. Foods. 13, 4131 (2024). https://doi.org/10.3390/foods13244131

32. Vásquez-Reyes, S., Bernal-Gámez, M., Domínguez-Chávez, J., Mondragón-Vásquez, K., Sánchez-Tapia, M., Ordaz, G., Granados-Portillo, O., Coutiño-Hernández, D., Barrera-Gómez, P., Torres, N., Tovar, A.R.: The Effects of Novel Co-Amorphous Naringenin and Fisetin Compounds on a Diet-Induced Obesity Murine Model. Nutrients. 16, 4425 (2024). https://doi.org/10.3390/nu16244425
33. Nepal, B., J. Stine, K.: Glycoalkaloids: Structure, Properties, and Interactions with Model Membrane Systems. Processes. 7, 513 (2019). https://doi.org/10.3390/pr7080513
34. Alum, E., Diana, M., P.C., U., Aja, P., Obeagu, E., Uti, D., Okon, M., Extension, K.P.: Phytochemical composition of Datura stramonium Ethanol leaf and seed extracts: A Comparative Study. 10, 118–125 (2023)
35. Fusco, W., Lorenzo, M.B., Cintoni, M., Porcari, S., Rinninella, E., Kaitsas, F., Lener, E., Mele, M.C., Gasbarrini, A., Collado, M.C., Cammarota, G., Ianiro, G.: Short-Chain Fatty-Acid-Producing Bacteria: Key Components of the Human Gut Microbiota. Nutrients. 15, 2211 (2023). https://doi.org/10.3390/nu15092211
36. Zhuang, Z., Zhou, P., Wang, J., Lu, X., Chen, Y.: The Characteristics, Mechanisms and Therapeutics: Exploring the Role of Gut Microbiota in Obesity. Diabetes Metab. Syndr. Obes. 16, 3691–3705 (2023). https://doi.org/10.2147/DMSO.S432344
37. 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
38. Bahrampour, N., Mirzababaei, A., Hosseininasab, D., Abaj, F., Clark, C.C.T., Mirzaei, K.: High intake of dietary phytochemical index may be related to reducing risk of diabetic nephropathy: a case–control study. BMC Nutr. 9, 14 (2023). https://doi.org/10.1186/s40795-023-00676-2
39. 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
40. 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
41. Saleh, H.A., Yousef, M.H., Abdelnaser, A.: The Anti-Inflammatory Properties of Phytochemicals and Their Effects on Epigenetic Mechanisms Involved in TLR4/NF-κB-Mediated Inflammation. Front. Immunol. 12, 606069 (2021). https://doi.org/10.3389/fimmu.2021.606069
42. 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
43. Rowland, I., Gibson, G., Heinken, A., Scott, K., Swann, J., Thiele, I., Tuohy, K.: Gut microbiota functions: metabolism of nutrients and other food components. Eur. J. Nutr. 57, 1–24 (2018). https://doi.org/10.1007/s00394-017-1445-8
44. Hossain, Md.S., Wazed, M.A., Asha, S., Amin, Md.R., Shimul, I.M.: Dietary Phytochemicals in Health and Disease: Mechanisms, Clinical Evidence, and Applications—A Comprehensive Review. Food Sci. Nutr. 13, e70101 (2025). https://doi.org/10.1002/fsn3.70101
45. Ugwu OPC, Nwodo OFC, Joshua EP, Abubakar B, Ossai EC, Odo CE. Phytochemical and acute toxicity studies of Moringa oleifera ethanol leaf extract. 2013;2(2):66-71.
46. 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.
47. Agbafor K, Ezeali C, Akubugwo E, Obiudu I, Uraku A, Ogbanshi M, Edwin N, Ugwu O. Cardioprotective effect of leaf and root extracts of Newbouldia laevis against carbon tetrachloride-induced cardiotoxicity in albino rats. Eur J Med Plants. 2015;9(3):1-7.
48. Offor CE, Nwankwegu NJ, Ugwu Okechukwu PC, Aja PM. The effects of ethanol leaf-extract of Pterocarpus santalinoides on liver enzymes of albino rats. 2015;15(5):920-922.
49. Ezekwe CI, Chinenye Ada A, Ugwu Okechukwu PC. Effects of methanol extract of Parkia biglobosa stem bark on the liver and kidney functions of albino rats. 2013;25(7):993-999.
50. Amalu PC, Chukwuezi FO, Ugwu OPC. Antimicrobial effects of bitter kola (Garcinia kola) nut on Staphylococcus aureus, Escherichia coli, and Candida albicans. J Dent Med Sci (IOSR-JDMS). 2014;13(4):29-32.
51. Okechukwu PU, Nzubechukwu Edwin, Ogbansh ME, Ezeani N, Nworie MO, Ezugwu A. The effect of ethanol leaf extract of Jatropha curcas on chloroform-induced hepatotoxicity in albino rats. Glob J Biotech Biochem. 2015;10:11-15.

52. Ezekwe CI, Okoro IJ, Ugwu OPC, Eze SC. The effect of methanol extract of Talinum triangulare on some selected hematological and kidney parameters of experimental rats. 2013;2(6):4383-4396.

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