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Winniefred
ISSN: 2550-794X

International Digital Organization for Scientific Research
IDOSR JOURNAL OF SCIENTIFIC RESEARCH 10(3):143-149, 2025.
https://doi.org/10.59298/IDOSRJSR/2024/10.3.143149

IDOSRJSR10.300000

# The Role of Gut Microbiota-Modulating Natural Products in Obesity-Associated Diabetes

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## ABSTRACT

The global rise in obesity-associated type 2 diabetes mellitus (T2DM) has sparked a paradigm shift in understanding metabolic diseases beyond mere caloric imbalance. Emerging evidence positions the gut microbiota as a critical modulator of host metabolism, immunity, and endocrine signaling. Alterations in gut microbial composition termed dysbiosis are intricately linked to chronic low-grade inflammation, insulin resistance, and lipid metabolism dysfunction, all of which are hallmarks of obesity-associated diabetes. Concurrently, natural products from plants, fungi, and marine sources have gained attention for their prebiotic, antimicrobial, and immunomodulatory properties that favorably reshape gut microbial ecology. This review examines the mechanistic pathways through which natural compounds modulate gut microbiota and attenuate metabolic dysregulation in obesity-associated T2DM. Specific focus is given to polyphenols, flavonoids, alkaloids, polysaccharides, and essential oils, highlighting their impact on microbial diversity, short-chain fatty acid production, intestinal barrier integrity, and inflammatory markers. We also explore clinical and translational implications, challenges in therapeutic implementation, and future directions for microbiota-targeted natural interventions in metabolic syndrome.

**Keywords:** Gut microbiota, Natural products, Obesity, Type 2 diabetes, Dysbiosis

## INTRODUCTION

Obesity and type 2 diabetes mellitus (T2DM) have emerged as two of the most pressing public health challenges of the 21st century, with their prevalence continuing to rise at an alarming rate [1, 2]. According to the World Health Organization (WHO), more than 650 million adults were classified as obese in 2023, while over 500 million individuals are currently living with T2DM [3]. The close association between these conditions is rooted in shared pathophysiological mechanisms, with insulin resistance acting as the primary bridge linking them. Excess adiposity, particularly visceral fat accumulation, leads to adipose tissue dysfunction, which manifests in chronic, low-grade systemic inflammation. This inflammatory state is fueled by increased secretion of pro-inflammatory cytokines, infiltration of immune cells into adipose tissue, and dysregulated adipokine production [4]. Concurrently, hepatic steatosis, or fat accumulation in the liver, disrupts glucose and lipid metabolism, further aggravating insulin resistance. Additionally, disturbances in gut-liver axis signaling mediated by changes in gut microbiota composition and function have been identified as significant contributors to metabolic imbalance [5]. Collectively, these factors create a vicious cycle where obesity promotes insulin resistance, and insulin resistance exacerbates obesity-driven metabolic dysfunction. Without targeted interventions, the synergistic progression of obesity and diabetes will continue to strain healthcare systems globally, driving an increase in cardiovascular disease, kidney dysfunction, and other debilitating complications.

### 1.2. Gut Microbiota: The Metabolic Gatekeeper

The human gastrointestinal tract is home to a diverse and dynamic community of trillions of microorganisms, collectively known as the gut microbiota. These microbial inhabitants play an integral role in maintaining host metabolic and immune homeostasis through their participation in nutrient breakdown, fermentation of indigestible fibers, production of bioactive metabolites, and modulation of immune responses [6, 7]. A balanced gut microbiota facilitates the generation of short-chain fatty acids (SCFAs), regulates bile acid metabolism, and strengthens the intestinal barrier, all of which contribute to optimal metabolic health. However, disturbances in the composition and function of this microbial ecosystem, termed dysbiosis can have far-reaching consequences for the host [8]. Dysbiosis has been implicated in the pathogenesis of obesity and T2DM by promoting endotoxemia, characterized by elevated systemic lipopolysaccharides (LPS) originating from gram-negative bacterial membranes. This condition activates inflammatory signaling pathways, impairs insulin sensitivity, and disrupts glucose metabolism [9]. Furthermore, altered microbial metabolism reduces SCFA production, leading to diminished gut barrier integrity and impaired energy regulation [10]. Changes in bile acid profiles and receptor signaling further aggravate metabolic disturbances. Increasing evidence underscores the concept that the gut microbiota acts as a metabolic gatekeeper, influencing energy homeostasis, glucose regulation, and lipid metabolism [11]. Therefore, modulating its composition and activity has emerged as a promising therapeutic target in combating obesity-associated diabetes.

### 1.3. Natural Products as Therapeutic Modulators

Natural products, comprising bioactive molecules derived from plants, animals, and microorganisms, have long been employed in traditional medicine systems to prevent and manage chronic diseases [12, 13]. Their therapeutic potential extends beyond direct pharmacological effects, as many natural compounds exert profound influences on the gut microbiota, thereby indirectly modulating host metabolism. Phytochemicals such as polyphenols, flavonoids, and alkaloids, along with bioactive peptides and polysaccharides, can selectively promote the growth of beneficial microbes, enhance microbial diversity, and suppress pathogenic species [14]. By doing so, they restore microbial balance, improve SCFA production, and strengthen intestinal barrier function. Additionally, certain natural products modulate bile acid metabolism, regulate inflammatory pathways, and improve insulin sensitivity, thereby targeting key mechanisms implicated in obesity and diabetes [15]. Recent advances in omics technologies have facilitated deeper understanding of the interactions between natural products and the gut microbiome, enabling the identification of specific microbial taxa and metabolites involved in therapeutic responses. Importantly, the widespread historical use of these agents supports their relative safety, though their efficacy depends on factors such as bioavailability, dosage, and individual microbiome composition. As global health systems grapple with the rising burden of obesity-associated diabetes, integrating natural product-based strategies into preventive and therapeutic regimens represents a cost-effective, sustainable, and culturally acceptable approach, particularly in regions with rich ethnomedicinal heritage.

### 2.1. Composition and Functional Diversity of Gut Microbiota

The gut microbiota is a highly complex microbial ecosystem dominated by four primary bacterial phyla: Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria. These microorganisms establish a symbiotic relationship with the human host, aiding in nutrient digestion, fermentation of dietary fibers, production of metabolites, and immune regulation. The Firmicutes/Bacteroidetes (F/B) ratio is commonly used as a marker of microbial composition, with an increased ratio frequently observed in obesity and T2DM [16]. This shift often reflects enhanced capacity for energy harvest from the diet, which may contribute to weight gain and metabolic dysfunction. While Firmicutes are known for their role in SCFA production, excessive abundance relative to Bacteroidetes may lead to altered energy balance and inflammation [17]. Actinobacteria, particularly Bifidobacterium species, are beneficial microbes associated with improved gut barrier function and anti-inflammatory effects, whereas Proteobacteria often include opportunistic pathogens that can promote dysbiosis and low-grade inflammation [18]. Beyond taxonomic composition, the functional diversity of the gut microbiota is equally critical. The stability and diversity of these microbial communities are essential for maintaining metabolic health, while reduced diversity is a hallmark of dysbiosis linked to insulin resistance and obesity-related complications[19].

### 2.2. Metabolic Roles of Gut Microbes

Gut microbiota exert profound influence on host metabolism through multiple interconnected mechanisms. One of their primary functions is the fermentation of dietary fibers into short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate. These metabolites serve as signaling molecules that regulate energy homeostasis, improve insulin sensitivity, and modulate glucose and lipid metabolism [20]. Butyrate, in particular, fuels colonocytes and strengthens gut barrier integrity, while propionate influences hepatic gluconeogenesis and acetate participates in lipid synthesis regulation [21]. Additionally, gut microbes play a central role in bile acid transformation, converting primary bile acids synthesized in the liver into secondary bile acids. These metabolites interact with host receptors, including the farnesoid X receptor (FXR) and Takeda G-protein-coupled receptor 5 (TGR5), to regulate lipid metabolism, glucose homeostasis, and inflammatory responses [22]. The gut microbiota also shape host immunity by maintaining mucosal immune balance, promoting the development of regulatory T cells, and preventing translocation of pathogens. Disruption of these processes due to dysbiosis can impair metabolic regulation, promote systemic inflammation, and contribute to the progression of obesity and T2DM [23]. Thus, the metabolic functions of gut microbes are indispensable for sustaining metabolic health, and their modulation offers a potential therapeutic pathway.

### 2.3. Gut Barrier Integrity and Endotoxemia

The intestinal barrier is a multifaceted defense system composed of epithelial cells, tight junction proteins, mucus layers, and immune components that collectively regulate the passage of nutrients while preventing harmful substances from entering the bloodstream. In the context of obesity and metabolic syndrome, gut microbiota dysbiosis often compromises this barrier, increasing intestinal permeability, a condition referred to as "leaky gut." This disruption allows lipopolysaccharides (LPS) from gram-negative bacteria to translocate into systemic circulation, initiating a state known as metabolic endotoxemia [24]. LPS interacts with toll-like receptor 4 (TLR4) on immune cells, triggering a cascade of pro-inflammatory cytokine production and activating nuclear factor kappa B (NF-κB) signaling. The resulting chronic, low-grade inflammation exacerbates insulin resistance, disrupts lipid metabolism, and promotes further weight gain [25]. Moreover, endotoxemia can impair pancreatic β-cell function, reducing insulin secretion and worsening glycemic control [26]. Factors such as reduced SCFA production, altered bile acid signaling, and diminished abundance of beneficial microbes like Bifidobacterium and Akkermansia further weaken gut barrier integrity. Restoring barrier function whether through prebiotics, probiotics, natural bioactive compounds, or lifestyle interventions can reduce endotoxemia and improve metabolic outcomes. This makes gut barrier preservation a central therapeutic goal in managing obesity-associated diabetes.

## 3. Natural Products That Modulate Gut Microbiota in Obesity and Diabetes

### 3.1. Polyphenols

**3.1.1. Resveratrol:** Resveratrol, a naturally occurring stilbene found in grapes, berries, and peanuts, exerts profound effects on gut microbiota composition and metabolic health. It selectively increases the abundance of *Akkermansia muciniphila*, a mucin-degrading bacterium known for enhancing gut barrier integrity and improving insulin sensitivity [27]. By strengthening the intestinal lining, resveratrol reduces translocation of harmful microbial products into circulation. It also decreases populations of lipopolysaccharide (LPS)-producing bacteria, thereby lowering systemic inflammation and metabolic endotoxemia. These microbiota-targeted actions, coupled with its antioxidant and anti-inflammatory properties, make resveratrol a promising dietary compound for preventing and managing metabolic disorders such as type 2 diabetes and obesity [28].

**3.1.2. Curcumin:** Curcumin, the primary bioactive compound in turmeric (*Curcuma longa*), exhibits prebiotic-like effects by promoting beneficial gut bacteria such as *Bifidobacterium* and *Lactobacillus.* Through modulation of NF-κB and activation of AMP-activated protein kinase (AMPK), curcumin exerts potent anti-inflammatory and anti-diabetic effects. It reduces intestinal permeability, suppresses pro-inflammatory cytokines, and improves glucose homeostasis [29]. Curcumin's influence on gut microbiota diversity enhances short-chain fatty acid (SCFA) production, further contributing to metabolic health. Its low bioavailability is partly offset by its local gut actions, making it a promising adjunct for managing insulin resistance, obesity, and related inflammatory conditions through both microbiota and molecular signaling pathways [30].

**3.2.1. Quercetin:** Quercetin, a flavonoid found in onions, apples, and leafy greens, modulates gut microbiota composition by reducing harmful *Proteobacteria* while enriching short-chain fatty acid (SCFA)-producing bacteria. These changes help improve gut health and metabolic balance [31]. Quercetin has been shown to attenuate glucose intolerance by enhancing insulin sensitivity and stimulating glucagon-like peptide-1 (GLP-1) secretion, which improves glycemic control. Its anti-inflammatory effects are mediated through the suppression of NF-κB signaling, while its antioxidant activity reduces oxidative stress. By reshaping gut microbiota and regulating host metabolism, quercetin offers therapeutic potential for managing type 2 diabetes, obesity, and related metabolic complications.

**3.2.2. Naringenin:** Naringenin, a citrus-derived flavonoid found in oranges, grapefruits, and tomatoes, plays a vital role in gut microbiota modulation and lipid metabolism regulation. It promotes the growth of butyrate-producing bacteria, particularly *Faecalibacterium prausnitzii*, which supports gut barrier integrity and reduces inflammation [32]. Naringenin lowers circulating endotoxins by reducing LPS-producing bacteria, thereby alleviating metabolic endotoxemia. It also exerts lipid-lowering effects by modulating genes involved in fatty acid oxidation and cholesterol metabolism [33]. These combined actions contribute to improved insulin sensitivity, reduced systemic inflammation, and better metabolic health, making naringenin a valuable dietary compound for preventing and managing obesity-associated metabolic disorders.

**3.3. Alkaloids – Berberine:** Berberine, an isoquinoline alkaloid extracted from *Coptis chinensis* and other medicinal plants, exerts potent anti-diabetic and lipid-lowering effects through gut microbiota modulation. It increases the abundance of SCFA-producing bacteria, enhances microbial diversity, and strengthens gut barrier function by upregulating tight junction proteins [34]. Berberine's ability to improve insulin sensitivity is linked to its suppression of pro-inflammatory cytokines and activation of AMPK signaling. Additionally, it reduces intestinal permeability, thereby preventing metabolic endotoxemia [35]. Its low systemic absorption suggests that many of its benefits are mediated locally in the gut, making berberine a promising natural therapeutic for type 2 diabetes and related metabolic disorders.

**3.4.1. Inulin:** Inulin, a fermentable prebiotic fiber found in chicory root, garlic, onions, and bananas, is metabolized by gut bacteria to produce short-chain fatty acids (SCFAs), particularly butyrate [36]. Butyrate plays a critical role in reinforcing intestinal epithelial integrity, reducing inflammation, and improving glucose metabolism. Inulin supplementation enhances microbial diversity, increases beneficial bacteria such as *Bifidobacterium* spp., and lowers circulating endotoxins. These effects translate into improved insulin sensitivity and reduced systemic inflammation. Its ability to modulate gut microbiota and support metabolic homeostasis has made inulin a widely studied dietary intervention for obesity, type 2 diabetes, and other metabolic syndrome components [37].

**3.4.2. β-Glucans:** β-glucans, soluble fibers found in oats, barley, and certain mushrooms, exert multiple health benefits through gut microbiota modulation. They increase the relative abundance of *Bacteroidetes* and promote the production of SCFAs, which improve gut barrier function and metabolic health [38]. β-glucans also exhibit immunomodulatory effects by reducing pro-inflammatory cytokines and enhancing anti-inflammatory responses. In metabolic disorders, they improve insulin sensitivity by enhancing glucose uptake and regulating lipid metabolism [39]. Their viscous nature slows gastric emptying, reduces postprandial glucose spikes, and supports satiety, making β-glucans an important dietary component for managing obesity, type 2 diabetes, and cardiovascular risk factors.

**3.5. Essential Oils:** Essential oils such as thymol, eugenol, and carvacrol, derived from herbs and spices like thyme, clove, and oregano, possess both antimicrobial and anti-inflammatory properties. They help maintain a healthy gut microbiota balance by suppressing pathogenic bacteria and promoting beneficial species [40]. These oils downregulate Toll-like receptor 4 (TLR4) expression, thereby reducing LPS-induced inflammation and improving insulin sensitivity. Their antioxidant properties further protect against oxidative stress-related tissue damage. While their systemic absorption is limited, their local actions in the gastrointestinal tract make them valuable for modulating microbiota composition and mitigating inflammation in metabolic disorders.

## 4. Molecular Mechanisms Underpinning Microbiota–Metabolite Interactions

**4.1. SCFA-Mediated Signaling:** Short-chain fatty acids (SCFAs), particularly butyrate and propionate, activate G-protein–coupled receptors GPR41 and GPR43 on intestinal L-cells. This activation stimulates the secretion of peptide YY (PYY) and glucagon-like peptide-1 (GLP-1), hormones that regulate appetite and glucose homeostasis. The signaling enhances insulin sensitivity, reduces energy intake, and promotes satiety [41]. These mechanisms position SCFAs as critical mediators linking gut microbiota activity to host metabolic regulation in obesity-associated diabetes.

**4.2. Epigenetic Regulation:** SCFAs, especially butyrate, act as histone deacetylase (HDAC) inhibitors, leading to hyperacetylation of histones and altered chromatin structure. This epigenetic modulation influences gene expression patterns governing inflammation, lipid metabolism, and glucose regulation. By controlling the transcription of key metabolic genes, SCFAs can suppress pro-inflammatory pathways and enhance insulin sensitivity [42]. This mechanism highlights their therapeutic potential in managing obesity-related diabetes through targeted regulation of gene networks.

**4.3. Crosstalk with Host Metabolism:** Microbial metabolites, including SCFAs and secondary bile acids, modulate host signaling pathways such as AMPK, PPARγ, and NF-κB. These pathways control vital processes like insulin signaling, adipogenesis, fatty acid oxidation, and inflammatory responses. By influencing these transcriptional programs, gut microbiota can shift the host's metabolic balance toward improved energy utilization and reduced fat storage [43]. Such interactions illustrate the dynamic bidirectional relationship between microbial metabolism and host metabolic health.

**5.1. Interindividual Variability:** The metabolic effects of natural products mediated via the gut microbiota vary greatly between individuals. This variability is driven by genetic differences, dietary habits, medication use, and baseline microbiome composition. As a result, interventions that work for one person may be less effective or ineffective in another. Understanding these personalized responses is essential for designing targeted therapies that maximize clinical benefits in obesity-associated diabetes [44].

**5.2. Bioavailability and Metabolism:** Many bioactive compounds from natural products undergo extensive chemical transformation in the gastrointestinal tract due to microbial metabolism and host enzymatic activity. These processes often reduce systemic bioavailability, thereby limiting therapeutic potency [45, 46]. Innovative strategies such as nanoemulsions, encapsulation, and targeted delivery systems are being developed to overcome these challenges, ensuring that active compounds reach their intended site of action at therapeutic concentrations [47].

**5.3. Complexity of Microbiota Interactions:** Gut microbiota-host interactions are highly complex, involving diverse microbial species and intricate metabolic networks. Determining causal links between specific microbes, their metabolites, and host health outcomes remains challenging. Multi-omics tools such as metagenomics, metabolomics, transcriptomics—are increasingly used to unravel these relationships. However, translating these findings into clinical interventions requires integrating large datasets with functional analyses to establish mechanistic insights and therapeutic targets in metabolic disorder [48].

**6.1. Personalized Nutrition:** Incorporating microbiome profiling into routine clinical practice could allow for precision dietary interventions using natural products tailored to an individual's microbial and metabolic profile. By targeting specific microbiota imbalances, such approaches could enhance therapeutic efficacy in obesity-associated diabetes [49]. Personalized nutrition would move beyond one-size-fits-all recommendations, enabling optimized diet-based treatments that align with an individual's genetic background, microbiome composition, and metabolic needs [50].

**6.2. Synbiotic Formulations:** Synbiotics, combinations of probiotics and prebiotics—offer a synergistic approach to restoring microbial balance and enhancing gut function. When probiotics are paired with prebiotic-rich natural products, they can promote the survival and activity of beneficial bacteria while boosting SCFA production [51]. Such formulations may improve insulin sensitivity, reduce inflammation, and modulate appetite-regulating hormones, making them promising adjuncts in obesity and diabetes management.

**6.3. Regulatory and Safety Considerations:** The therapeutic use of natural products in microbiome-targeted interventions requires rigorous standardization and quality control. Variations in raw materials, extraction methods, and formulation can affect efficacy and safety. Regulatory oversight and robust clinical trials are necessary to confirm reproducibility, ensure proper dosing, and minimize adverse effects. These steps will help translate promising experimental findings into safe, effective treatments for diverse populations.

### 7. Future Directions

High-resolution microbial mapping will facilitate the discovery of novel biomarkers and therapeutic targets, enabling precision interventions for obesity-associated diabetes. Longitudinal cohort studies are crucial to establish the long-term safety, sustainability, and clinical benefits of natural product-based therapies. Additionally, advances in microbial engineering and synthetic biology may enable the creation of customized probiotics capable of producing bioactive metabolites in situ, opening new frontiers in microbiome-driven metabolic health management.

## CONCLUSION

The gut microbiota emerges as a central player in the pathogenesis and potential treatment of obesity-associated diabetes. Natural products, with their rich chemical diversity and multi-targeted effects, hold immense promise as modulators of the gut ecosystem. By reshaping microbial composition, enhancing SCFA production, and reducing inflammation, these agents offer a holistic approach to metabolic disease management. Despite existing challenges, advances in systems biology, nutrigenomics, and translational research will accelerate the development of microbiota-targeted natural therapies. A personalized, microbiota-informed strategy represents the future frontier in combating the twin epidemics of obesity and diabetes.

## REFERENCES

1. Alfaris, N., Alqahtani, A.M., Alamuddin, N., Rigas, G.: Global Impact of Obesity. Gastroenterology Clinics of North America. 52, 277–293 (2023). https://doi.org/10.1016/j.gtc.2023.03.002
2. 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
3. Obesity and overweight, https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
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. Obesity Medicine. 54, 100585 (2025). https://doi.org/10.1016/j.obmed.2025.100585
5. 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. 103, e38088 (2024). https://doi.org/10.1097/MD.0000000000038088
6. Ainebyoona, C., Uti, D.E., Ugwu, O.P.-C., Edeh, F.O.: Unveiling the microbial orchestra: exploring the role of microbiota in cancer development and treatment. Discov Onc. 16, 646 (2025). https://doi.org/10.1007/s12672-025-02352-2
7. ALTVEŞ, S., YILDIZ, H.K., VURAL, H.C.: Interaction of the microbiota with the human body in health and diseases. Biosci Microbiota Food Health. 39, 23–32 (2020). https://doi.org/10.12938/bmfh.19-023
8. Ugwu, O.P.-C., Okon, M.B., Alum, E.U., Ugwu, C.N., Anyanwu, E.G., Mariam, B., Ogenyi, F.C., Eze, V.H.U., Anyanwu, C.N., Ezeonwumelu, J.O.C., Egba, S.I., Uti, D.E., Onohuean, H., Aja, P.M., Ugwu, M.N.: Unveiling the therapeutic potential of the gut microbiota–brain axis: Novel insights and clinical applications in neurological disorders. Medicine. 104, e43542 (2025). https://doi.org/10.1097/MD.0000000000043542
9. 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
10. Nogal, A., Valdes, A.M., Menni, C.: The role of short-chain fatty acids in the interplay between gut microbiota and diet in cardio-metabolic health. Gut Microbes. 13, 1897212. https://doi.org/10.1080/19490976.2021.1897212
11. Riedl, R.A., Atkinson, S.N., Burnett, C.M.L., Grobe, J.L., Kirby, J.R.: The Gut Microbiome, Energy Homeostasis, and Implications for Hypertension. Curr Hypertens Rep. 19, 27 (2017). https://doi.org/10.1007/s11906-017-0721-6
12. Famurewa, A.C., Orji, O.U., Aja, P.M., Nwite, F., Ohuche, S.E., Ukasoanya, S.C., Nnaji, L.O., Joshua, D., Igwe, K.U., Chima, S.F.: Nephroprotective effects of Datura stramonium leaves against methotrexate nephrotoxicity via attenuation of oxidative stress-mediated inflammation and apoptosis in rats. Avicenna J Phytomed. 13, 377–387 (2023). https://doi.org/10.22038/AJP.2023.21903
13. 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. Journal of Chemical Society of Nigeria. 47, (2022). https://doi.org/10.46602/jcsn.v47i5.819
14. Khameneh, B., Eskin, N.A.M., Iranshahy, M., Fazly Bazzaz, B.S.: Phytochemicals: A Promising Weapon in the Arsenal against Antibiotic-Resistant Bacteria. Antibiotics (Basel). 10, 1044 (2021). https://doi.org/10.3390/antibiotics10091044
15. Wu, Y., Zhou, A., Tang, L., Lei, Y., Tang, B., Zhang, L.: Bile Acids: Key Regulators and Novel Treatment Targets for Type 2 Diabetes. J Diabetes Res. 2020, 6138438 (2020). https://doi.org/10.1155/2020/6138438

16. Magne, F., Gotteland, M., Gauthier, L., Zazueta, A., Pesoa, S., Navarrete, P., Balamurugan, R.: The Firmicutes/Bacteroidetes Ratio: A Relevant Marker of Gut Dysbiosis in Obese Patients? Nutrients. 12, 1474 (2020). https://doi.org/10.3390/nu12051474
17. 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
18. Matera, M.: *Bifidobacteria*, *Lactobacilli*... when, how and why to use them. Global Pediatrics. 8, 100139 (2024). https://doi.org/10.1016/j.gpeds.2024.100139
19. Lozupone, C.A., Stombaugh, J.I., Gordon, J.I., Jansson, J.K., Knight, R.: Diversity, stability and resilience of the human gut microbiota. Nature. 489, 220–230 (2012). https://doi.org/10.1038/nature11550
20. Akhtar, M., Chen, Y., Ma, Z., Zhang, X., Shi, D., Khan, J.A., Liu, H.: Gut microbiota-derived short chain fatty acids are potential mediators in gut inflammation. Animal Nutrition. 8, 350–360 (2022). https://doi.org/10.1016/j.aninu.2021.11.005
21. van Deuren, T., Blaak, E.E., Canfora, E.E.: Butyrate to combat obesity and obesity-associated metabolic disorders: Current status and future implications for therapeutic use. Obes Rev. 23, e13498 (2022). https://doi.org/10.1111/obr.13498
22. Larabi, A.B., Masson, H.L.P., Bäumler, A.J.: Bile acids as modulators of gut microbiota composition and function. Gut Microbes. 15, 2172671. https://doi.org/10.1080/19490976.2023.2172671
23. Shen, Y., Fan, N., Ma, S., Cheng, X., Yang, X., Wang, G.: Gut Microbiota Dysbiosis: Pathogenesis, Diseases, Prevention, and Therapy. MedComm (2020). 6, e70168 (2025). https://doi.org/10.1002/mco2.70168
24. Di Vincenzo, F., Del Gaudio, A., Petito, V., Lopetuso, L.R., Scaldaferri, F.: Gut microbiota, intestinal permeability, and systemic inflammation: a narrative review. Intern Emerg Med. 19, 275–293 (2024). https://doi.org/10.1007/s11739-023-03374-w
25. Kim, H.-J., Kim, H., Lee, J.-H., Hwangbo, C.: Toll-like receptor 4 (TLR4): new insight immune and aging. Immun Ageing. 20, 67 (2023). https://doi.org/10.1186/s12979-023-00383-3
26. Dludla, P.V., Mabhida, S.E., Ziqubu, K., Nkambule, B.B., Mazibuko-Mbeje, S.E., Hanser, S., Basson, A.K., Pheiffer, C., Kengne, A.P.: Pancreatic β-cell dysfunction in type 2 diabetes: Implications of inflammation and oxidative stress. World J Diabetes. 14, 130–146 (2023). https://doi.org/10.4239/wjd.v14.i3.130
27. Prakash, V., Bose, C., Sunilkumar, D., Cherian, R.M., Thomas, S.S., Nair, B.G.: Resveratrol as a Promising Nutraceutical: Implications in Gut Microbiota Modulation, Inflammatory Disorders, and Colorectal Cancer. Int J Mol Sci. 25, 3370 (2024). https://doi.org/10.3390/ijms25063370
28. Chaplin, A., Carpéné, C., Mercader, J.: Resveratrol, Metabolic Syndrome, and Gut Microbiota. Nutrients. 10, 1651 (2018). https://doi.org/10.3390/nu10111651
29. Zhu, J., He, L.: The Modulatory Effects of Curcumin on the Gut Microbiota: A Potential Strategy for Disease Treatment and Health Promotion. Microorganisms. 12, 642 (2024). https://doi.org/10.3390/microorganisms12040642
30. Servida, S., Piontini, A., Gori, F., Tomaino, L., Moroncini, G., De Gennaro Colonna, V., La Vecchia, C., Vigna, L.: Curcumin and Gut Microbiota: A Narrative Overview with Focus on Glycemic Control. Int J Mol Sci. 25, 7710 (2024). https://doi.org/10.3390/ijms25147710
31. Xiong, H.-H., Lin, S.-Y., Chen, L.-L., Ouyang, K.-H., Wang, W.-J.: The Interaction between Flavonoids and Intestinal Microbes: A Review. Foods. 12, 320 (2023). https://doi.org/10.3390/foods12020320
32. Yang, Y., Trevethan, M., Wang, S., Zhao, L.: Beneficial Effects of Citrus Flavanones Naringin and Naringenin and Their Food Sources on Lipid Metabolism: An Update on Bioavailability, Pharmacokinetics, and Mechanisms. J Nutr Biochem. 104, 108967 (2022). https://doi.org/10.1016/j.jnutbio.2022.108967
33. Gao, J., Yuan, L., Jiang, H., Li, G., Zhang, Y., Zhou, R., Xian, W., Zou, Y., Du, Q., Zhou, X.: Naringenin modulates oxidative stress and lipid metabolism: Insights from network pharmacology, mendelian randomization, and molecular docking. Front Pharmacol. 15, 1448308 (2024). https://doi.org/10.3389/fphar.2024.1448308
34. Wang, H., Zhang, H., Gao, Z., Zhang, Q., Gu, C.: The mechanism of berberine alleviating metabolic disorder based on gut microbiome. Front Cell Infect Microbiol. 12, 854885 (2022). https://doi.org/10.3389/fcimb.2022.854885
35. Cortez-Navarrete, M., Pérez-Rubio, K.G., Escobedo-Gutiérrez, M. de J.: Role of Fenugreek, Cinnamon, Curcuma longa, Berberine and Momordica charantia in Type 2 Diabetes Mellitus Treatment: A Review. Pharmaceuticals (Basel). 16, 515 (2023). https://doi.org/10.3390/ph16040515
36. Sheng, W., Ji, G., Zhang, L.: Immunomodulatory effects of inulin and its intestinal metabolites. Front Immunol. 14, 1224092 (2023). https://doi.org/10.3389/fimmu.2023.1224092
37. Hughes, R.L., Alvarado, D.A., Swanson, K.S., Holscher, H.D.: The Prebiotic Potential of Inulin-Type Fructans: A Systematic Review. Advances in Nutrition. 13, 492–529 (2022). https://doi.org/10.1093/advances/nmab119

38. Edo, G.I., Mafe, A.N., Ali, A.B.M., Akpoghelie, P.O., Yousif, E., Isoje, E.F., Igbuku, U.A., Zainulabdeen, K., Owheruo, J.O., Essaghah, A.E.A., Umar, H., Ahmed, D.S., Alamiery, A.A.: A critical review on the impacts of β-glucans on gut microbiota and human health. The Microbe. 7, 100394 (2025). https://doi.org/10.1016/j.microb.2025.100394
39. Murphy, E.J., Rezoagli, E., Major, I., Rowan, N.J., Laffey, J.G.: β-Glucan Metabolic and Immunomodulatory Properties and Potential for Clinical Application. J Fungi (Basel). 6, 356 (2020). https://doi.org/10.3390/jof6040356
40. Vassiliou, E., Awoleye, O., Davis, A., Mishra, S.: Anti-Inflammatory and Antimicrobial Properties of Thyme Oil and Its Main Constituents. Int J Mol Sci. 24, 6936 (2023). https://doi.org/10.3390/ijms24086936
41. Kim, M.H., Kang, S.G., Park, J.H., Yanagisawa, M., Kim, C.H.: Short-chain fatty acids activate GPR41 and GPR43 on intestinal epithelial cells to promote inflammatory responses in mice. Gastroenterology. 145, 396-406.e1–10 (2013). https://doi.org/10.1053/j.gastro.2013.04.056
42. Liu, X., Shao, J., Liao, Y.-T., Wang, L.-N., Jia, Y., Dong, P., Liu, Z., He, D., Li, C., Zhang, X.: Regulation of short-chain fatty acids in the immune system. Front Immunol. 14, 1186892 (2023). https://doi.org/10.3389/fimmu.2023.1186892
43. Iqbal, M., Yu, Q., Tang, J., Xiang, J.: Unraveling the gut microbiota's role in obesity: key metabolites, microbial species, and therapeutic insights. J Bacteriol. 207, e00479-24. https://doi.org/10.1128/jb.00479-24
44. 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
45. 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
46. Saeed, E., Javed, F., Rana, Z., Perveen, R., Mallhi, I.Y., Amjad, I., Maqsood, Q., Chaudhary, N.A., Tahir, S.B., Fatima, A., Rasheed, N.F.: Bioactive Compounds, Their Mechanisms of Action, and Cardioprotective Effects of Pomegranate (Punica granatum): A Comprehensive Review. eFood. 6, e70075 (2025). https://doi.org/10.1002/efd2.70075
47. Nwuruku, O.A., 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
48. Alum, E.U., Ugwu, O.P.-C.: Artificial intelligence in personalized medicine: transforming diagnosis and treatment. Discov Appl Sci. 7, 193 (2025). https://doi.org/10.1007/s42452-025-06625-x
49. Hitch, T.C.A., Hall, L.J., Walsh, S.K., Leventhal, G.E., Slack, E., de Wouters, T., Walter, J., Clavel, T.: Microbiome-based interventions to modulate gut ecology and the immune system. Mucosal Immunology. 15, 1095–1113 (2022). https://doi.org/10.1038/s41385-022-00564-1
50. 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
51. Markowiak, P., Śliżewska, K.: Effects of Probiotics, Prebiotics, and Synbiotics on Human Health. Nutrients. 9, 1021 (2017). https://doi.org/10.3390/nu9091021

**CITE AS: Winniefred Nankya (2025). The Role of Gut Microbiota-Modulating Natural Products in Obesity-Associated Diabetes. IDOSR JOURNAL OF SCIENTIFIC RESEARCH 10(3):143-149. https://doi.org/10.59298/IDOSRJSR/2024/10.3.143149**