



# Natural Plant-Derived Inhibitors of Digestive Enzymes: A Novel Approach for Managing Obesity and Type 2 Diabetes-

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## ABSTRACT

Obesity and Type 2 Diabetes Mellitus (T2DM) are prevalent global health concerns, with an increasing incidence linked to modern lifestyle factors. The regulation of glucose and lipid metabolism is a crucial aspect of managing these conditions. Natural plant-derived inhibitors targeting digestive enzymes such as  $\alpha$ -amylase,  $\alpha$ -glucosidase, and lipase have emerged as promising therapeutic agents. These enzymes are pivotal in the breakdown of carbohydrates and fats in the digestive system. Inhibition of these enzymes reduces the absorption of glucose and lipids, contributing to better control of postprandial blood glucose levels and lipid profiles. This review aims to examine the plant compounds that have shown inhibitory activity against  $\alpha$ -amylase,  $\alpha$ -glucosidase, and lipase, discussing their mechanisms of action, therapeutic potential, and implications for managing obesity and T2DM. A selection of medicinal plants, including flavonoids, alkaloids, phenolics, and terpenoids, are highlighted for their potential to modulate digestive enzyme activity, thus providing an innovative and natural approach for managing metabolic disorders. The review also explores the clinical relevance of these inhibitors, their bioavailability, and the prospects for future development of natural enzyme inhibitors as adjunctive therapies for metabolic disease management.

**Keywords:** Obesity, Type 2 Diabetes Mellitus,  $\alpha$ -amylase,  $\alpha$ -glucosidase, lipase, digestive enzymes, plant-derived inhibitors, glucose metabolism, lipid metabolism.

## INTRODUCTION

Obesity and Type 2 Diabetes Mellitus (T2DM) are multifactorial metabolic diseases that have reached epidemic proportions globally, contributing significantly to healthcare costs and morbidity [1-4]. One of the central features of these conditions is dysregulated glucose and lipid metabolism, which leads to elevated blood glucose and abnormal lipid profiles, both of which are risk factors for cardiovascular diseases and other metabolic complications [1, 5, 6]. Lifestyle modifications, including diet and exercise, remain the cornerstone of managing these diseases, but pharmacological interventions are often required for effective disease control. Traditional pharmacological agents for managing T2DM, such as  $\alpha$ -glucosidase inhibitors (e.g., acarbose) and lipase inhibitors (e.g., orlistat), have limitations such as gastrointestinal side effects, poor patient adherence, and long-term safety concerns [7]. As a result, there has been increasing interest in alternative therapeutic options derived from natural sources. Plant-derived compounds have long been recognized for their therapeutic potential, and numerous studies have explored their effects on digestive enzyme inhibition as a means of regulating glucose and lipid metabolism [7]. The inhibition of digestive enzymes, particularly  $\alpha$ -amylase,  $\alpha$ -glucosidase, and lipase, represents a novel and effective approach to controlling postprandial glucose levels and lipid absorption, both of which are critical in managing obesity and T2DM.  $\alpha$ -Amylase and  $\alpha$ -glucosidase are enzymes responsible for breaking down complex carbohydrates into simpler sugars, which are then absorbed into the bloodstream, raising blood glucose levels [8]. Lipase, on the other hand, is responsible for breaking down dietary fats into free fatty acids and glycerol for absorption. By inhibiting these enzymes, the absorption of glucose and lipids can be reduced, thereby modulating blood sugar and lipid profiles in individuals with metabolic disorders [9]. This review aims to provide a comprehensive analysis of plant-derived inhibitors of  $\alpha$ -amylase,  $\alpha$ -glucosidase,

### Mechanisms of Action of Digestive Enzyme Inhibitors:

**$\alpha$ -Amylase Inhibition:**  $\alpha$ -Amylase plays a crucial role in carbohydrate metabolism by breaking down complex starches into smaller polysaccharides, maltose, and dextrins, which are then further hydrolyzed into glucose by other digestive enzymes such as maltase and isomaltase[10]. This enzymatic activity facilitates the rapid absorption of glucose into the bloodstream, which can lead to postprandial hyperglycemia, a major concern in type 2 diabetes mellitus (T2DM). By inhibiting  $\alpha$ -amylase, the breakdown of carbohydrates is significantly slowed, resulting in a gradual and controlled release of glucose[11]. This approach helps in stabilizing blood glucose levels, reducing insulin spikes, and improving overall glycemic control. Several plant-derived bioactive compounds, such as polyphenols, flavonoids, alkaloids, and tannins, have been identified as potent  $\alpha$ -amylase inhibitors[12, 13]. For instance, flavonoids from green tea (*Camellia sinensis*), phenolic acids from cinnamon (*Cinnamomum verum*), and tannins from pomegranate (*Punica granatum*) have shown substantial inhibitory activity against  $\alpha$ -amylase in various in vitro and in vivo studies. These natural inhibitors not only reduce carbohydrate digestion but also offer additional benefits such as antioxidant and anti-inflammatory properties, which further contribute to the management of T2DM. Unlike synthetic  $\alpha$ -amylase inhibitors such as acarbose, which can cause gastrointestinal discomfort and bloating due to undigested carbohydrates reaching the colon, plant-based inhibitors may offer a more tolerable and sustainable approach to managing diabetes.

**$\alpha$ -Glucosidase Inhibition:**  $\alpha$ -Glucosidase, an enzyme located in the brush border of the small intestine, is responsible for the final step in carbohydrate digestion, breaking down disaccharides like sucrose and maltose into glucose for absorption into the bloodstream. The inhibition of  $\alpha$ -glucosidase slows this conversion, thereby attenuating the rapid rise in postprandial blood glucose levels[14]. This mechanism is particularly beneficial for individuals with impaired glucose tolerance or insulin resistance, as it mitigates the excessive release of glucose into circulation after meals. Many plant-derived compounds, including flavonoids, terpenoids, saponins, and polyphenols, have been extensively studied for their  $\alpha$ -glucosidase inhibitory activity[15, 16]. For example, quercetin from onions (*Allium cepa*), ellagic acid from berries, and triterpenoids from bitter melon (*Momordica charantia*) have demonstrated potent inhibition of  $\alpha$ -glucosidase, effectively reducing postprandial hyperglycemia[17]. These natural inhibitors not only help in glycemic control but also provide additional metabolic benefits such as reducing oxidative stress and improving insulin sensitivity. Compared to pharmaceutical  $\alpha$ -glucosidase inhibitors like miglitol and voglibose, which can cause side effects like diarrhea, bloating, and flatulence, plant-based alternatives are often better tolerated due to their mild action and synergistic health benefits. The integration of these natural compounds into dietary interventions or nutraceutical formulations represents a promising strategy for managing T2DM with fewer side effects and improved patient compliance.

**Lipase Inhibition:** Lipase is a key digestive enzyme responsible for breaking down dietary triglycerides into free fatty acids and monoglycerides, which are then absorbed through the intestinal mucosa and transported into systemic circulation[17]. Excessive lipid absorption contributes to obesity, dyslipidemia, and insulin resistance, all of which are closely associated with metabolic disorders like T2DM. The inhibition of pancreatic lipase reduces the hydrolysis and absorption of dietary fats, thereby decreasing postprandial triglyceride levels and overall fat accumulation in the body[18, 19]. Plant-derived lipase inhibitors, such as polyphenols, flavonoids, and alkaloids, have gained considerable attention as potential anti-obesity agents. For instance, epigallocatechin gallate (EGCG) from green tea, curcumin from turmeric (*Curcuma longa*), and saponins from ginseng (*Panax ginseng*) have demonstrated strong lipase inhibitory effects in preclinical and clinical studies[20–22]. These bioactive compounds not only prevent excessive fat absorption but also exhibit anti-inflammatory and lipid-lowering properties, which are essential for cardiovascular health. Unlike synthetic lipase inhibitors like orlistat, which is associated with adverse gastrointestinal effects such as steatorrhea (fatty stools), bloating, and nutrient malabsorption, plant-based inhibitors provide a gentler and more holistic approach to weight and lipid management[20]. Additionally, these natural compounds have been shown to modulate gut microbiota, promoting the growth of beneficial bacteria that contribute to metabolic health. By incorporating plant-derived lipase inhibitors into functional foods or dietary supplements, it is possible to support weight management and lipid control in individuals with obesity and T2DM, offering a sustainable and natural alternative to conventional pharmaceutical treatments.

### Plant-Derived Inhibitors of Digestive Enzymes

Several plant-derived compounds have demonstrated inhibitory activity against digestive enzymes, with a variety of mechanisms contributing to their efficacy. These bioactive compounds include flavonoids, polyphenols, alkaloids, terpenoids, and other secondary metabolites. The following sections explore some of the most notable plant-derived inhibitors of  $\alpha$ -amylase,  $\alpha$ -glucosidase, and lipase.

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**Flavonoids:** Flavonoids are a diverse class of polyphenolic compounds widely found in fruits, vegetables, tea, and medicinal plants[23]. These naturally occurring compounds have garnered significant attention in scientific research due to their potential in preventing and managing metabolic disorders, including diabetes, obesity, and dyslipidemia. One of the primary mechanisms through which flavonoids exert their metabolic benefits is by inhibiting key digestive enzymes involved in carbohydrate and lipid metabolism[24]. By targeting enzymes such as  $\alpha$ -amylase,  $\alpha$ -glucosidase, and pancreatic lipase, flavonoids help regulate postprandial glucose levels, reduce lipid absorption, and mitigate obesity-related complications. Their multifunctional properties, including antioxidant, anti-inflammatory, and insulin-sensitizing effects, further enhance their therapeutic potential. This section highlights some of the most well-researched flavonoids—quercetin, kaempferol, and epigallocatechin gallate (EGCG)—and their enzyme-inhibitory properties in metabolic regulation.

Quercetin, a flavonol commonly found in apples, onions, berries, and tea, has been extensively studied for its metabolic benefits[25, 26]. Research indicates that quercetin inhibits  $\alpha$ -amylase and  $\alpha$ -glucosidase, two key enzymes responsible for breaking down complex carbohydrates into simple sugars. By slowing carbohydrate digestion, quercetin reduces the rapid spikes in blood glucose levels following meals, making it a promising natural agent for managing type 2 diabetes[27]. Additionally, quercetin exhibits inhibitory activity against pancreatic lipase, an enzyme essential for fat digestion and absorption. This mechanism contributes to its potential role in weight management and lipid metabolism regulation. Beyond its enzyme-inhibitory effects, quercetin has demonstrated anti-inflammatory and antioxidant properties, which may further support cardiovascular health by reducing oxidative stress and improving endothelial function. These combined effects make quercetin an important bioactive compound in functional foods and nutraceuticals targeting metabolic disorders.

Kaempferol, another flavonoid with promising metabolic effects, is abundant in foods such as kale, spinach, and tea[28]. Similar to quercetin, kaempferol has been shown to inhibit  $\alpha$ -amylase and  $\alpha$ -glucosidase, leading to reduced glucose absorption and improved glycemic control. Studies suggest that kaempferol supplementation can help lower postprandial glucose levels, thereby reducing the risk of insulin resistance and type 2 diabetes. Additionally, kaempferol's anti-obesity potential stems from its ability to modulate lipid metabolism and reduce fat accumulation in adipose tissues. By influencing key signaling pathways involved in energy balance, kaempferol may offer protective effects against obesity-related metabolic disturbances. Furthermore, its anti-inflammatory and antioxidative properties contribute to its ability to mitigate chronic diseases associated with metabolic syndrome.[28] The growing body of evidence supporting kaempferol's role in metabolic health suggests that it could be an essential component of dietary interventions and plant-based therapies for diabetes and obesity management.

Epigallocatechin gallate (EGCG), the most abundant catechin in green tea, is widely recognized for its potent metabolic benefits[20, 21]. EGCG has been shown to significantly inhibit  $\alpha$ -glucosidase, delaying carbohydrate breakdown and reducing postprandial hyperglycemia. Additionally, EGCG's inhibition of pancreatic lipase contributes to decreased fat absorption, making it a valuable natural agent for weight management. Studies have also highlighted EGCG's role in enhancing insulin sensitivity, promoting fat oxidation, and modulating gut microbiota composition—factors that collectively support metabolic homeostasis. Moreover, EGCG's antioxidant properties play a crucial role in protecting pancreatic  $\beta$ -cells from oxidative damage, which is a key factor in diabetes progression[20]. The combination of these mechanisms makes EGCG a promising compound for developing functional foods, dietary supplements, and pharmacological agents aimed at controlling metabolic disorders. Given the substantial evidence supporting its benefits, EGCG continues to be a focal point of research in the field of metabolic health and nutrition.

**Phenolic Acids:** Phenolic acids are a diverse group of bioactive compounds commonly found in fruits, vegetables, and whole grains, known for their potent antioxidant and enzyme-inhibitory properties[29]. Among the most studied phenolic acids are caffeic acid, chlorogenic acid, and ferulic acid, all of which have demonstrated significant inhibitory effects on  $\alpha$ -amylase and  $\alpha$ -glucosidase—two key enzymes involved in carbohydrate digestion[30]. These compounds exert their effects by binding to the active sites of digestive enzymes, thereby obstructing substrate access and reducing enzymatic activity. This mechanism effectively slows down the breakdown of complex carbohydrates into simple sugars, leading to a lower postprandial blood glucose level[31]. Consequently, the inhibition of these enzymes by phenolic acids plays a crucial role in glycemic control and the management of hyperglycemia, particularly in individuals with type 2 diabetes mellitus (T2DM). Additionally, phenolic acids contribute to overall metabolic health by exhibiting anti-inflammatory and antioxidant effects, which may further support insulin sensitivity and pancreatic function [32].

**Alkaloids:** Alkaloids are nitrogen-containing secondary metabolites widely distributed in medicinal plants, many of which possess significant biological activities, including enzyme inhibition[33, 34]. A well-known alkaloid, **berberine**, derived from *Berberis* species and other medicinal plants, has been extensively studied for its potential in diabetes management[35, 36]. Berberine has been shown to strongly inhibit  $\alpha$ -glucosidase and

$\alpha$ -amylase, thereby limiting carbohydrate digestion and reducing glucose absorption in the intestine. Additionally, berberine exerts beneficial effects on glucose metabolism by improving insulin sensitivity, enhancing glucose uptake in peripheral tissues, and modulating gut microbiota composition. Beyond its enzyme-inhibitory properties, berberine is also known for its anti-inflammatory, antioxidant, and lipid-lowering effects, making it a multifunctional compound in the fight against T2DM and related metabolic disorders[36]. These findings underscore the therapeutic potential of alkaloids as natural inhibitors of digestive enzymes, providing a complementary approach to conventional diabetes treatments.

**Terpenoids:** Terpenoids, a large and diverse class of naturally occurring plant compounds, include bioactive molecules such as saponins, essential oils, and various phytochemicals with significant medicinal properties[37, 38]. Among these, **ginsenosides**, the primary active components of *Panax ginseng*, have garnered substantial attention for their potential in diabetes management. Ginsenosides have been shown to inhibit both  $\alpha$ -amylase and  $\alpha$ -glucosidase, thereby reducing carbohydrate breakdown and postprandial glucose spikes[39,40,41,42,43,44,45]. Moreover, studies suggest that ginsenosides can enhance insulin sensitivity by modulating insulin receptor signaling pathways and promoting glucose uptake in skeletal muscle and adipose tissues. Beyond their hypoglycemic effects, terpenoids also exhibit anti-inflammatory and antioxidant properties, which may help mitigate diabetes-associated complications such as oxidative stress and chronic inflammation. Given these multifaceted benefits, terpenoids hold great promise as natural therapeutic agents for controlling blood glucose levels and improving metabolic health.

**Tannins:** Tannins, a subgroup of polyphenolic compounds abundantly present in tea, berries, nuts, and other plant-based foods, have been recognized for their ability to modulate metabolic pathways and inhibit digestive enzymes[46,47,48,49,50]. These compounds have demonstrated significant inhibitory effects on  $\alpha$ -amylase and lipase, which are key enzymes involved in carbohydrate and lipid metabolism. By blocking  $\alpha$ -amylase activity, tannins slow the digestion of starches and reduce glucose absorption, contributing to improved glycemic control[51,52,53]. In addition, their inhibitory effect on lipase reduces fat absorption in the intestine, which may help in the management of obesity and dyslipidemia. Beyond their enzyme-inhibitory functions, tannins exhibit strong antioxidant and anti-inflammatory activities, protecting against oxidative stress and inflammation commonly associated with metabolic diseases[41]. This dual action of tannins—regulating both glucose and lipid metabolism—positions them as potential therapeutic agents for the prevention and management of diabetes and obesity-related complications.

#### Other Compounds

Several other bioactive compounds have demonstrated promising enzyme-inhibitory effects, contributing to their potential role in diabetes and metabolic disease management. Curcumin, the principal bioactive compound in *Curcuma longa* (turmeric), has been shown to inhibit  $\alpha$ -amylase and lipase activity, thereby modulating glucose and lipid metabolism[42]. Curcumin's ability to reduce postprandial glucose levels and prevent fat accumulation highlights its potential for managing both hyperglycemia and dyslipidemia. Additionally, curcumin possesses strong anti-inflammatory and antioxidant properties, which may further enhance insulin sensitivity and pancreatic  $\beta$ -cell function[42]. Similarly, gingerol, the bioactive component of *Zingiber officinale* (ginger), has been reported to inhibit  $\alpha$ -amylase and  $\alpha$ -glucosidase activity, thereby slowing carbohydrate digestion and glucose absorption[43]. This effect makes gingerol a valuable natural compound for controlling postprandial glucose fluctuations. Furthermore, gingerol has been associated with anti-inflammatory and insulin-sensitizing properties, which may contribute to better glycemic control in individuals with insulin resistance[44]. Given the broad spectrum of benefits offered by these bioactive compounds, they hold significant potential as natural adjuncts to conventional therapies for managing diabetes and metabolic disorders.

#### Therapeutic Implications and Clinical Relevance:

The development of natural enzyme inhibitors as adjunctive therapies for obesity and T2DM has several advantages over conventional pharmaceutical agents. These plant-derived compounds generally have fewer side effects, are widely available, and are often more affordable. Furthermore, they can be incorporated into dietary interventions, making them an appealing option for long-term management. However, there are several challenges that need to be addressed before plant-derived inhibitors can be widely used in clinical settings. These include issues of bioavailability, formulation, and the need for clinical trials to validate their efficacy and safety. Many bioactive compounds from plants exhibit low bioavailability due to poor absorption in the gastrointestinal tract, which limits their effectiveness. Therefore, innovative delivery systems and strategies, such as nano formulations and adjuvants, are required to enhance the bioavailability and therapeutic potential of these compounds.

#### CONCLUSION

Plant-derived inhibitors of digestive enzymes represent a promising strategy for managing obesity and Type 2 Diabetes Mellitus. By targeting  $\alpha$ -amylase,  $\alpha$ -glucosidase, and lipase, these natural compounds can modulate glucose and lipid metabolism, helping to control postprandial blood sugar and lipid levels. A diverse range of

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plant-based compounds, including flavonoids, alkaloids, phenolic acids, and terpenoids, have shown potential for therapeutic use in metabolic disorders. However, further research, including clinical trials and exploration of formulation strategies, is essential to translate these findings into effective treatments. Natural enzyme inhibitors may provide an important complementary approach to conventional therapies for the management of obesity and T2DM, supporting better metabolic control and improving patient outcomes.

#### REFERENCES

1. 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>
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., Gatashah, 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., 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. Annett, S., Moore, G., Robson, T.: Obesity and Cancer Metastasis: Molecular and Translational Perspectives. *Cancers.* 12, 3798 (2020). <https://doi.org/10.3390/cancers12123798>
6. 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>
7. Akmal, M., Patel, P., Wadhwa, R.: Alpha Glucosidase Inhibitors. In: *StatPearls*. StatPearls Publishing, Treasure Island (FL) (2025)
8. Benrahou, K., Naceiri Mrabti, H., Bouyahya, A., Daoudi, N.E., Bnouham, M., Mezzour, H., Mahmud, S., Alshahrani, M.M., Obaidullah, A.J., Cherrah, Y., Faouzi, M.E.A.: Inhibition of  $\alpha$ -Amylase,  $\alpha$ -Glucosidase, and Lipase, Intestinal Glucose Absorption, and Antidiabetic Properties by Extracts of *Erodium guttatum*. *Evid.-Based Complement. Altern. Med. ECAM.* 2022, 5868682 (2022). <https://doi.org/10.1155/2022/5868682>
9. Haguët, Q., Le Joubioux, F., Chavanelle, V., Groult, H., Schoonjans, N., Langhi, C., Michaux, A., Otero, Y.F., Boisseau, N., Peltier, S.L., Sirvent, P., Maugard, T.: Inhibitory Potential of  $\alpha$ -Amylase,  $\alpha$ -Glucosidase, and Pancreatic Lipase by a Formulation of Five Plant Extracts: TOTUM-63. *Int. J. Mol. Sci.* 24, 3652 (2023). <https://doi.org/10.3390/ijms24043652>
10. des Gachons, C.P., Breslin, P.A.S.: Salivary Amylase: Digestion and Metabolic Syndrome. *Curr. Diab. Rep.* 16, 102 (2016). <https://doi.org/10.1007/s11892-016-0794-7>
11. González, P., Lozano, P., Ros, G., Solano, F.: Hyperglycemia and Oxidative Stress: An Integral, Updated and Critical Overview of Their Metabolic Interconnections. *Int. J. Mol. Sci.* 24, 9352 (2023). <https://doi.org/10.3390/ijms24119352>
12. Intharuksa, A., Kuljarusnont, S., Sasaki, Y., Tungmunnithum, D.: Flavonoids and Other Polyphenols: Bioactive Molecules from Traditional Medicine Recipes/Medicinal Plants and Their Potential for Phytopharmaceutical and Medical Application. *Molecules.* 29, 5760 (2024). <https://doi.org/10.3390/molecules29235760>
13. 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>
14. Khoo, C.M.: Diabetes Mellitus Treatment. In: Quah, S.R. (ed.) *International Encyclopedia of Public Health (Second Edition)*. pp. 288–293. Academic Press, Oxford (2017)
15. Sharma, K., Kaur, R., Kumar, S., Saini, R.K., Sharma, S., Pawde, S.V., Kumar, V.: Saponins: A concise review on food related aspects, applications and health implications. *Food Chem. Adv.* 2, 100191 (2023). <https://doi.org/10.1016/j.focha.2023.100191>
16. Suryavanshi, S.V., Kulkarni, Y.A.: Toxicity of escin-triterpene saponins from *Aesculus*. *Toxicol. Environ. Chem.* 104, 141–148 (2022). <https://doi.org/10.1080/02772248.2021.1996577>
17. 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>

18. 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>
19. Górczyńska-Kosiorz, S., Kosiorz, M., Dziegielewska-Gęsiak, S.: Exploring the Interplay of Genetics and Nutrition in the Rising Epidemic of Obesity and Metabolic Diseases. *Nutrients*. 16, 3562 (2024). <https://doi.org/10.3390/nu16203562>
20. Andreu Fernández, V., Almeida Toledano, L., Pizarro Lozano, N., Navarro Tapia, E., Gómez Roig, M.D., De la Torre Fornell, R., García Algar, Ó.: Bioavailability of Epigallocatechin Gallate Administered with Different Nutritional Strategies in Healthy Volunteers. *Antioxidants*. 9, 440 (2020). <https://doi.org/10.3390/antiox9050440>
21. Bakun, P., Mlynarczyk, D.T., Koczorowski, T., Cerbin-Koczorowska, M., Piwowarczyk, L., Kolasiński, E., Stawny, M., Kuźmińska, J., Jelińska, A., Goslinski, T.: Tea-break with epigallocatechin gallate derivatives – Powerful polyphenols of great potential for medicine. *Eur. J. Med. Chem.* 261, 115820 (2023). <https://doi.org/10.1016/j.ejmech.2023.115820>
22. 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>
23. Ioannou, I., Chekir, L., Ghoul, M.: Effect of Heat Treatment and Light Exposure on the Antioxidant Activity of Flavonoids. *Processes*. 8, 1078 (2020). <https://doi.org/10.3390/pr8091078>
24. Sandoval, V., Sanz-Lamora, H., Arias, G., Marrero, P.F., Haro, D., Relat, J.: Metabolic Impact of Flavonoids Consumption in Obesity: From Central to Peripheral. *Nutrients*. 12, 2393 (2020). <https://doi.org/10.3390/nu12082393>
25. Aghababaei, F., Hadidi, M.: Recent Advances in Potential Health Benefits of Quercetin. *Pharmaceuticals*. 16, 1020 (2023). <https://doi.org/10.3390/ph16071020>
26. Chiang, M.-C., Tsai, T.-Y., Wang, C.-J.: The Potential Benefits of Quercetin for Brain Health: A Review of Anti-Inflammatory and Neuroprotective Mechanisms. *Int. J. Mol. Sci.* 24, 6328 (2023). <https://doi.org/10.3390/ijms24076328>
27. Dong, J., Zhang, X., Zhang, L., Bian, H.-X., Xu, N., Bao, B., Liu, J.: Quercetin reduces obesity-associated ATM infiltration and inflammation in mice: a mechanism including AMPK $\alpha$ 1/SIRT1. *J. Lipid Res.* 55, 363 (2014). <https://doi.org/10.1194/jlr.M038786>
28. Chen, A.Y., Chen, Y.C.: A review of the dietary flavonoid, kaempferol on human health and cancer chemoprevention. *Food Chem.* 138, 2099–2107 (2013). <https://doi.org/10.1016/j.foodchem.2012.11.139>
29. 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>
30. Kanchanasurakit, S., Saokaew, S., Phisalprapa, P., Duangjai, A.: Chlorogenic acid in green bean coffee on body weight: a systematic review and meta-analysis of randomized controlled trials. *Syst. Rev.* 12, 163 (2023). <https://doi.org/10.1186/s13643-023-02311-4>
31. Nguyen, V., Taine, E.G., Meng, D., Cui, T., Tan, W.: Chlorogenic Acid: A Systematic Review on the Biological Functions, Mechanistic Actions, and Therapeutic Potentials. *Nutrients*. 16, 924 (2024). <https://doi.org/10.3390/nu16070924>
32. Alum, E.U., Nwuruku, A.O., Edwin, N.: Targeting oxidative stress in cancer management: The role of antioxidant phytochemicals. *KIU J. Health Sci.* 4, 1–10 (2024). <https://doi.org/10.59568/KJHS-2024-4-2-01>
33. Heinrich, M., Mah, J., Amirikia, V.: Alkaloids Used as Medicines: Structural Phytochemistry Meets Biodiversity—An Update and Forward Look. *Molecules*. 26, 1836 (2021). <https://doi.org/10.3390/molecules26071836>
34. Ma, Z., Wang, S., Miao, W., Zhang, Z., Yu, L., Liu, S., Luo, Z., Liang, H., Yu, J., Huang, T., Li, M., Gao, J., Su, S., Li, Y., Zhou, L.: The Roles of Natural Alkaloids and Polyphenols in Lipid Metabolism: Therapeutic Implications and Potential Targets in Metabolic Diseases. *Curr. Med. Chem.* 30, 3649–3667 (2023). <https://doi.org/10.2174/0929867330666221107095646>
35. 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>
36. 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)
37. 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>

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

38. Siddiqui, T., Khan, M.U., Sharma, V., Gupta, K.: Terpenoids in essential oils: Chemistry, classification, and potential impact on human health and industry. *Phytomedicine Plus*. 4, 100549 (2024). <https://doi.org/10.1016/j.phyplu.2024.100549>
39. Tang, P., Liu, S., Zhang, J., Ai, Z., Hu, Y., Cui, L., Zou, H., Li, X., Wang, Y., Nan, B., Wang, Y.: Ginsenosides as dietary supplements with immunomodulatory effects: a review. *Appl. Biol. Chem.* 67, 27 (2024). <https://doi.org/10.1186/s13765-024-00881-y>
40. Ozogul, Y., Ucar, Y., Tadesse, E.E., Rathod, N., Kulawik, P., Trif, M., Esatbeyoglu, T., Ozogul, F.: Tannins for food preservation and human health: A review of current knowledge. *Appl. Food Res.* 5, 100738 (2025). <https://doi.org/10.1016/j.afres.2025.100738>
41. Alum, E.U.: Role of Phytochemicals in Cardiovascular Disease Management: Insights into Mechanisms, Efficacy, and Clinical Application. *Phytomedicine Plus*. 100695 (2024). <https://doi.org/10.1016/j.phyplu.2024.100695>
42. El-Saadony, M.T., Yang, T., Korma, S.A., Sitohy, M., Abd El-Mageed, T.A., Selim, S., Al Jaouni, S.K., Salem, H.M., Mahmmoud, Y., Soliman, S.M., Mo'men, S.A.A., Mosa, W.F.A., El-Wafai, N.A., Abou-Aly, H.E., Sitohy, B., Abd El-Hack, M.E., El-Tarabily, K.A., Saad, A.M.: Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. *Front. Nutr.* 9, 1040259 (2023). <https://doi.org/10.3389/fnut.2022.1040259>
43. Ebrahimzadeh Attari, V., Malek Mahdavi, A., Javadivala, Z., Mahluji, S., Zununi Vahed, S., Ostadrahimi, A.: A systematic review of the anti-obesity and weight lowering effect of ginger (*Zingiber officinale* Roscoe) and its mechanisms of action. *Phytother. Res. PTR.* 32, 577-585 (2018). <https://doi.org/10.1002/ptr.5986>
44. Seo, S.H., Fang, F., Kang, I.: Ginger (*Zingiber officinale*) Attenuates Obesity and Adipose Tissue Remodeling in High-Fat Diet-Fed C57BL/6 Mice. *Int. J. Environ. Res. Public Health.* 18, 631 (2021). <https://doi.org/10.3390/ijerph18020631>
45. Aja PM, IO Igwenyi, PU Okechukwu, OU Orji, EU Alum. Evaluation of anti-diabetic effect and liver function indices of ethanol extracts of *Moringa oleifera* and *Cajanus cajan* leaves in alloxan induced diabetic albino rats *Global Veterinaria* 14(3) 439-447 (2015).
46. Offor CE, OPC Ugwu, EU Alum. The anti-diabetic effect of ethanol leaf-extract of *Allium sativum* on Albino rats. *International Journal of Pharmacy and Medical Sciences*, 4, (1), 01-03 (2014).
47. Enechi OC, H Ikenna Oluka, PC Okechukwu Ugwu. Acute toxicity, lipid peroxidation and ameliorative properties of *Alstonia boonei* ethanol leaf extract on the kidney markers of alloxan induced diabetic rats. *African journal of biotechnology*, 13, 5 (2014).
48. Adonu CC, OP Ugwu, A Bawa, EC Ossai, AC Nwaka. Intrinsic blood coagulation studies in patients suffering from both diabetes and hypertension. *Int Journal of Pharmaceutical Medicine and Bio Science*, 2 (2), 36-45 (2013).
49. Okechukwu Paul-Chima Ugwu, Esther Ugo Alum, Michael Ben Okon, Patrick M Aja, Emmanuel Ifeanyi Obeagu, EC Onyeneke Ethanol root extract and fractions of *Sphenocentrum jollyanum* abrogate hyperglycaemia and low body weight in streptozotocin-induced diabetic Wistar albino rats Oxford University Press 2(2) 10 (2023).
50. Mariam Oyedeki Amusa and Adeyinka Olufemi Adepoju Okechukwu P. C. Ugwu, Esther Ugo Alum, Emmanuel I. Obeagu, Michael Ben Okon, Patrick M. Aja , Awotunde Oluwasegun Samson Effect of Ethanol leaf extract of *Chromolaena odorata* on lipid profile of streptozotocin induced diabetic wistar albino rats. *IAA Journal of Biological Sciences*, 10, (1), 109-117 (2023).
51. Alum EU, GU Umoru, DE Utu, PM Aja, OP Ugwu, OU Orji, BU Nwali, NN Ezeani, N Edwin, FO Orinya HEPATO-PROTECTIVE EFFECT OF ETHANOL LEAF EXTRACT OF *Datura stramonium* in ALLOXAN-INDUCED DIABETIC ALBINO RATS. *Journal of Chemical Society of Nigeria*, 47, 5 (2022).
52. Ugwu Okechukwu P.C. and Amasiorah V.I. The effects of the crude ethanol root extract and fractions of *Sphenocentrum jollyanum* on hematological indices and glycosylated haemoglobin of streptozotocin-induced diabetic. *INOSR Scientific Research*, 6, (1), 61-74 (2020).
53. Enechi OC, IH Oluka, OPC Ugwu, YS Omeh Effect of ethanol leaf extract of *Alstonia boonei* on the lipid profile of alloxan induced diabetic rats. *World Journal of Pharmacy and Pharmaceutical Sciences (WJPPS)*, 2013, Vol. 2, No. 3, 782-795(2012).

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