16 Phenolic Bioactive as Promising Natural Therapeutics for Obesity Control

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Abstract

Obesity has emerged as a major global health concern and is now considered to have reached epidemic or pandemic levels worldwide. Although growing research highlights the potential role of phenolic compounds in the management of obesity, their exact mechanisms and overall effectiveness are still not fully clarified. Various in vitro and in vivo investigations have indicated that phenolic compounds may contribute to obesity control through multiple mechanisms, including reduction of food consumption, suppression of lipogenesis, enhancement of lipolysis, stimulation of fatty acid β-oxidation, inhibition of adipocyte formation and proliferation, reduction of inflammatory responses, and mitigation of oxidative stress. This review summarizes recent findings regarding the anti-obesity potential of phenolic compounds derived from plants, nutraceuticals, and functional foods, based on experimental, animal, and clinical studies. Particular emphasis has been placed on widely consumed plant-based products such as cocoa, cinnamon, olive oil, and beverages including red wine, green, white and black tea, as well as Hibiscus sabdariffa L. tea, among others.

Keywords: Obesity, Phenolic Compounds, Natural Products, Metabolic Syndrome.

Introduction

The globe Health Organization (WHO) has designated obesity as a global epidemic, and it is widely acknowledged as one of the biggest public health issues facing the globe today. The body mass index (BMI), which measures body weight in relation to height (kg/m2), is frequently used to determine whether a person is overweight or obese. People with a BMI of 25–29.9 kg/m² are typically classified as overweight, while those with a BMI of 30 kg/m² or greater are considered obese, though BMI thresholds may fluctuate among other populations and ethnic groups. A BMI of 40 kg/m² or higher is usually considered severe or class III obesity. Genetic predisposition, environmental variables, and behavioral factors interact to cause obesity, a complicated disorder. Its development is significantly influenced by dietary practices, lifestyle decisions, and socioeconomic circumstances. A prolonged imbalance between energy intake and energy expenditure is the main cause of the disease, which is frequently linked to excessive calorie intake and decreased physical activity. Obesity is associated with substantial changes in the physiology and function of adipose tissue in addition to the build-up of extra fat. Obesity has been shown to induce a chronic state of low-grade inflammation in human white adipose tissue. There is growing evidence that this inflammatory environment has a role in the development of several metabolic illnesses associated with obesity, such as dyslipidemia, cardiovascular diseases, and type 2 diabetes mellitus (T2DM). Elevated triglyceride concentrations and decreased high-density lipoprotein (HDL) cholesterol levels are common characteristics of these problems, which raise the risk of unfavorable health outcomes.

Although managing and preventing obesity necessitates a multifaceted strategy, food adjustment continues to be one of the most significant and manageable aspects. Eating habits have changed significantly across populations in recent decades. Modern diets differ from traditional ones in that they consume more meat, fish, alcoholic beverages, and some fruits while consuming fewer vegetables, legumes, grains, olive oil, and wine. The total consumption of bioactive phytochemicals, especially phenolic compounds, has been impacted by these changes in dietary preferences. Dietary polyphenols have garnered significant attention from researchers, nutritionists, and the food industry due to their possible health benefits. Since the 1990s, there has been a significant increase in scientific interest in phenolic compounds due to epidemiological evidence that regular consumption of foods high in polyphenols is linked to a lower risk of various chronic disorders, such as cancer and cardiovascular diseases. Additionally, results from dietary intervention and observational studies suggest that consuming more dietary polyphenols may be associated with a lower incidence of obesity, underscoring the possible function of these substances in controlling body weight and metabolic health.

Worldwide Status of Obesity

As a significant contributor to the incidence of non-communicable illnesses, obesity has emerged as one of the most urgent global public health issues. According to recent estimates from the World Health Organization, over one billion people worldwide suffer from obesity. Approximately 2.5 billion adults were considered overweight in 2022, with nearly 890 million of them being obese. Additionally, 16% of adults worldwide were obese, and 43% of adults were overweight. Over the past three decades, there has been a significant increase in the incidence of obesity; since 1990, adult obesity rates have more than doubled, while

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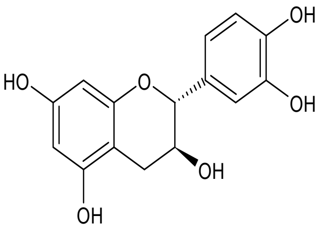
juvenile obesity rates have increased fourfold. Globally, there are significant health, social, and economic issues as a result of the rising incidence of obesity in both adults and children. Excessive adipose tissue formation brought on by a lack of balance between energy consumption and expenditure is the hallmark of obesity. The contemporary obesity epidemic is primarily caused by environmental factors, food choices, and sedentary lifestyles, even though genetic predisposition plays a role in obesity susceptibility. The illness greatly raises morbidity, mortality, and healthcare costs globally since it is closely linked to a number of metabolic disorders, such as type 2 diabetes mellitus, cardiovascular diseases, dyslipidemia, and several types of cancer. It is becoming more widely acknowledged that obesity is a chronic inflammatory disease that has a substantial impact on metabolic balance and immunological function. Adipocytes, preadipocytes, fibroblasts, vascular cells, and different immune cells, especially macrophages, make up adipose tissue, which is now regarded as a dynamic endocrine organ rather than just a passive energy storage location. Increased macrophage infiltration and increased adipocyte release of a variety of bioactive chemicals known as adipokines are linked to the growth of adipose tissue in obesity. These adipokines are essential for maintaining a low-grade systemic inflammatory state.

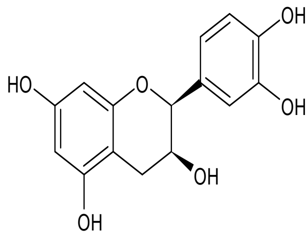
Role of Phenolic Compounds in Nutraceuticals and Functional Foods

The idea of a nutritious diet has changed significantly over the past few decades due to increased healthcare costs, longer life expectancies, improvements in science, and the quick development of cutting-edge technologies. Consumer awareness of the connection between diet and health has increased as a result of these factors, which has stimulated study in the fields of food, nutrition, and biochemical sciences with the goal of creating goods that promote optimal physiological function, fend off disease, and improve general quality of life. In this regard, functional foods and nutraceuticals have drawn a lot of attention as successful methods for managing and preventing nutrition-related illnesses while enhancing physical and mental health. At the same time, natural products have gained popularity as important sources of bioactive substances with potential medical applications. Over half of the medications currently utilized in clinical practice globally are thought to be derived from natural sources. Because of their high concentration of phenolic compounds, which have a variety of biological and pharmacological properties, higher plants make up a significant portion of these sources.

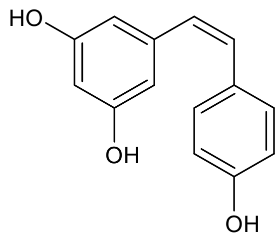
One of the biggest and most varied families of non-essential dietary phytochemicals that plants produce as secondary metabolites in response to environmental and physiological stress is phenolic compounds. These compounds are distinguished structurally by the existence of one or more aromatic rings with one or more hydroxyl groups. Over 8,000 phenolic compounds with a wide range of structural variations have been found in nature to date. Despite the fact that phenolics have long been used as naturally occurring food colorants and additives, scholarly interest in these substances grew significantly in the 1990s after epidemiological data showed a negative correlation between the occurrence of chronic diseases, such as cancer and cardiovascular disorders, and the consumption of foods high in phenolics. Phenolic chemicals are divided into flavonoids and non-flavonoids according to their chemical structure. While non-flavonoid phenolics include substances like phenolic acids, which make up a significant fraction of dietary phenolics, flavonoids are a broad class of polyphenolic molecules with a fifteen-carbon skeleton structured as two aromatic rings connected by a carbon bridge. The potential anti-obesity properties of phenolic compounds, such as epigallocatechin gallate, resveratrol, catechins, quercetin, and anthocyanins, have garnered significant scientific interest in recent years.



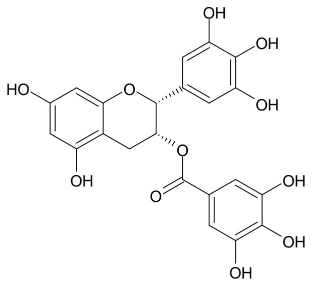
Catechin



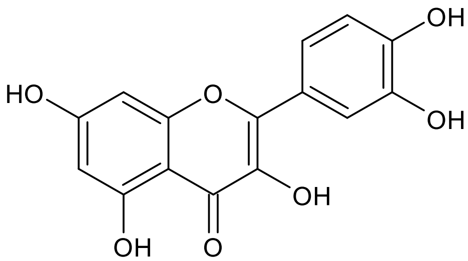
Epicatechin



Resveratrol



Epigallocatechin Gallate



Quercetin

Figure 1: Structure of the most studied Phenolic Compounds

Phenolic Compounds as Bioactive Agents Against Obesity and Related Non-Communicable Diseases

Many efforts have been made to prevent obesity and its associated comorbidities from an early age, as well as to develop effective anti-obesity therapeutic strategies. However, lifestyle interventions based only on dietary adjustments and physical activity frequently yield limited long-term success. As a result, many preclinical and clinical studies have been conducted to find new pharmacological and dietary strategies for managing obesity. The positive effect of phenolic compounds in the treatment and prevention of non-communicable illnesses,

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such as obesity, cancer, and metabolic disorders linked to obesity, has been amply demonstrated during the past ten years. These bioactive compounds have anti-obesity effects through a variety of mechanisms, including controlling appetite and energy intake, suppressing adipogenesis and lipogenesis, increasing lipid metabolism and fatty acid β-oxidation, inhibiting the proliferation and differentiation of adipocytes, and modifying oxidative stress and inflammatory pathways. Phenolic chemicals have shown promise in preventing and treating the effects of obesity and its associated metabolic problems due to their varied biological activities.

- **In Vitro and in Vivo Studies of Phenolic Compounds with Anti-Obesity Properties**
    - **Studies on Plant Extracts Performed in Vitro**

Finding and creating natural substitutes for synthetic medications to treat and prevent a range of illnesses has become a major focus of plant and food science research in recent years. Amongst these, obesity and overweight have become significant public health issues, underscoring the need for practical and long-lasting preventative measures. The use of nutraceuticals, functional foods, and beverages enhanced with plant-derived bioactive chemicals has drawn a lot of attention as a weight-management strategy, in addition to lifestyle changes incorporating dietary control and increased physical activity. These goods' natural origin increases customer acceptance, but questions about their effectiveness and scientific validity still exist. In this regard, in vitro screening techniques offer useful initial instruments for assessing the anti-obesity potential of compounds derived from plants. For initial detection and evaluation of bioactive phytochemicals, these methods provide a quick, economical, and effective substitute for animal investigations. Thus, the main in vitro tests used to evaluate the anti-obesity activity of plant extracts and food-derived products are reviewed in this section, with a focus on the phenolic chemicals that underlie their biological effects.

Sergent and colleagues used an in vitro digestion model using pancreatin, which is generated from the pig pancreas and contains lipase along with other digestive enzymes like trypsin and amylase, to better mimic circumstances. Oleic acid leakage was tracked in this method as a sign of lipid breakdown. Their results showed that phenolic substances, such as quercetin, resveratrol, and epigallocatechin-3-gallate, decreased triolein hydrolysis by 50%, indicating their ability to postpone intestinal lipid breakdown and hence limit fatty acid absorption in vivo. Recent studies have also looked into other therapeutic targets related to glycemic and lipid homeostasis because obesity is closely linked to metabolic illnesses like cardiovascular illness and type 2 diabetes mellitus.

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Table 1: *In vitro* Anti-obesity Targets and Phenolic compounds from Plant-Derived Sources

S. No.	Molecular Target/Assay	Biological Role	Plant Source/Extract	Major Phenolic/ Bioactive Compounds	Key Findings
1	**Pancreatic Lipase Inhibition**	Reduces digestion and absorption of dietary fats by inhibiting triglyceride hydrolysis	*Salicis radicis cortex*, *Corni fructus*, *Rubi fructus*, *Geranium nepalense*	Various plant phenolics	Significant lipase inhibitory activity observed at 100 µg/mL
2	**Pancreatic Lipase Inhibition**	Suppresses lipid digestion and fat absorption	Grape seed (*Vitis vinifera*), Tea (*Camellia sinensis*), Pomegranate (*Punica granatum*)	Polyphenols, catechins, flavonoids	Demonstrated potent anti-lipase activity based on IC_{50} values
3	**Simulated Gastrointestinal Lipid Digestion Assay**	Delays fatty acid release and intestinal lipid absorption	Phenolic standards	Resveratrol, EGCG, Quercetin	Reduced triolein hydrolysis by approximately 50%
4	**Fatty Acid Synthase (FAS) Inhibition**	Inhibits de novo fatty acid biosynthesis and adipose tissue accumulation	*Garcinia mangostana* hulls	Xanthones, Benzophenones	Exhibited promising FAS inhibitory activity
5	**α-Amylase Inhibition**	Slows carbohydrate digestion and glucose release	*Ficus lutea*, *F. craterostoma*, *F. natalensis*	Polyphenolic constituents	*F. lutea* showed strongest α-amylase inhibition (IC_{50} = 9.4 µg/mL)
6	**α-Glucosidase Inhibition**	Reduces postprandial glucose absorption	*Ficus* species	Polyphenolic compounds	*F. lutea* exhibited highest inhibitory activity among tested species
7	**α-Amylase and α-Glucosidase Inhibition**	Modulates carbohydrate metabolism and glycemic response	Extra Virgin Olive Oil (EVOO)	Hydroxytyrosol, Dihydroxytyrosol and related phenolics	Stronger inhibition against α-glucosidase than α-amylase
8	**Digestive Enzyme Inhibition**	Interferes with lipid digestion and absorption	Tea, Cocoa, Cinnamon	Catechins	Inhibited pancreatic lipase and α-amylase; affected lipid emulsification and micellar solubilization
9	**ACE (Angiotensin-Converting Enzyme) Inhibition**	Regulates blood pressure and reduces cardiovascular risk	Extra Virgin Olive Oil (EVOO)	Hydroxytyrosol, Dihydroxytyrosol, 3,4-DHPEA-EDA, p-HPEA-EDA, Luteolin	ACE inhibitory activity with IC_{50} values ranging from 98.6–164 µg/mL

10	**ACE Inhibition**	Potential cardioprotective effect associated with obesity management	EVOO phenolic fractions	3,4-DHPEA-EDA, p-HPEA-EDA, Luteolin	Exhibited greater ACE inhibitory potency than major olive phenolics

- **Studies on plant extracts performed in animal models**

In animal models, a number of plant-derived compounds that have shown substantial biological activity in vitro have also shown encouraging anti-obesity effects. These include wine-derived polyphenols and grape seed extracts; tea; pomegranate and lemon verbena leaves; fruits; juice and seed oil; chocolate; olive oil and leaves; and Hibiscus sabdariffa. Other plant sources that have been shown to have anti-obesity potential include common fig (Ficus carica), cinnamon (Cinnamomum zeylanicum), and Cornelian cherry (Cornus mas). A common finding across research is a decrease in body weight increase, adipose tissue formation, and energy intake, even if the mechanisms behind their biological activities vary based on the plant extract and animal model used.

These plant-derived bioactive chemicals have been demonstrated to promote metabolic health by improving glucose homeostasis and reducing dyslipidemia, in addition to their effects on body weight management. Following supplementation with phenolic-rich extracts, several studies have shown decreases in blood glucose concentrations, triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL) cholesterol. Additionally, by increasing nitric oxide (NO) bioavailability—either by boosting endothelial nitric oxide synthase (eNOS) activity, producing more NO, or decreasing the production of reactive oxygen species like superoxide anions—these natural products may have positive cardiovascular effects.

- **Clinical Evaluation of Phenolic Compounds, Plant Extracts and Functional Foods in Obesity Management**

Despite the widespread use of botanical supplements with alleged antidiabetic, antihypertensive, and cholesterol-lowering effects, only a small number of them have undergone rigorous evaluation through carefully planned, controlled clinical trials utilizing standardized and well-characterized preparations. On the other hand, research on botanical products for managing obesity has gained more attention, and a number of clinical studies have shown promising results. Green tea and its derivative components have been identified as some of the most researched therapies for weight management among the different phenolic-rich plant matrices assessed. The processes behind their possible anti-obesity actions have been the subject of numerous reviews, especially those pertaining to catechin polyphenols.

An ideal and consistent amount of green tea catechins (GTCs) is still not determined, despite the large amount of clinical evidence demonstrating the positive benefits of green tea on obesity-related parameters. Results from clinical trials using comparatively modest doses have been mixed. For example, supplementing overweight and obese postmenopausal women with 150 mg of epigallocatechin-3-gallate (EGCG) had varying results in reducing body fat. Conversely, research employing greater catechin dosages—typically between 270 and 1200 mg/day—has generally shown better results. When moderately obese people were given a commercial green tea extract containing 375 mg of entire catechins, including 270 mg of EGCG, their body weight and waist circumference significantly decreased, but their lipid profile did not significantly improve. Similarly, in women with central obesity, supplementing with higher doses of EGCG (roughly 857 mg/day) resulted in significant reductions in body weight, body mass index (BMI), and waist circumference. It also improved plasma lipid parameters by lowering concentrations of total and standard cholesterol and low-density lipoprotein (LDL) cholesterol without compromising safety.

Table 2: Clinical Evidence Supporting the Anti-Obesity Effects of Phenolic-Rich Plant Extracts in Humans

S. No.	Plant Source	Major Bioactive Compounds	Study Population	Dose & Duration	Key Outcomes
1	**Green Tea Extract** (*Camellia sinensis*)	EGCG and Green Tea Catechins (GTCs)	Overweight/obese postmenopausal women	150 mg EGCG	Inconsistent effects on body fat reduction
2	**Green Tea Extract**	270 mg EGCG (375 mg total GTCs)	70 moderately obese adults	Daily supplementation	↓ Body weight (4.6%); ↓ Waist circumference (4.48%); no significant effect on lipid profile
3	**Green Tea Extract**	856.8 mg EGCG/day	115 women with central obesity	Daily supplementation	Significant reductions in body weight, BMI, waist circumference, total cholesterol, and LDL-C
4	**Green Tea Catechins (GTCs)**	Catechin polyphenols	56 obese hypertensive patients	379 mg/day	Improved lipid profile; no significant change in BMI
5	**Green Tea Extract**	302 mg EGCG (1200 mg extract/day)	78 obese women	12 weeks	Significant reduction in LDL and triglycerides; increased HDL; minimal effect on body weight
6	**EGCG Supplementation**	EGCG	Obese women	300 mg/day for 12 weeks	No significant changes in body weight or body fat composition

7	**Hibiscus sabdariffa Extract**	Anthocyanins and polyphenols	Obese participants	Extract capsules, 12 weeks	Significant reductions in BMI, body weight, and waist-to-hip ratio; no significant changes in lipid profile
8	**Hibiscus sabdariffa Calyx Extract**	Polyphenol-rich extract	Patients with metabolic syndrome	125 mg/kg/day for 6 weeks	Increased HDL cholesterol and reduced total cholesterol levels
9	**Hibiscus sabdariffa Extract**	Anthocyanins	Apparently healthy volunteers	100 mg/day for 4 weeks	Reduced glucose, total cholesterol, and LDL-C; increased HDL by 37.5%
10	**Hibiscus sabdariffa Leaf Extract**	Phenolic compounds	Healthy participants (n = 60)	1 g/day for 12 weeks	No significant changes in anthropometric or lipid parameters

Conclusion & Future Perspectives

The European guidelines for clinical practice state that evidence-based therapeutic strategies and excellent clinical care should be the cornerstones of obesity management. Phenolic compounds have been shown to have potential anti-obesity activities in numerous research conducted on animals and in vitro over the past few decades. For the initial evaluation and identification of bioactive plant extracts with possible medicinal uses, these experimental models have proven useful. However, many preclinical discoveries still have little translational relevance since many experimental models fail to accurately capture the complexities of real obesity, producing results that are frequently challenging to repeat in clinical settings. Although the amount of research on the potency of polyphenols in managing and preventing obesity is increasing, the evidence from human trials is still comparatively small and frequently contradictory. As a result, more carefully planned clinical studies are needed to bolster the existing body of information and make it easier to create dietary guidelines with scientific backing for lowering obesity and its related metabolic problems. Additionally, there is a great deal of variation in study design, therapy duration, dosage, participant characteristics, and outcome indicators in the current clinical literature, which makes it difficult to evaluate and compare results across studies.

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