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The role of plant-derived compounds in anti-obesity drug discovery: A molecular perspective

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Obesity is a complex and multifaceted disease associated with metabolic diseases and severe health problems worldwide. There is an urgent need for novel therapeutic strategies since the currently available treatment options are often ineffective or cause adverse effects. Since they can modulate crucial biochemical pathways,phytochemicals, which are plant-derived compounds, provide a promising approach to the design of anti-obesity drugs. Such ways through which these substances work are preventing adipogenesis, regulating lipid metabolism, dropping inflammation, improving insulin sensitivity, and reestablishing energy balance. These are some of the main topics of this review. Numerous phytochemicals have emerged as auspicious agents targeting adipocytes, gut bacteria, and essential enzymes elaborate in metabolic pathways associated to obesity, such as polyphenols, flavonoids, and terpenes. Additional preclinical and clinical data testify to the rationality of these molecules toward their intended therapy aims. Prospects for incorporating phytochemicals into treatment plans for obesity are deliberated next, along with potential synergistic effects of plant bioactives and allegations for polyherbal formulations.

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Introduction

The global obesity epidemic brings about grave health and economic impacts. Obesity, according to Blüher (2019), affects over 650 million persons worldwide [1]. Incidence has sharply escalated in the last few decades; this rise can be traced back to factors including urbanization, sedentary lifestyles, and low-quality diets [2]. Current management of obesity comprises pharmacotherapy, surgery, and lifestyle changes. The limitations of conventional treatments underscore the need to explore alternative options, such as the possibility of plant-based compounds as anti-obesity drugs. Phytochemicals, which are plant-derived substances, have emerged as beneficial in the treatment of obesity. Active components from plants control lipid metabolism and reduce adipogenesis, as Mir et al. (2019) highlighted [3]. Using a molecular-level understanding, the current study focuses on the therapeutic potential of chemicals originating from plants in creating potent anti-obesity medicines. However, as all of these processes are essential for controlling obesity, the scope should be broadened to fully cover talks on adipogenesis, lipid metabolism, inflammation, and energy balance in order

to meet the stated goals. Alternatively, the aim should be changed to appropriately reflect this more limited scope if the primary focus is still inflammation and specific chemical kinds. This change will improve the manuscript's cohesion and clarity by ensuring that the content and the stated aims are consistent.

Molecular targets of plant-based compounds in obesity control

Obesity is a chronic metabolic illness that has several interconnected causes. It is closely linked to numerous comorbidities, such as diabetes, cardiovascular diseases, and certain types of cancer, making it a major global health concern. In this sense, understanding the molecular targets of compounds derived from plants offers promising strategies for managing obesity and related issues [3,4]. Obesity is mainly an energy imbalance where the body retains excess fat due to a higher intake of calories than it spends [5]. Recent research has demonstrated that dysregulated adipogenesis, chronic inflammation, and altered gut microbiota composition all contribute to obesity, in addition to lifestyle choices, such as diet, exercise habits [6,7] and smoking. The Tobacco present in cigarettes damages the body by increasing oxidative stress and DNA damage. The risk of morbidity and premature mortality is significantly higher in smokers with obesity compared to non-smokers without obesity [8]. These basic processes provide potential targets for therapeutic intervention, especially when utilizing plant-based bioactive chemical agents [9]. Numerous preclinical studies have shown that plant-derived chemicals are useful in the management of obesity [10]. Table 1 shows Plant-Derived Compounds and Their Molecular Targets for Obesity Management: Mechanisms, Evidence, and Therapeutic Potential.

Prominently, the significant pathways and systems that control inflammation, lipid metabolism, and energy balance need to be targeted effectively to address obesity. Through the interface with crucial transcription features, such as PPARγ and C/EBPs, plant-derived

Table 1

Plant-derived compounds and their molecular targets for obesity management: Mechanisms, evidence, and therapeutic potential.

Molecular Target	Plant-Derived Compound/s	Mechanism of Action	Preclinical Evidence	Clinical Evidence	Therapeutic Potential	Ref
Adipocytes	Polyphenols from *Hibiscus sabdariffa*	Inhibition of adipogenesis, lipid accumulation	Reduced lipid content in 3T3-L1 cells; suppressed adipogenic transcription factors	Limited clinical evidence on metabolic outcomes	Potential for anti-adipogenic therapy	[11]
Hypothalamus	Alkaloids (e.g., capsaicin)	Modulation of appetite-regulating neuropeptides	Animal models show appetite suppression	Clinical trials indicate modest weight loss	Adjunctive appetite suppressant	[12]
Gut Microbiota	Flavonoids (e.g., quercetin)	Modulation of gut microbiota composition	Improved gut microbiota diversity and metabolic profiles in animal studies	Early clinical studies suggest benefits for gut health	Microbiota-targeted interventions	[13]
PI3K/AKT Pathway	*Alchemilla monticola* extract	Downregulation of PI3K/AKT signaling in adipocytes	Suppressed lipid storage in human adipocytes	No clinical trials reported	Promising target for adipogenesis inhibition	[14]
Lipid Metabolism	Diterpenes (e.g., forskolin)	Activation of lipolysis and thermogenesis	Enhanced lipolysis in adipose tissue in rodent models	Reported increased basal metabolic rate in humans	Thermogenic agent for obesity management	[12]
α-Amylase/α-Glucosidase	Phenolic acids (e.g., chlorogenic acid)	Inhibition of carbohydrate digestion and glucose absorption	Decreased postprandial glucose levels in animal models	Significant reduction in postprandial glucose in human trials	Prevention of diet-induced obesity and metabolic disorders	[15]
Adipose Tissue Inflammation	Flavonoids (e.g., kaempferol)	Suppression of pro-inflammatory cytokine secretion	Reduced TNF-α and IL-6 levels in obese animal models	Few clinical trials but promising outcomes	Reduction of obesity-associated chronic inflammation	[16]
Wnt/β-Catenin Pathway	Rhubarb-derived anthraquinones	Modulation of Wnt/β-catenin signaling	Promoted lipid metabolism and reduced adipocyte differentiation in vitro	Not yet clinically evaluated	New avenue for multi-pathway targeting	[17]
Lipogenesis	Green tea catechins	Inhibition of fatty acid synthesis	Decreased fatty acid synthase expression in mice	Reduction in visceral fat in human studies	Prevention of excess fat deposition	[18]
Thermogenesis	Resveratrol	Activation of brown adipose tissue	Enhanced thermogenic gene expression in mice	Minor thermogenic effects in clinical studies	Potential adjuvant for increasing energy expenditure	[19]

Table 1 (*continued*)

Molecular Target	Plant-Derived Compound/s	Mechanism of Action	Preclinical Evidence	Clinical Evidence	Therapeutic Potential	Ref
Lipid Transport	Saponins	Promotion of cholesterol excretion	Improved lipid profiles in animal models	Preliminary clinical evidence suggests improved lipid metabolism	Lipid-lowering therapy	[20]
Appetite Regulation	*Garcinia cambogia* extract	Inhibition of serotonin reuptake	Appetite suppression in rodent studies	Mixed results in human trials	Needs optimization for efficacy	[3]
Gut Hormones	Anthocyanins	Modulation of GLP-1 secretion	Enhanced GLP-1 levels in preclinical studies	Clinical studies demonstrate improved satiety	Hormonal regulation for appetite control	[21]
Adipocyte Differentiation	Curcumin	Inhibition of adipogenic transcription factors	Suppressed PPARγ and C/EBPα expression in adipocyte cells	Limited human evidence	Prevention of fat cell development	[5]
Mitochondrial Activity	Berberine	Enhancement of mitochondrial biogenesis	Improved mitochondrial function in preclinical obesity models	Reports of weight loss in small-scale clinical trials	Improves energy metabolism	[22]
Reactive Oxygen Species	Catechins	Antioxidant activity reducing oxidative stress	Improved mitochondrial health in vitro	Antioxidant supplementation showed modest effects on obesity outcomes	Supportive therapy for oxidative-stress-related obesity	[4]
Hepatic Lipid Metabolism	Silymarin	Modulation of lipogenesis and fatty acid oxidation	Reduced hepatic fat accumulation in NAFLD models	Limited clinical trials	Obesity-associated liver disease management	[7]
Gut Barrier Function	Polysaccharides	Strengthening intestinal barrier	Reduced intestinal permeability and inflammation in animal models	Clinical evidence is emerging	Prevention of obesity-linked metabolic endotoxemia	[9]

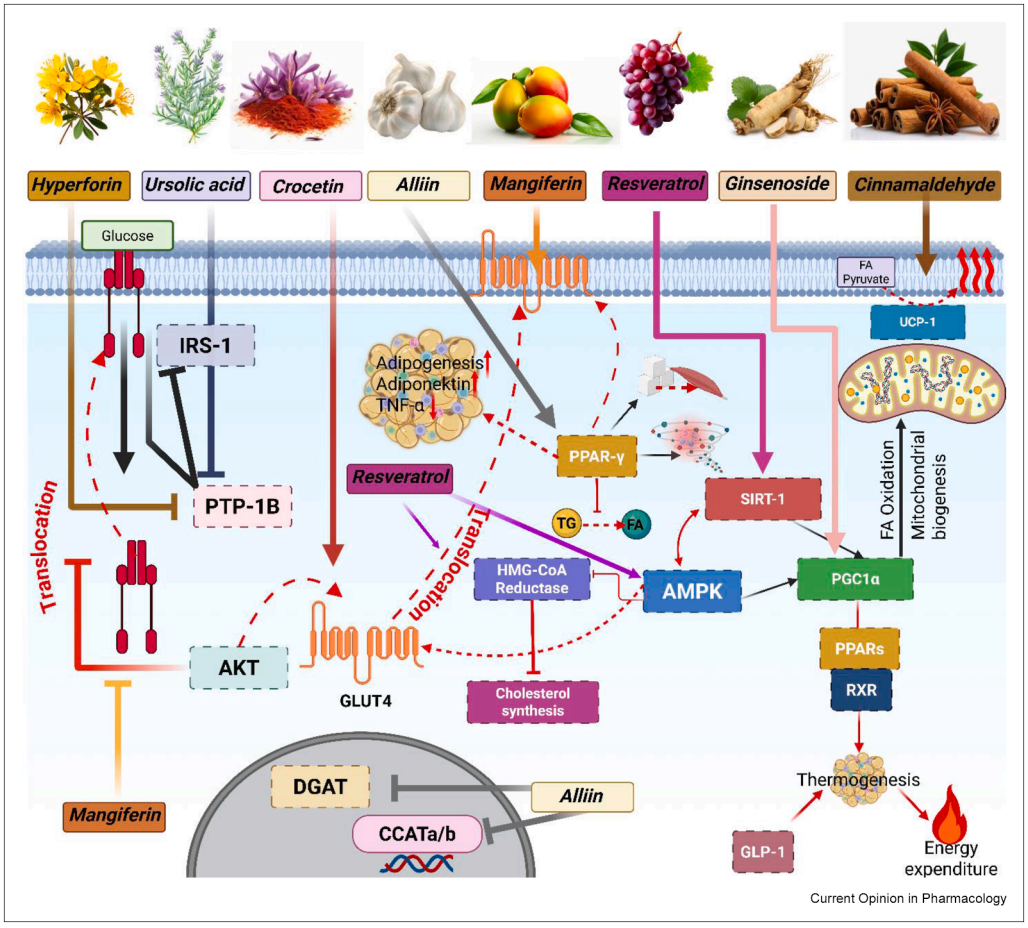
chemicals can control adipogenesis and lipolysis [23]. Another significant objective of obesity therapies is the hypothalamus, the body's 'center' of hunger and satiety. Phytochemicals have been shown to modify hypothalamic neuropeptides such as ghrelin and leptin [12,21]. Plant-derived substances such polyphenols and prebiotics, as shown in Figure 1, are crucial in regulating the makeup of gut microbes, which can reduce inflammation and enhance metabolic control [24]. Targeting lipid metabolism is also an important tactic, especially by inhibiting pancreatic lipase, a vital enzyme involved in the digestion of fat. As natural lipase inhibitors, a number of plant-based compounds, such as flavonoids and polyphenols, reduce the absorption of dietary fat and help control obesity. The discussion of important ideas would be strengthened if this section were expanded to include a more thorough explanation of these mechanisms and their molecular routes [6,25].

Important pathways linked to obesity, such as adipogenesis, lipid metabolism, inflammation, energy balance, and gut microbiota, are influenced by substances originating from plants. They work via altering transcription factors like PPARγ and C/EBPs, hypothalamic neuropeptides like ghrelin and leptin, and enzymes like pancreatic lipase. Preclinical research is encouraging, but more work is required to elucidate mechanisms, enhance bioavailability, and convert results into clinical uses.

Exploring the anti-adipogenic potential of phytochemicals in obesity treatment

The process of adipogenesis is a strictly controlled differentiation of preadipocytes into mature adipocytes, on which energy homeostasis relies [26]. In obesity, this mechanism becomes dysregulated and leads to an overaccumulation of lipids within the adipocytes. Transcription factors such as CCAAT/enhancer-binding protein alpha (C/EBPα) and peroxisome proliferator-activated receptor gamma (PPARγ) are required for adipogenesis as they are necessary for regulating genes involved in lipid storage and adipocyte differentiation [23]. This pathway is also important because the Wnt/β-catenin pathway suppresses the expression of PPARγ and C/EBPα, which also leads to an inhibition of adipogenesis. Dysregulation in these pathways contributes to adipose tissue growth, amplifying metabolic diseases associated with obesity [17]. This way, chronic overnutrition endorses adipogenesis and grounds hypertrophy and hyperplasia in the adipocytes, which clues to insulin resistance and inflammation and many other metabolic disturbances. Thus, targeting adipogenesis has occurred as a potential therapeutic approach for management obesity. Due to fewer opposing effects and more health benefits associated to synthetic medications, phytochemicals are natural inhibitors of adipogenesis [27]. Table 2 illustrates Plant-Based Bioactive:

Figure 1



Different Plant-Derived Compounds in Obesity Management. This schematic illustration depicts the mechanisms by which selected plant-derived bioactive compounds influence key signaling pathways related to adipogenesis, glucose metabolism, lipid metabolism, and thermogenesis, thereby contributing to anti-obesity effects. **IRS-1:** Insulin receptor substrate-1; **PTP-1B:** Protein tyrosine phosphatase 1B; **AKT:** Protein kinase B; **GLUT4:** Glucose transporter type 4; **PPAR-γ:** Peroxisome proliferator-activated receptor gamma; **FA:** Fatty acids; **TG:** Triglycerides; **TNF-α:** Tumor necrosis factor; **AMPK:** AMP-activated protein kinase; **HMG-CoA:** 3-hydroxy-3-methylglutaryl coenzyme A; **SIRT-1:** Sirtuin 1; **PGC1α:** Peroxisome proliferator-activated receptor gamma coactivator 1-alpha; **RXR:** Retinoid X receptor; **UCP-1:** Uncoupling protein 1; **GLP-1:** Glucagon-like peptide-1; **DGAT:** Diacylglycerol acyltransferase; **CCATa/b:** Carbohydrate response element-binding protein alpha/beta.

Mechanisms, Effects, and Evidence in Lipid Metabolism and Weight Management.

Numerous kinds of phytochemicals, such as polyphenols, flavonoids, terpenes, and alkaloids, have been established to have significant anti-adipogenic effects. For example, Urolithin from pomegranate (*Punica granatum*) demonstrated anti-obesity effects by regulation of lipid and glucose homeostasis without any adverse events in mice [39], anthocyanin from blueberries (*Vaccinium corymbosum*) exhibited anti-obesity effects by ameliorating obesity-associated metabolic dysfunction through TLR4 pathway inhibition and gut microbiota dysbiosis [40], EGCG from Green tea (*Camellia sinensis*) effectively reduced obesity in C57BL/6 J mice induced by olive oil-based and unsaturated fatty acid-enriched high fat diet by activation of PPARδ pathway in White adipose tissue [40], Cyanidin from red cabbage (*Brassica oleracea* var. *capitata f. rubra*) showed anti-obesity effect by reducing hypertrophy, inflammation, and insulin resistance induced by high concentration of free fatty acids in murine 3T3-L1 adipocyte [41], Isorhamnetin from almonds (*Prunus dulcis*) demonstrated anti-obesity effects by upregulation of enoyl-CoA hydratase and adipose triglyceride lipase via NHR-49-dependent pathway in *Caenorhabditis elegans* [42] , Quercetin from kale (*Brassica oleracea* var. sabellica) showed anti-obesity effects by increasing expression of non-shivering thermogenesis genes in brown adipose tissue, including uncoupling protein 1 (UCP1) and mitochondrial transcriptional factor A (mtTFA) in mice [43]. These bioactive compounds impact the signaling pathways that regulate adipocyte development (As shown in Figure 2).

Table 2

Plant-based bioactives: Mechanisms, effects, and evidence in lipid metabolism and weight management.

Category	Bioactive compound/s	Key insights and Mechanism of Action	Model used	Ref
Phytochemicals in Lipid Metabolism	Polyphenols, flavonoids, saponins	Inhibits lipogenesis enzymes (e.g., FAS) and downregulates fatty acid synthase (FAS).	Animal Models	[28]
Impact on Lipases	Catechins	Inhibits pancreatic lipase activity and reduces fat absorption in the gut.	Human Trials	[29]
Bioactives in Lipogenesis	Mandelamide	Blocks differentiation of 3T3-L1 adipocytes and regulates PPARγ and C/EBPα pathways.	*In vitro*	[30]
Role in Lipolysis	Resveratrol	Enhances lipolysis via AMPK activation and promotes breakdown of triglycerides.	Animal Models	[31]
Weight Reduction Evidence	Curcumin	Decreases body weight and fat mass by suppressing inflammatory cytokines.	Human Trials	[32]
Fat Burning	Capsaicin	Increases thermogenesis and fat oxidation by stimulating beta-adrenergic receptors.	Human Trials	[33]
Epigenetic Modifications	Genistein	Modulates DNA methylation in adipocytes and prevents adipogenesis.	*In vitro*	[19]
Anti-inflammatory Effects	Quercetin	Reduces TNF-α and IL-6 in adipose tissue and alleviates inflammation in obesity.	Human Trials	[34]
Regulation of Adipocyte Metabolism	Anthocyanins	Enhances insulin sensitivity by improving glucose uptake in adipocytes.	Animal Models	[35]
Mechanisms in Fat Oxidation	Caffeine	Increases mitochondrial activity by enhancing fatty acid oxidation.	Human Trials	[36]
Lipid Metabolism in NAFLD	Silymarin	Inhibits hepatic lipogenesis by activating PPARα pathways.	Animal Models	[37]
Inflammation in Obesity	Terpenoids	Suppresses the NF-κB pathway and decreases systemic inflammation.	*In vitro*	[38]
Adipose Tissue Inflammation	Flavonoids	Inhibit adipokine secretion and reduces macrophage infiltration in adipose tissue.	Animal Models	[16]
Bioactives and Mitochondrial Function	Curcuminoids	Enhance mitochondrial biogenesis and improve energy metabolism.	Human Trials	[4]

Plant-based bioactives: mechanisms of action in lipid metabolism and weight control

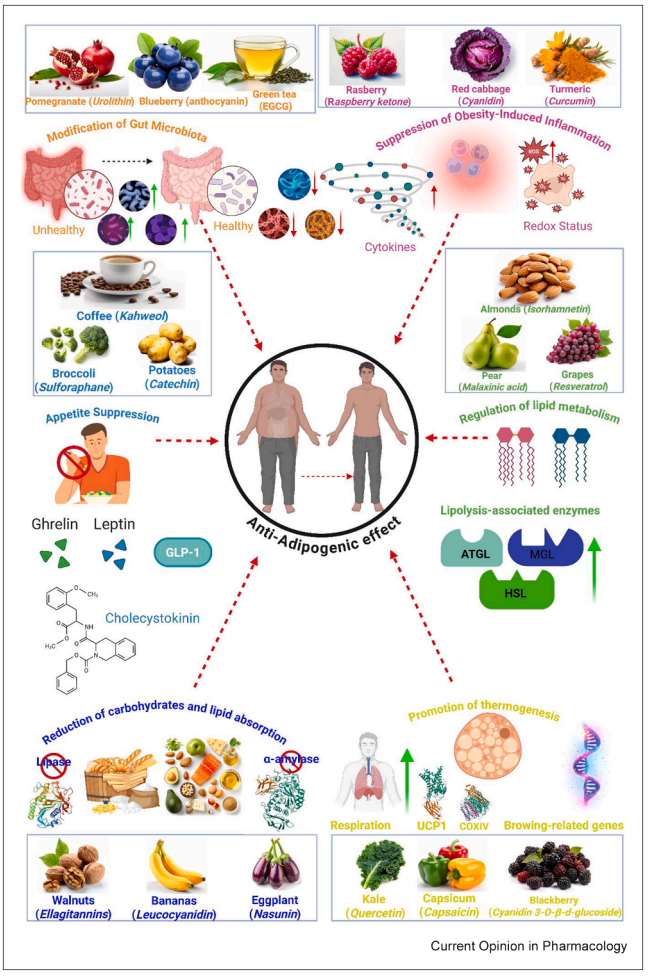
Lipid metabolism is a complex process by which lipids must be amalgamated, stored, and broken down to supply energy to body tissues [44]. One of the central processes in lipid metabolism is fatty acid oxidation, followed closely by the two interrelated processes of lipolysis the breakdown of triglycerides to free fatty acids, and lipogenesis those processes concerned with the synthesis of fatty acids and triglycerides. Dysregulation of these pathways leads to an imbalance between energy intake and expenditure, producing and exacerbating obesity [35].

Impact of plant bioactives on fat synthesis and breakdown

Through the coordination of the regulation of lipogenesis and lipolysis, phytochemicals minimize obesity. By inhibiting PPARγ and C/EBPα, two transcription factors important for adipocyte differentiation and lipid accumulation, polyphenols decrease lipogenesis [28]. Moreover, by activating AMP-activated protein kinase (AMPK), a key regulator of energy metabolism, bioactives like flavonoids increase lipolysis [37]. An alkaloid, berberine, from the *Berberis* species, has shown noteworthy activity in stimulating lipolysis and constraining lipogenesis. It decreases lipid synthesis in adipocytes, blocks SREBP-1c, and activates AMPK [19]. Citrus flavonoids, naringenin, and hesperidin also stimulate lipolysis by refining mitochondrial function in adipocytes, cumulative energy expenditure, and lowering fat levels [45]. These results show how plant-based bioactives are potent in reducing fat through the reduction of numerous lipid metabolic pathways. Further results are established through human clinical studies. As shown in Figure 3, the treatment with green tea extract, containing EGCG, resulted in considerable reduction in body weight, waist measurement, and the total level of cholesterol among the overweight participants [46].

Current investigation is still attempting to clarify the molecular procedures of these substances but offers a gateway for a wider use of these substances in the fight in contradiction of obesity and linked conditions [19].

Figure 2



Anti-Adipogenic Potential of Phytochemicals in Obesity. Schematic illustration showing key mechanisms by which dietary components reduce adiposity through modulation of gut microbiota, suppression of inflammation and appetite, regulation of lipid metabolism, inhibition of lipolytic enzymes, and promotion of thermogenesis. **ATGL**, adipose triglyceride lipase; **MGL**, monoacylglycerol lipase; **HSL**, hormone-sensitive lipase; **UCP1**, uncoupling protein 1; **COXIV**, cytochrome c oxidase subunit IV; **GLP-1**, glucagon-like peptide-1.

Anti-inflammatory properties of plant-derived compounds in obesity therapy

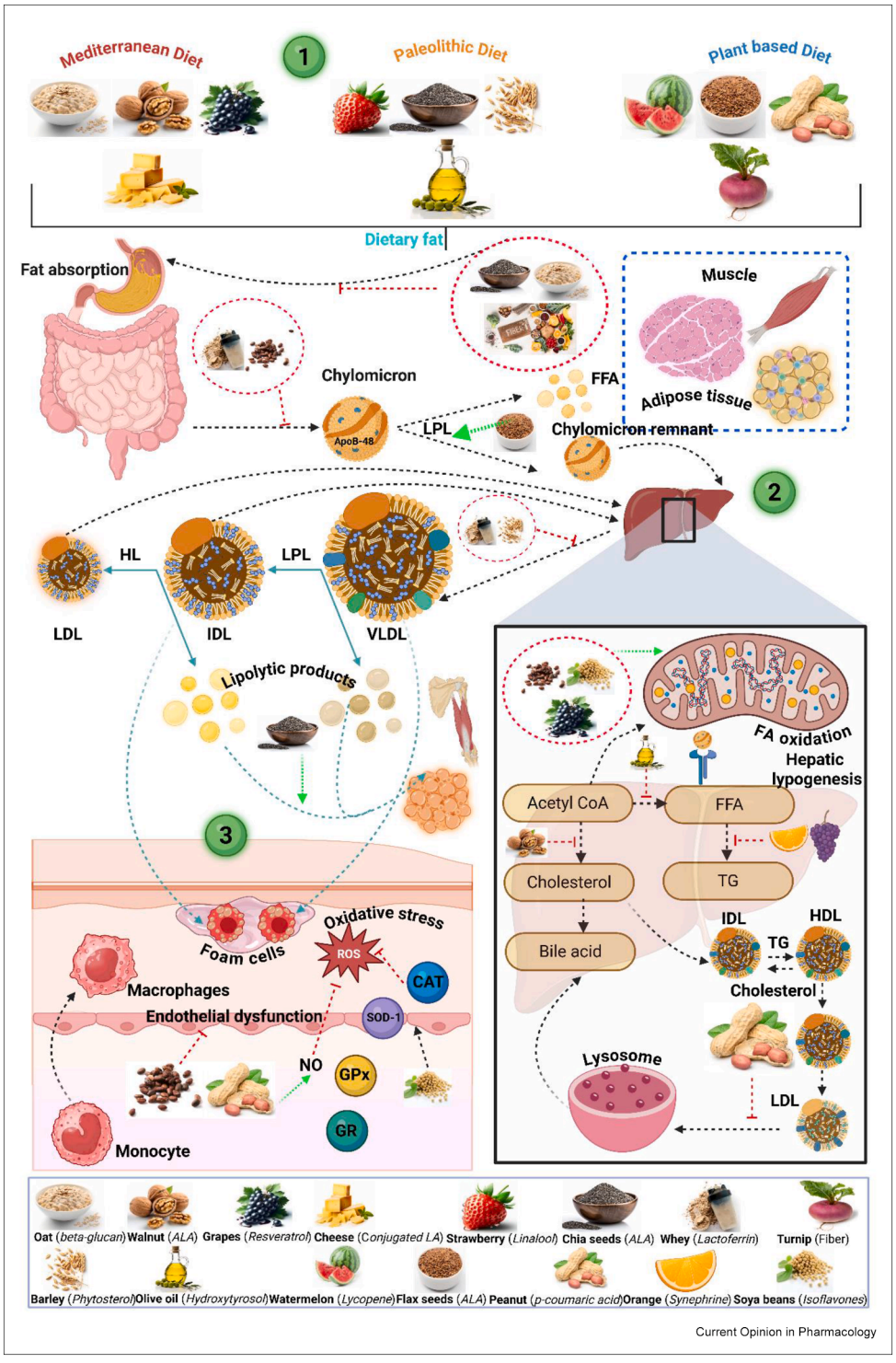
Chronic low-grade inflammation is also highly linked to obesity, and this disorder is related to metabolic disturbances, including type 2 diabetes, insulin resistance, and cardiovascular diseases [16] (Illustrated in Figure 4). Hypertrophic adipocytes produce pro-inflammatory mediators including TNF-α, IL-6, and MCP-1, that attract macrophages and further enhance inflammation. Adipose tissue plays an important role in the process [16]. Such a chronic inflammatory disease, often referred to as "metabolic inflammation," plays a key role in disease etiology associated with obesity. Furthermore, oxidative stress and reactive oxygen species (ROS) are the amplifiers of this inflammatory cascade [4]. For the deterrence of obesity along with its morbidities, successful therapeutic interferences are obligatory that tackle both oxidative stress and inflammation.

Plant-derived anti-inflammatory compounds

Compounds extracted from plants have gained a lot of attention since they provide anti-inflammatory and metabolic benefits in obesity treatment. Some of the significant phytochemicals include:

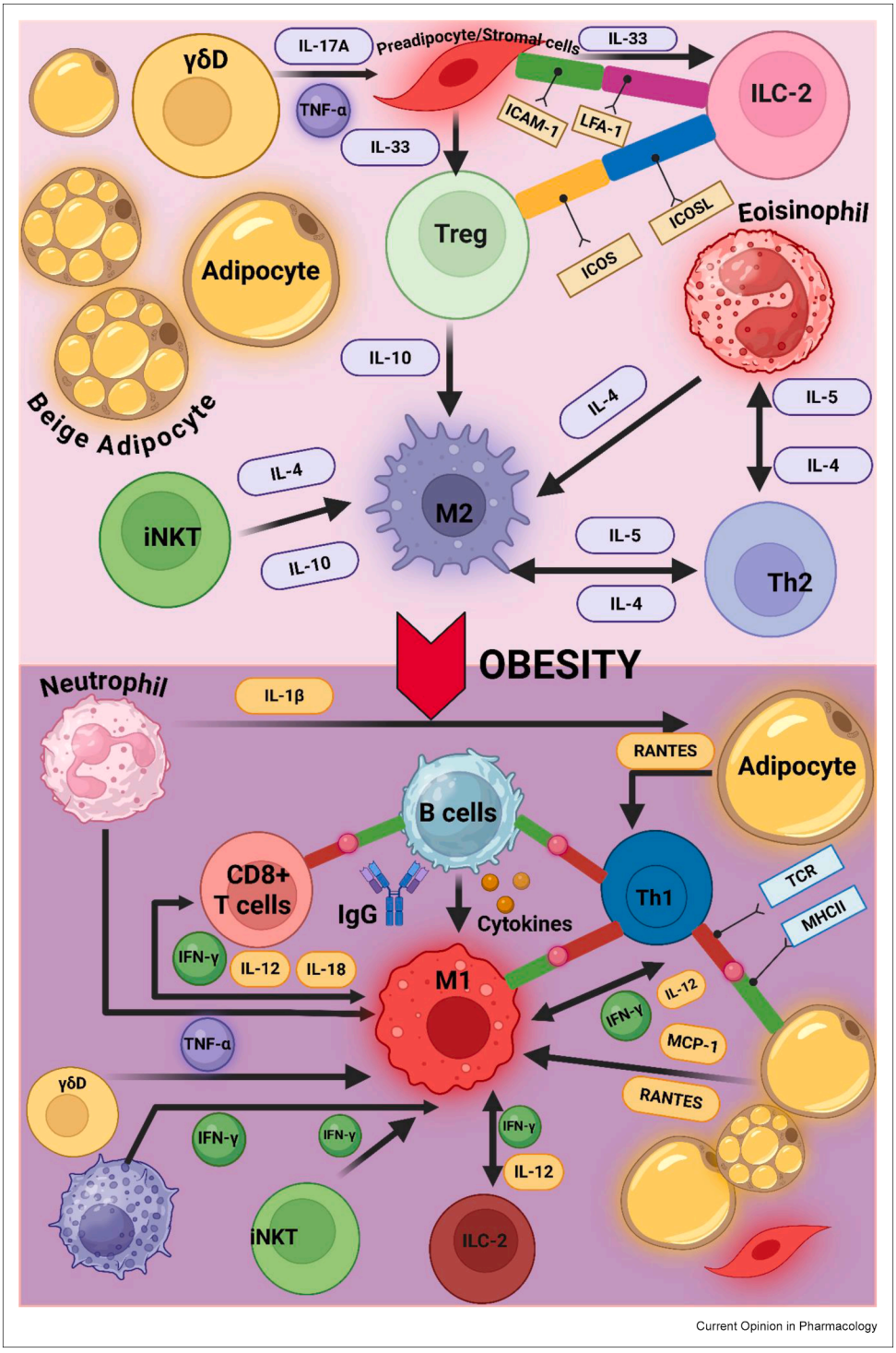
1. **Curcumin**: Curcumin is an anti-inflammatory compound which has been well studied and found in turmeric (*Curcuma longa*). It inhibits the activation of NF-κB, reducing the expression of pro-inflammatory cytokines such as TNF-α and IL-6. Curcumin has been proven to be beneficial in reducing inflammation in adipose tissue and cumulative insulin sensitivity [36,4].

Figure 3



Effect of Bioactive Plant Compounds on Lipogenesis and Lipolysis. Schematic illustration showing how different dietary patterns (Mediterranean, Paleolithic, and Plant-Based diets) influence lipid metabolism and cardiovascular health. Dietary fats are absorbed and processed into lipoproteins (chylomicrons, VLDL, LDL, HDL), while bioactive compounds (e.g., resveratrol, ALA, hydroxytyrosol) modulate oxidative stress and inflammation through antioxidant enzymes and nitric oxide pathways. **ALA**, α-linolenic acid; **ApoB-48**, apolipoprotein B-48; **CAT**, catalase; **FFA**, free fatty acids; **GPx**, glutathione peroxidase; **GR**, glutathione reductase; **HDL**, high-density lipoprotein; **HL**, hepatic lipase; **IDL**, intermediate-density lipoprotein; **LDL**, low-density lipoprotein; **LPL**, lipoprotein lipase; **NO**, nitric oxide; **ROS**, reactive oxygen species; **SOD-1**, superoxide dismutase 1; **TG**, triglycerides; **VLDL**, very-low-density lipoprotein.

Figure 4



Interplay of Inflammation in the adipose tissue and obesity. Schematic representation of immune regulation in adipose tissue under lean and obese conditions. In lean adipose tissue, anti-inflammatory immune cells (e.g., M2 macrophages, eosinophils, Th2 cells, Tregs, ILC-2, iNKT, and γδ T cells) maintain metabolic homeostasis via cytokines such as IL-4, IL-5, IL-10, and IL-33. In obesity, pro-inflammatory cells (e.g., M1 macrophages, CD8+ T cells, Th1 cells, B cells, neutrophils) secrete IFN-γ, IL-1β, TNF-α, and MCP-1, promoting chronic inflammation and insulin resistance. **γδ T**, gamma delta T cells; **iNKT**, invariant natural killer T cells; **Treg**, regulatory T cells; M1, pro-inflammatory macrophages; M2, anti-inflammatory macrophages; **ILC-2**, group 2 innate lymphoid cells; **Th1**, T helper type 1; **Th2**, T helper type 2; **IL**, interleukin; **IFN-γ**, interferon-gamma; **TNF-α**, tumor necrosis factor-alpha; **MCP-1**, monocyte chemoattractant protein-1; **RANTES**, regulated on activation normal T cell expressed and secreted**; ICAM-1**, intercellular adhesion molecule 1; **LFA-1**, lymphocyte function-associated antigen 1; **TCR**, T cell receptor; **MHCII**, major histocompatibility complex class II; **IgG**, immunoglobulin G.

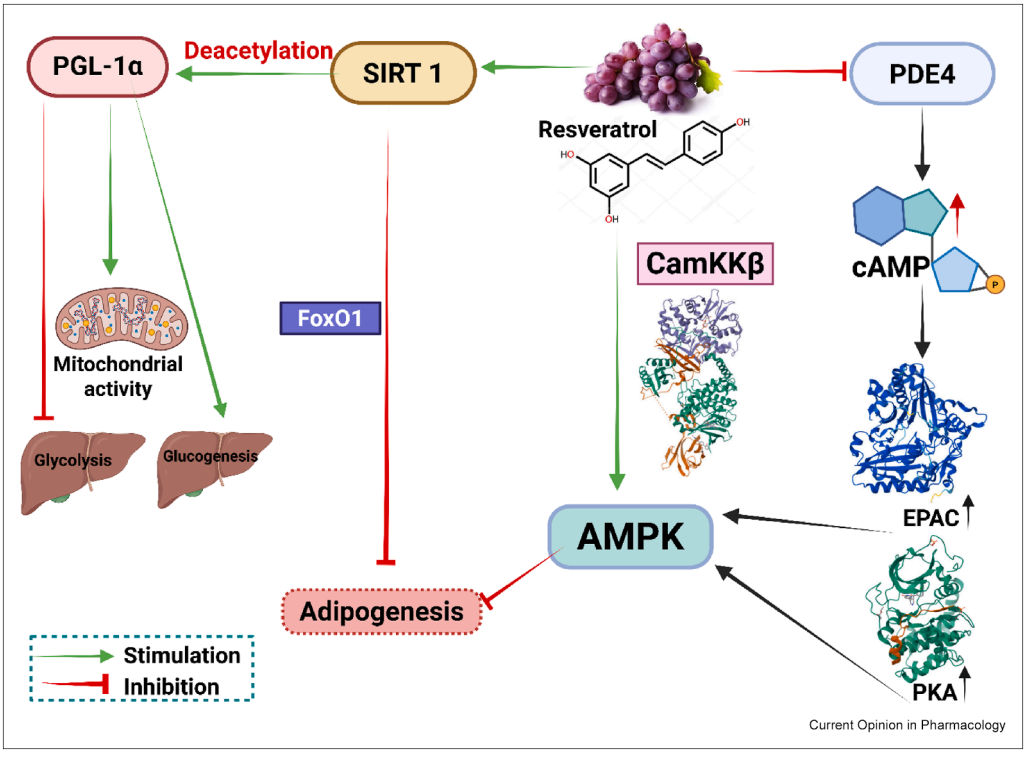
2. **Resveratrol**: This polyphenol that is rich in berries and grapes mediates anti-inflammation via its ability to stimulate SIRT1 to inhibit NF-κB activity and initiate AMPK pathways [Illustrated in Figure. 5]. Plant-produced resveratrol inhibits macrophage infiltration in adipose tissue, hence reducing systemic inflammation [47,48].
3. **Gingerol**: Gingerol, derived from ginger, exerts anti-inflammatory actions through NF-κB and COX-2 inhibition. It may also be considered for obesity therapy since it has reduced systemic inflammatory markers and increased insulin sensitivity [46].

These compounds can be crucial in controlling obesity because they act through different mechanisms on inflammation.

Mechanisms of action: NF-κB inhibition and cytokine reduction

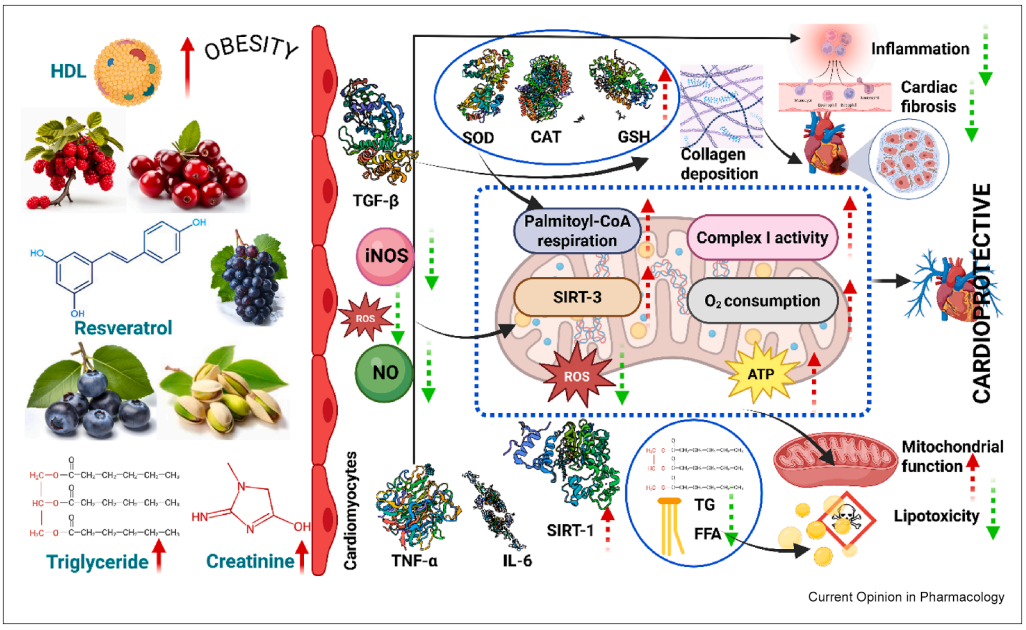
Compounds produced from plants impact critical molecular pathways, mainly through their mechanism of action against NF-κB, which is crucial in inflammation within obesity. Its activation in the adipose tissue often enhances systemic inflammation via the production of pro-inflammatory cytokines [49]. Some of the phytochemicals that have been found to block the translocation of NF-κB, thus reducing the expression of inflammatory genes [50]. Apart from decreasing NF-κB, plant bioactive also suppress the production of cytokines. Gingerol have been found to decrease MCP-1 and other proinflammatory mediators, while resveratrol has been proven to reduce levels of IL-6 and TNF-α [51]. The effectiveness of the chemotherapeutic approach of these chemicals derived from plants in alleviating the inflammation related to obesity lies in their additive mechanism of reducing cytokines and lessening NF-κB. Major contributing factors to the obesity associated metabolic dysfunctions include chronic low-grade inflammation. In addition to being accountable for insulin signaling and glucose homeostasis, malfunction in adipose tissue upsurges macrophage infiltration and inflammatory cytokine release [16]. Anti-inflammatory treatments are important as the chronic inflammatory state also plays a role in conditions like atherosclerosis, hypertension, and fatty liver disease [38]. This inflammation is relieved by dropping macrophage infiltration and restoring adipose tissue homeostasis through compounds derived from plants (As shown in Figure 6). For instance, polyphenols

Figure 5



Resveratrol-mediated activation of the SIRT1-AMPK signaling cascade and its regulation of metabolic pathways. Resveratrol activates SIRT1 and inhibits PDE4, elevating cAMP levels that stimulate EPAC, PKA, and AMPK. Together with CaMKKβ, AMPK and SIRT1 activate PGC-1α, enhancing mitochondrial biogenesis and oxidative metabolism while suppressing adipogenesis. (Green arrows indicate activation; red bars indicate inhibition). **SIRT1**, sirtuin 1; **PGC-1α**, peroxisome proliferator-activated receptor gamma coactivator-1 alpha; **PDE4**, phosphodiesterase 4; **cAMP**, cyclic adenosine monophosphate; **EPAC**, exchange protein directly activated by cAMP; **PKA**, protein kinase A; **AMPK**, AMP-activated protein kinase; **CaMKKβ**, calcium/calmodulin-dependent protein kinase kinase beta.

Figure 6



Mechanism of action of Resveratrol in Obesity. Proposed mechanism of natural compounds in mitigating obesity-induced cardiovascular dysfunction. Natural sources (e.g., berries, grapes, pistachios) elevate HDL and counteract TG and creatinine increases. Obesity enhances TGF-β and iNOS expression, elevating ROS and inflammatory cytokines (TNF-α, IL-6), leading to mitochondrial dysfunction, fibrosis, and lipotoxicity. Resveratrol restores antioxidant defense, activates SIRT-1/3, and improves mitochondrial function, promoting cardioprotection. **HDL**, high-density lipoprotein; **TGF-β**, transforming growth factor-beta; **iNOS**, inducible nitric oxide synthase; **NO**, nitric oxide; **ROS**, reactive oxygen species; **TNF-α**, tumor necrosis factor-alpha; **IL-6**, interleukin-6; **SOD**, superoxide dismutase; **CAT**, catalase; **GSH**, glutathione; **SIRT-1/3**, sirtuin-1/3; **TG**, triglycerides; **FFA**, free fatty acids; **ATP**, adenosine triphosphate.

has been shown to decrease inflammation, improve lipid profiles, and improve glucose metabolism [36]. Besides, curcumin and gingerol are essential in decreasing the systemic inflammatory markers, thus refining the metabolic outcomes [48]. This study looks at the molecular effects of plant-derived chemicals on processes linked to obesity, with a focus on pathways that control inflammation, lipid metabolism, and adipogenesis. Important signaling cascades that mediate these effects are highlighted, including AMPK, PI3K/AKT, NF-κB, and SIRT1. This work provides a molecular insight into how plant-derived compounds contribute to obesity management by targeting pathways involved in adipogenesis, lipid metabolism, inflammation, and energy regulation. It highlights key phytochemicals and their mechanisms of action, emphasizing their potential as natural alternatives to current anti-obesity therapies. Moreover, it underscores existing gaps in pharmacological validation, dosage optimization, and bioavailability, calling for comprehensive translational studies to advance these compounds from experimental models to clinical application. Bioactive substances produced from plants promote the breakdown of fat and decrease its synthesis, which helps control body weight and lipid metabolism. While curcumin, resveratrol, and gingerol lower inflammation and improve insulin sensitivity, compounds like berberine, naringenin, and hesperidin boost mitochondrial activity and energy expenditure. Although more study is required to elucidate routes, improve dosage, and validate clinical efficacy, these mechanisms highlight their promise as natural anti-obesity medicines [48].

Conclusion and future perspectives

Using plant-derived chemicals to treat obesity offers a scientifically grounded and health-conscious strategy to address this global challenge. The bioactive substances under discussion work via a variety of pathways, such as enhancing insulin sensitivity, reducing inflammation, inhibiting adipogenesis, and modifying lipid metabolism. Research on both humans and animals has shown that certain substances, like berberine can alter the metabolic processes linked to obesity. Nanotechnology-based delivery systems (e.g., liposomes and nanoparticles) and other sophisticated formulation techniques could be investigated to solve issues including low solubility, instability, and restricted bioavailability. Furthermore, combining several phytochemicals or incorporating plant-derived substances with traditional anti-obesity medications may have synergistic effects. To address ADME considerations, formulation techniques, target validation, and

approaches for creating next-generation, long-acting anti-obesity medicines, a special section titled "Challenges and Future Directions in Translating Phytochemicals into Anti-Obesity Drugs" ought to be included.

Authors' contribution

All authors contributed equally to the conceptualization, literature review, analysis, and interpretation of data for this study. VS; RNR; SM; SKS; VC; KD: Composed the preliminary manuscript. BGO; SD; GG; TGS: Conducted a critical revision and editing of the paper. All authors evaluated and sanctioned the final version of the manuscript for publication.

Ethics approval and consent to participate

Not applicable.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
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