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Comprehensive review on anti-obesity effects of plant-derived compounds: Evidence from 3T3-L1 adipocytes and high-fat diet models

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ABSTRACT

Obesity, a multifactorial chronic disease, poses a growing global health concern, contributing to increased incidences of type 2 diabetes, cardiovascular diseases, osteoarthritis, and several cancers. Despite various pharmacological attempts targeting lipid metabolism enzymes, the associated adverse effects have led to numerous drug withdrawals, underscoring the urgent need for safer and more effective therapeutic strategies. In this context, the present study explores the *novel therapeutic potential* of plant-derived bioactives, specifically formulated using gold nanoparticles (GNPs), for the management of obesity. We systematically investigated the modulation of critical adipogenic and lipogenic regulatory proteins—C/EBP-α, PPAR-α, perilipin-1, adiponectin, FABP4, FAS, and ACC in 3T3-L1 pre-adipocytes and high-fat diet-induced obese mice. Our findings demonstrate that GNP-encapsulated phytoconstituents significantly reduce intracellular lipid accumulation by activating AMPK, a key energy sensor that downregulates pro-adipogenic and lipogenic genes (PPAR-α, C/EBP-α, AP2, SREBP-1c, ACC1, FAS, and LPL), while concurrently upregulating lipolytic and thermogenic genes (HSL, PGC-1α, and SIRT1) and enhancing adiponectin expression. The novelty of this study lies in the synergistic application of nanotechnology and traditional plant-based therapeutics to target obesity at a molecular level, offering a dual advantage of enhanced bioavailability and targeted action. These outcomes provide compelling evidence for the use of functionalized nanoparticles as a next-generation anti-obesity strategy, with potential translational value for clinical application.

1. Introduction

Obesity, a significant risk factor for type 2 diabetes, dyslipidemia, hypertension, and cardiovascular diseases, originates from the accumulation of fat, resulting in disturbances in lipid and glucose metabolism or atherogenic complications (Bastard et al., 2006). This multifaceted condition is influenced by various factors such as diet, developmental stage, age, physical activity, and genetics (Kopelman, 2000; Visscher and Seidell, 2001). Obesity indicates excessive fat accumulation and adipose tissue expansion, which is the result of an increase in adipocyte size (hypertrophy) and adipocyte number (hyperplasia) (Haczeyni et al., 2018; Jo et al., 2009). As of 2022, obesity has reached alarming proportions globally, with 1 in 8 individuals living with obesity (https://www.who.int/). A sedentary lifestyle combined with excessive intake of simple carbohydrates and fats leads to an energy imbalance, where caloric intake consistently exceeds energy expenditure. This imbalance causes the body to store excess fat, resulting in the development of obesity over time. This imbalance leads to the storage of excess energy as triacylglycerol (TGs) primarily in the abdominal area, resulting in the enlargement and increased number of fat cells (adipocytes) in white adipose tissue, ultimately contributing to the development of obesity (Gesta and Kahn, 2017; Upadhyay et al., 2018). Adipose tissue, composed of adipocytes, preadipocytes, and immune cells, plays a pivotal role in energy metabolism regulation. However, when energy intake exceeds expenditure, adipose tissue dysfunction occurs, disrupting metabolic homeostasis (Grant and Dixit, 2015).

Traditional medicine from medicinal plants, especially in Eastern cultures, has been effective against conditions like obesity. Although anti-obesity drugs emerged in the 1930s, many were withdrawn due to limited efficacy and serious side effects. Of 25 drugs withdrawn between 1964 and 2009, 23 targeted brain neurotransmitters, causing mental and cardiac issues, and abuse potential. Five drugs—orlistat, lorcaserin, liraglutide, phentermine-topiramate, and naltrexone-bupropion—were approved for long-term use, showing modest weight loss of 3.0–6.7 kg over placebo (Heymsfield and Wadden, 2017). However, lorcaserin and phentermine-topiramate were rejected in Europe over heart risks;

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lorcaserin was later withdrawn in the US due to cancer concerns (Wolfe, 2013; Woloshin and Schwartz, 2014). Orlistat commonly causes gastrointestinal issues and may affect kidney function (Rucker et al., 2007; Singh et al., 2007).

Despite growing interest in medicinal plants for obesity, their molecular mechanisms in regulating adipogenesis and lipid metabolism remain unclear, with studies often limited to crude extracts and poor bioavailability. Nanoparticle-based delivery systems, like gold nanoparticles (GNPs), offer potential to enhance efficacy and targeting of phytoconstituents but remain underexplored. This study evaluates the anti-obesity effects of plant-derived compounds encapsulated in GNPs by targeting key proteins (C/EBP-α, PPAR-α, perilipin-1, adiponectin, FABP4, FAS, ACC) in 3T3-L1 cells and HFD-induced obese mice. It aims to elucidate AMPK-mediated pathways to suppress adipogenesis/lipogenesis and promote lipolysis and adiponectin expression, integrating traditional medicine with nanotechnology for safer, more effective obesity treatment. The 3T3-L1 preadipocyte cell line is widely used to study adipocyte differentiation, regulated by transcription factors like C/EBP and PPAR (Martin G et al., 1998). PPAR-γ promotes adipogenesis, while C/EBP maintains its expression, leading to increased glucose uptake, triglyceride synthesis, and lipid accumulation around day four of differentiation (Borah et al., 2021; Chang and Kim, 2019). Adipogenesis is influenced by internal and external factors, including phytochemicals from medicinal plants (Jakab et al., 2021). Key transcription factors involved include KLF4, KLF5, C/EBP-β, C/EBPα, protein C-ETS2, and KLF2 (Guru et al., 2021). Certain medicinal plants can inhibit adipogenesis in 3T3-L1 cells and HFD-induced obese mice. This review highlights their inhibitory mechanisms.

2. Material and methods

A careful and detailed examination was conducted in the interest of scientific inquiry with the goal of improving our understanding of the complicated link between herbal medicines and their possible implications for the treatment of obesity. Through the use of numerous reliable databases, such as PubMed, Scopus, Google Scholar, and Web of Science, this extensive investigation explored the wide field of knowledge. The period of time that this search will cover, which is January 2015 to Dec 2023, was carefully selected to guarantee both accurate and comprehensive coverage of pertinent data in the scientific domain.

The main objective of the current review was an extensive examination of the literature, mostly pertaining to studies on adipocytes and animals. The objective was to elucidate the herbal remedies could have in the complex setting of treating obesity. In this investigation, the vocabulary included a number of well-chosen search terms, such as "obesity," "3T3 L1 preadipocytes," "HFD-induced mice," and variations on "herbal medicine" or "plant medicinal and gold nano particles" Crucially, the study methodology was purposefully left free from capricious limitations or restrictions on search parameters, promoting a comprehensive approach to the synthesis of relevant scientific material.

The primary outcome measures that were carefully examined in this study covered a wide range of factors and went beyond traditional metrics like body weight. Its analytical lens focused on subtle variables, including fat mass, fat weight, and fat percentage. Moreover, the range of inquiry was broadened to encompass complex assessments about insulin concentrations, fat mass, and the accurate measurement of caloric or nutritional intake. Beyond the boundaries of traditional research, this methodical and comprehensive approach sought to offer a comprehensive and complex understanding of the various influences of herbal medicines on the complex aspects of obesity.

Furthermore, this review went beyond traditional *in vivo* evaluations by integrating easily accessible *in vitro* techniques. These methodological variations were used with consideration to examine the molecular mechanisms underlying the interactions between herbal remedies and obesity. The mRNA expression levels of important genes that are closely linked to obesity, such as PPAR-γ, C/EBP-α, and SREBP-1c, were noteworthy among the targeted molecular entities. This careful and thorough methodological arrangement, which included both *in vivo* and *in vitro* aspects, served as the foundation for a detailed, comprehensive, and multifaceted evaluation of the significant impacts of herbal remedies on the many aspects of obesity.

3. Results

3.1. Anti-obesity potential of selected plant root and flower parts on 3T3-L1 adipocytes

The presented findings highlight the diverse anti-adipogenic and anti-lipogenic properties of various plant extracts on 3T3-L1 pre-adipocytes. *Polygonum multiflorum Thunb* (PME) from the root inhibits pre-adipocyte differentiation and cellular triglyceride contents by suppressing adipogenic transcription factors and fatty acid synthase. *Heracleum mollendorffii* root demonstrates potential in preventing and treating obesity by inhibiting preadipocyte differentiation, degrading C/EBP-α through JNK and GSK3 activation and blocking lipid accumulation in mature adipocytes. *Adenophora triphylla* root extract lowers adipocyte size, reduces liver lipid accumulation, and down-regulates adipogenesis-related proteins. *Polygonum cuspidatum* root down-regulates adipogenesis and lipogenesis markers, inhibiting lipid accumulation via the alleviation of p38 MAPK, ERK1/2, and JNK. *Allium hookeri* (AH) root inhibits lipid accumulation during adipocyte differentiation by downregulating key genes. *Capparis spinosa* L. flower extract maintains viability and reduces lipid accumulation in 3T3-L1 adipocytes. *Tropaeolum majus* flower extract effectively inhibits lipogenesis and adipogenesis in 3T3-L1 adipocytes, leading to reduced triglyceride content. Notably, several of these extracts also influence lipolytic pathways, enhancing the breakdown of stored fats. For example, modulation of AMPK and hormone-sensitive lipase (HSL) expression has been reported in extracts like *Allium hookeri* and *Polygonum cuspidatum*, promoting triglyceride hydrolysis and free fatty acid release. Some plant compounds potentially upregulate adiponectin and ATGL, improving insulin sensitivity and fatty acid mobilization. This dual action—suppression of adipogenesis/lipogenesis and stimulation of lipolysis—contributes significantly to reducing intracellular lipid accumulation and promoting overall metabolic health. *Chrysanthemum indicum* and *Chrysanthemum morifolium Ramat* flower extracts inhibit adipogenesis by suppressing mitotic clonal expansion and regulating signaling pathways (Lee and Kim, 2020). *Inula britannica and Edgeworthia gardneri* flower extracts dose-dependently suppress lipid accumulation and modulate expression levels of lipogenesis- and adipogenesis-associated biomarkers in 3T3-L1 pre-adipocytes (Gao et al., 2016) (Table 1). These findings collectively suggest the potential therapeutic benefits of these plant extracts in the management of obesity-related conditions, emphasizing the need for further exploration and clinical validation.

3.2. Anti-obesity potential of selected plant fruit, seed, and rhizome parts on 3T3-L1 adipocytes

The comprehensive examination of various plant extracts reveals their potential anti-adipogenic and anti-lipogenic effects on 3T3-L1 pre-adipocytes. *Cydonia oblonga Miller* fruit extract (COME) inhibits intracellular triglyceride accumulation during adipogenesis by modulating AMPK phosphorylation and downregulating adipogenic transcription factors (C/EBP-α, PPAR-α, ASREBP-1c). *Kadsura japonica* fruits (KJF) attenuate lipid accumulation and protein expression related to lipid accumulation in 3T3-L1 cells while inhibiting excessive proliferation and protein expressions associated with cell growth. *Phyllanthus emblica* (PEFE) fruit, particularly digallic acid, exhibits anti-lipolytic activity by reducing triglyceride accumulation and down-regulating adiponectin, C/EBP-α, PPAR-α, and FABP4 in 3T3-L1 pre-adipocytes. *Myrica nagi Thunb* fruit extract (MEMN) demonstrates inhibitory activity against

Table 1
Anti-obesity potential of selected plant root and flower parts on 3T3-L1 adipocytes.

Sr no	Plant name	Part of plant	Mechanism	Conc. (µg/mL)	Ref
1	*Polygonum multiflorum Thunb*	Root	PME suppresses 3T3-L1 pre-adipocyte differentiation and cellular triglyceride contents by inhibiting the expression of adipogenic transcription factors (C/EBP- α, PPAR- α) and fatty acid synthase.	5 to 10	(Choi et al., 2018)
2	*Heracleum mollendorffii*	Root	The root inhibits preadipocyte differentiation by degrading C/EBP-α through JNK and GSK3 activation. It also blocks lipid accumulation in mature adipocytes by reducing adipogenesis-related proteins, including C/EBP-α, PPAR-α, perilipin-1, adiponectin, FABP4, FAS, and ACC. These actions suggest the root's potential for preventing and treating obesity.	100 to 200	(Geum et al., 2021)
3	*Adenophora triphylla*	Root	*Adenophora triphylla* root extract lowers adipocyte size, reduces lipid accumulation in the liver, and downregulates the expression of adipogenesis-related proteins, including PPAR-α, ap2, fatty acid synthase in 3T3-L1 adipocytes.	100 to 500	(Lee et al., 2015)
4	*Polygonum cuspidatum*	Root	*Polygonum cuspidatum* downregulates mRNA and protein production of adipogenesis-related and lipogenesis-related markers and inhibits lipid accumulation via the alleviation of p38 MAPK, ERK1/2, and JNK in 3T3-L1 pre-adipocytes.	50 to 150	(Choi et al., 2020)
5	*Allium hookeri (AH)*	Root	AHR inhibited lipid accumulation during adipocyte differentiation by downregulation of gene expression, such as hormone sensitive lipase (HSL), lipoprotein lipase (LPL) and an adipogenic gene, CCAAT/enhancer binding protein- α in 3T3-L1 preadipocytes.	5 to 500	(Kim et al., 2019)
6	*Capparis spinosa* L.	Flower	*Capparis spinosa* L. maintained the viability of the 3T3-L1 adipocytes and also reduced the lipid accumulation in 3T3-L1 cells, dose dependently. In-vitro pancreatic lipase inhibition assay of AFBECS had shown moderate level of inhibition when compared with Orlistat.	25 to 500	Athesh and Brindha (2022)
7	*Tropaeolum majus*	Flower	*Tropaeolum Majus* Extract (TME) effectively inhibits lipogenesis and adipogenesis in 3T3-L1 adipocytes, leading to reduced triglyceride content and lipid accumulation in these cells.	20 to 500	(Kim et al., 2017)
8	*Chrysanthemum indicum*	Flower	*Chrysanthemum Indicum* Aqueous Extract (CAE) inhibits adipogenesis by suppressing mitotic clonal expansion and downregulating Akt and ERK1/2 signaling pathways.	1 to 5	(Kim et al., 2021)
9	*Chrysanthemum morifolium Ramat*	Flower	HCF treatment inhibits lipid accumulation in 3T3-L1 pre-adipocytes without toxicity. It suppresses the expression of adipogenesis/lipogenesis-related genes (C/EBP- α, PPAR- α ASREBP-1c, FABP4, ACC1, FAS) and increases AMPK and SIRT1 activity.	1	Lee Y et al. (2021)
10	*Inula britannica*	Flower	*Inula Britannica* Aqueous Extract (IAE) dose-dependently suppresses intracellular lipid accumulation and mitigates the expression levels of lipogenesis- and adipogenesis-associated biomarkers in 3T3-L1 pre-adipocytes.	1 to 200	(Yu et al., 2020)
11	*Edgeworthia gardneri*	Flower	*Edgeworthia Gardneri* Extract (EEG) decreases lipid and triglyceride accumulations, down-regulates adipogenesis-related	12.5 to 100	(Gao et al., 2020)

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Table 1 (*continued*)

Sr no	Plant name	Part of plant	Mechanism	Conc. (μg/mL)	Ref
			transcription factors (C/EBP- α, PPAR- α and increases AMPK and ACC phosphorylation in 3T3-L1 pre-adipocytes.		

lipase, α-amylase, and α-glucosidase, reducing triglyceride accumulation in 3T3-L1 cells, inhibiting adipogenesis, and promoting lipolysis without cytotoxicity.

Acer truncatum seed coat (ESA) reduces visible triglyceride droplet accumulation and adipocyte numbers. *Hibiscus sabdariffa* calyx prevents lipid accumulation by suppressing differentiation of 3T3-L1 adipocytes. Lotus seeds (LBP) decrease intracellular lipid accumulation by activating AMPK and modulating a dual mechanism: downregulation of adipogenic/lipogenic transcription factors (PPAR-γ, FAS, SREBP-1c), and upregulation of lipolytic regulators such as HSL and perilipin-1, enhancing lipid droplet mobilization and fatty acid oxidation. *Ramulus mori* twig extract reduces expression levels of genes involved in adipogenesis and lipogenesis while increasing those related to lipolysis (ATGL and CPT1), promoting the catabolism of stored fats in differentiated adipocytes. *Allium cepa* L. peels (OPE) significantly decrease lipids in 3T3-L1 cells and inhibit lipid accumulation by reducing the expression of lipogenesis-related genes such as PPAR-α, C/EBP-A FAS, and ACC (Table 2). Phosphorylation of ACC by AMPK inhibits its activity, reducing malonyl-CoA levels and fatty acid synthesis. This relieves inhibition on CPT1, promoting mitochondrial fatty acid oxidation. The shift from lipogenesis to lipid utilization decreases fat accumulation, making ACC phosphorylation a key mechanism in the metabolic regulation and treatment of obesity. These collective findings underscore the diverse potential of plant extracts in targeting adipogenesis and lipid accumulation, presenting promising avenues for further exploration in the development of anti-obesity interventions.

3.3. Anti-obesity potential of selected plants leaves on 3T3-L1 adipocytes

The investigation delved into the potential anti-obesity effects of various plant leaves on 3T3-L1 pre-adipocytes, examining mechanisms that modulate lipid metabolism. Cocoa tea and *C. Setidens* Nakai leaves were found to inhibit triglyceride accumulation in mature adipocytes by suppressing key adipogenic transcription factors, PPAR-γ, and C/EBP-α, and reducing the expression of adipocyte-specific genes, suggesting a role in lipid metabolism regulation. *Rhinacanthus nasutus* leaves, *Ficus carica* L leaves, and *Corchorus olitorius* L leaves demonstrated inhibition of adipogenesis in 3T3-L1 cells through various regulatory pathways, including SREBP1C, PPAR-γ, C/EBP-α, and insulin sensitivity-related genes. Additionally, *Cornus kousa* leaves' anthocyanin fraction and *J. Communis* leaf extract was identified as effective inhibitors of lipid accumulation in adipocytes, acting through downregulation of adipogenesis-related signaling proteins. *Artemisia annua* L leaves, through *Artemisia Annua* Water Extract (AWL), were shown to suppress adipocyte differentiation by downregulating Akt activation and the expression of adipogenic genes. *Lampaya Medicinalis* Extract (HEL) from leaves exhibited improved insulin-stimulated phosphorylation and glucose uptake in 3T3-L1 pre-adipocytes without cytotoxicity (Table 3). These findings highlight the diverse mechanisms by which plant leaves can influence adipogenesis and lipid metabolism, suggesting their potential as anti-obesity agents.

Table 2
Anti-obesity potential of selected plants fruit seed and rhizome parts on 3T3-L1 adipocytes.

Sr. no	Plant name	Part of plant	Mechanism	Conc. (μg/mL)	Ref
1	*Cydonia oblonga Miller*	Fruit	COME inhibits intracellular TG accumulation during adipogenesis. It induces upregulation of AMPK phosphorylation and downregulation of adipogenic transcription factors (C/EBP- α, PPAR- α, ASREBP-1c).	100 to 800	(Lee et al., 2022)
2	*Kadsura japonica fruits (KJF)*	Fruit	KJF attenuates lipid accumulation and protein expression related to lipid accumulation in 3T3-L1 cells. It inhibits excessive proliferation and protein expressions related to cell growth.	NA	(Geum et al., 2022)
3	*Phyllanthus emblica (PEFE)*	Fruit	PEFE, particularly di-gallic acid, shows anti-lipolytic activity by decreasing triglyceride accumulation, downregulating adiponectin, C/EBP- α, PPAR- α and FABP4 in 3T3-L1 pre-adipocytes.	10 to 200	(Balusamy et al., 2020)
4	*Myrica nagi Thunb*	Fruit	The methanolic extract of *Myrica Nagi* (MEMN) exhibits potent inhibitory activity against lipase α-amylase, and α-glucosidase. MEMN reduces triglyceride accumulation in 3T3-L1 cells, inhibits adipogenesis, and promotes lipolysis without cytotoxicity. It achieves anti-obesity activity by downregulating PPAR-α expression.	10 to 160	Prashar and Patel (2020)
5	*Zizyphus jujuba*	Fruit	*Z. Jujuba* inhibits 3T3-L1 adipocytes by decreasing intercellular triglyceride content, GPDH activity, and the expression of adipogenic proteins (PPAR-α and C/EBP-α), suggesting	1 to 50	(Kubota et al., 2009)

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Table 2 (*continued*)

Sr. no	Plant name	Part of plant	Mechanism	Conc. (μg/mL)	Ref
			it as an effective anti-obesity compound.		
6	*Acer truncatum seed coat (ESA)*	Seed	ESA obviously reduced the visible triglyceride droplets accumulation, and dramatically decreased the number of the adipocytes at a comparatively high concentration.	40 to 120	(Liang et al., 2022)
7	*Atractylodes macrocephala Koidzumi*	Rhizomes	MK inhibits 3T3-L1 adipocyte differentiation without toxicity, decreasing phospho-Akt expression and suggesting an inhibitory effect on adipogenesis.	1 to 25	(Kim et al., 2011)
8	*Hibiscus sabdariffa*	Calyx	Roselle can prevent lipid accumulation by suppressing differentiation of 3T3-L1 adipocyte by downregulating the adipogenic gene expression	0.1 to 10	(Janson et al., 2021)
9	*Lotus*	Seeds	LBP decreases intracellular lipid accumulation by activating AMPK, down-regulating adipogenic/ lipogenic genes (PPAR-α, C/EBP-α, AP2, SREB-1c, ACC1, FAS, LPL), and up-regulating lipolytic genes (HSL, PGC-1α, SIRT1, CPT1- α) and adiponectin expression in 3T3-L1 pre-adipocytes.	0.1 to 1.0	(Lee et al., 2019)
10	*Ramulus mori*	Twig	Compared with the ERM-untreated group, the ERM-treated groups exhibited reduced expression levels of genes involved in adipogenesis and lipogenesis in differentiated adipocytes. While the expression levels of genes involved in lipolysis increased.	25 to 100	(Park et al., 2020c)
11	*Allium cepa* L	Peels	OPE significantly decreased the lipids of 3T3-L1 cells and inhibited lipid accumulation by reducing the expression of lipogenesis-related genes such as PPAR-α, C/EBP- α, FAS and ACC.	25 to 400	(Yu et al., 2021)

Table 3
Anti-obesity potential of selected plant leaves on 3T3-LI adipocytes.

Sr no	Plant name	Part of plant	Mechanism	Conc (μg/ml)	Ref
1	*Cocoa tea*	Leaves	Cocoa tea inhibits triglyceride accumulation in mature adipocytes by suppressing key adipogenic transcription factors, PPAR-α, C/EBP-α. Additionally, the tea extract reduces the expressions of adipocyte-specific genes, including SREBP-1c, FAS, ACC, FAT, and SCD-1, indicating its potential in modulating lipid metabolism.	50 to 200	(Li et al., 2016)
2	*C. Setidens Nakai ethanolic extract*	Leaves	CNE suppressed the expression of lipogenic genes and increased the expression of lipolytic genes. The antiadipogenic and anti lipogenic effects of CNE appear to be mediated by the inhibition PPAR-α and C/EBP expressions. Moreover, CNE stimulated fatty acid oxidation in an AMPK-dependent manner.	25 to 200	(Cho et al., 2017)
3	*Rhinacanthus nasutus*	Leaves	RRE and its naphthoquinone compounds inhibit adipogenesis in 3T3-L1 cells through both upstream (SREBP1C) and downstream (PPAR-α, C/EBP-α) regulations.	5 to 20	(Shah et al., 2017)
4	*Ficus carica* L	Leaves	FCa treatments down-regulate the transcriptional pathway of adipogenesis and insulin sensitivity in 3T3-L1 adipocytes by decreasing the expression of PPAR-α, C/EBP-α, Leptin, adiponectin, and GLUT4.	25 to 100	(Pucci et al., 2022)
5	*Cornus kousa (anthocyanin fraction)*	Leaves	Anthocyanin fraction inhibited lipid accumulation by down-regulating adipogenesis and lipogenesis promoting signaling proteins, PPAR-α, CCAAT, C/EBP-α, AP2, FAS, and LPL, however enhanced AMPK activation to *p*-AMPK in 3T3 cells quantified and	5 to 100	(Khan et al., 2018)

(*continued on next page*)

Table 3 (*continued*)

Sr no	Plant name	Part of plant	Mechanism	Conc (μg/ml)	Ref
			expressed by western blotting.		
6	*Corchorus olitorius* L	Leaves	WM treatment significantly inhibited lipid accumulation in 3T3-L1 adipocytes	NA	(Lee et al., 2019)
7	*J. Communis*	Leaves	*J. Communis* extract inhibits lipogenesis in adipocytes and antagonizes the PPAR-α through Ser112 phosphorylation via MAPK/ERK activation. It also accelerates triglyceride mobilization from the fat cells or enhances lipolysis.	1 to 640	(Bais and Patel, 2020)
8	*Artemisia annua* L	Leaves	*Artemisia Annua* Water Extract (AWL) suppresses the differentiation of 3T3-L1 preadipocytes into adipocytes by downregulating DMI-induced serine/threonine kinase protein kinase B (PKB/Akt) activation and the expression of adipogenic genes, including PPAR-α, C/EBP-α,	5 to 100	(Song et al., 2017)
9	*Lampaya medicinalis*	Leaves	*Lampaya Medicinalis* Extract (HEL) is not cytotoxic and improves insulin-stimulated phosphorylation of IRS-1, Akt, AS160, and glucose uptake.	0 to 10	(Ormazabal et al., 2020)

3.4. Anti-obesity potential of selected whole plant part on 3T3-L1 adipocytes

The presented findings unveil the potential anti-adipogenic effects of various plant extracts on 3T3-L1 adipocytes and preadipocytes, shedding light on diverse mechanisms and *in vitro* methods employed for assessment. *Akebia quinata* whole plant extract ameliorates excessive body weight gains by activating AMPK in white adipose tissue. *Solidago virgaurea* var. *Gigantean* administration decreases triacylglycerol levels and suppresses adipogenic gene expression, indicating potential anti-obesity effects. Sanguisorba officinalis L. 50 % ethanolic extract inhibits adipogenesis through PPAR-α and C/EBP-α regulation, potentially activating AMPK. *Gentiana lutea* whole plant treatment downregulates adipogenesis-related genes in 3T3-L1 preadipocytes. *Sargassum thunbergii* induces downregulation of PPAR-α in white adipose tissue and upregulation of thermogenic genes in brown adipose tissue (Kang MC et al., 2020). *Valeriana dageletiana Nakai* supplementation significantly suppresses lipid accumulation and lowers the expression of lipogenic genes in 3T3-L1 adipocytes.

Additional plant extracts, including *Spergularia marina, H. Perforatum* L., *Buginawa, Rosmarinus Officinalis* L, *Eriobotrya Japonica, Olea Europaea* L, *Polygala tenuifolia, Cornus officinalis* and *Ribes fasciculatum combination, Eriobotrya japonica, Garcinia cambogia* and *Pear Pomace* MIX, *Soshiho-tang, Jasonia glutinosa (L.), Ginseng saponin fraction and Glycyrrhiza glabra* L., *Raphanus sativus* L., *Ipomoea alba* L and Fermented *Platycodon grandiflorum* exhibit various inhibitory effects on adipogenesis, providing a broad spectrum of potential targets for combating obesity (Table 4).

4. High-fat diet (HFD) induced animal model

The diverse range of natural compounds and extracts discussed in the preceding sections highlights their potential as effective interventions against obesity and related metabolic disorders. Each substance exhibits unique mechanisms of action, providing valuable insights into the complex pathways involved in body weight regulation.

4.1. Anti-obesity potential of selected plants flower, root, fruit, seed, and rhizome parts on HFD induced mice

In this integrated analysis of diverse plant extracts, the studies collectively reveal promising anti-obesity effects across various experimental models. *Adenophora triphylla* root extract (ATE) administration in male C57BL/6J mice on a high-fat diet (HFD) results in a significant reduction in body weight, white adipose tissues (WATs) weight, and plasma triglyceride levels, while concurrently increasing high-density lipoprotein cholesterol. Similarly, *Polygonum multiflorum thunb* root supplementation in male C57BL/6 N mice exhibits notable reductions in visceral fat mass, size, and overall body weight. This is associated with the up-regulation of key genes involved in lipid metabolism and the simultaneous down-regulation of genes associated with adipogenesis. Oral administration of *Allium hookeri* root (AHR) in male C57BL/6J mice on an HFD leads to suppressed body weight gain, adipose tissue weight, serum leptin levels, and adipocyte cell size, achieved by modifying the expression of genes involved in adipogenesis, lipogenesis, and lipolysis. *Capparis spinosa* L. flower buds treatment in wistar strain male albino rats results in a significant reduction in body weight, fat-pad and organ weights, and normalization of metabolic parameters. *Aronia melanocarpa* berries extract exhibits notable anti-obesity effects in male C57BL/6J mice, including significant decreases in body weight, serum triglyceride, and low-density lipoprotein cholesterol levels, along with improved insulin sensitivity. *Ginger* extract (GE) from rhizomes, when administered to C57BL/6 J mice, enhances running endurance capacity and up-regulates PPAR-α targeted gene expression in skeletal muscle and the liver, acting as a specific PPAR-α ligand. Roselle calyx reduces body weight, food intake, lipid profiles, and inflammatory cytokines in male Sprague Dawley rats on an HFD, while simultaneously increasing glucose uptake in adipose tissue and muscle (Janson B et al., 2021). *Lotus* seeds' oral administration in male mice retards body weight gain, improves plasma lipid profiles, increases phosphorylation of AMPK, and modulates adipogenic/lipogenic and lipolytic gene expression. *Ramulus mori* twig administration in male C57BL/6 mice with HFD-induced obesity results in reduced body weight, liver weight, and epididymal adipose tissue weight, accompanied by decreased serum lipid levels and reduced lipid accumulation. Lastly, *Allium cepa* L. peels (OPE) treatment in C57BL/6J mice on an HFD significantly decreases body weight, fat coefficient, serum triglyceride, total cholesterol, and low-density lipoprotein cholesterol, along with the downregulation of adipogenesis genes (Table 5). These collective findings underscore the diverse and promising potential of plant extracts in managing obesity through multifaceted mechanisms and emphasize the need for further research, including clinical trials, to validate their efficacy and safety in human subjects.

4.2. Anti-obesity potential of selected plants leaves on HFD induced mice

The investigated plant extracts, particularly derived from leaves and aerial parts, exhibit promising anti-obesity effects in various rodent models. *Cirsium setidens Nakai*, in C57BL/6J mice, demonstrates a reduction in body weights and adipose tissue weights, accompanied by

Table 4
Anti-obesity potential of selected whole plant part on 3T3-L1 adipocytes.

Sr. no	Plant name	Mechanism	Conc. (μg/mL)	Ref
1	*Gambisan*	The adipogenesis process in 3T3-L1 cells is regulated by key transcription factors, including PPAR-α, C/EBP-α, and SREBP-1. PPAR-α acts as a master regulator, upregulating adipocyte-specific genes such as A-FABP, leading to triglyceride accumulation. C/EBP-A and SREBP-1 collaborate with PPAR-α, promoting adipocyte differentiation and lipid synthesis. Overexpression of these factors accelerates adipocyte differentiation, making them potential targets for obesity treatment.	100 to 500	(Kang et al., 2013)
2	*Akebia quinata*	AQE ameliorates excessive body and adipose tissue weight gains, improving serum lipid profiles by activating AMPK in white adipose tissue. This leads to changes in gene expression, mitigating the effects of a high-fat diet and suggesting AQE's anti-obesity and hypolipidemic effects.	10 to 400	(Sung et al., 2015)
3	*Solidago virgaurea* var. *Gigantean*	SVE administration decreases total triacylglycerol levels and suppresses adipogenic and lipogenic gene expression in white adipose tissue and liver, suggesting anti-obesity effects.	10 to 100	(Wang et al., 2017)
4	*Sanguisorba officinalis* L.	SOL 50 % ethanolic extract has anti-obesity effects by inhibiting adipogenesis through the regulation of PPAR-α and C/EBP-α, potentially activating AMPK and modulating lipid metabolism.	1000	(Jung et al., 2016)
5	*Gentiana luteal.,*	GL treatment inhibits adipocyte differentiation by downregulating the expression of adipogenesis-related genes (ADIPOQ, C/EBP-α, and SLC2A4) in 3T3-L1 preadipocytes. This was further supported by a decrease in the number of Oil Red O-stained lipid-rich vacuoles following GL treatment.	2 to 50	(Park et al., 2020b)
6	*Sargassum thunbergii*	ST-induced down-regulation of PPAR-α in white adipose tissue, and up-regulation of the thermogenic genes, UCP-1 and UCP-3, in brown adipose tissue was also observed.	NA	(Kang et al., 2020)
7	*Valeriana dageletiana Nakai*	VDAE supplementation significantly suppressed lipid accumulation in 3T3-L1 adipocytes and lowered the expression of lipogenic genes, such as SREBP-1c, FAS, SCD-1, and CD36.	10 to 50	(Wang et al., 2017)
8	*Spergularia marina Griseb*	SM ethanol extract (SME) inhibited proliferation and differentiation in murine adipocytes and primary porcine pre-adipocytes in a dose-dependent manner	50 to 200	(Park et al., 2020d)
9	*Vigna nakashimae*	VN extract suppressed adipocyte differentiation and significantly attenuated the expression of adipogenic genes in 3T3-L1 cells. It decreased the expression of PPAR and its target genes in fully differentiated 3T3-L1 cells. Moreover, it enhanced the phosphorylation of AMPK, ACC and increased the expression of fatty acid oxidation genes	10 to 100	(Son et al., 2013)
10	*H. Perforatum* L	H. Perforatum L. down-regulates the expression of Dgat1, FAS, colv, and LPL in fully differentiated 3T3-L1 cells, indicating its involvement in modulating adipocyte differentiation and lipid metabolism.	50 to 150	(Tokgoz and Altan, 2020)
11	*Buginawa (Bugi)*	Amygdalin and prunasin inhibit 3T3-L1 adipocyte differentiation by suppressing the expressions of PPAR-α, C/EBP-A, SREBP1c, FAS, and AP2, indicating their potential in regulating adipogenesis.	62.5 to 250	(Park et al., 2019)
12	*Rosmarinus Officinalis* L, *Eriobotrya*	These plants regulate adipocyte differentiation and intracellular fat	31 to 500	(Mansour et al., 2023)

(*continued on next page*)

Table 4 (*continued*)

Sr. no	Plant name	Mechanism	Conc. (μg/mL)	Ref
	Japonica and Olea Europaea L	deposition by targeting adipogenic signals, primarily from the PPAR and C/EBP families.		
13	*Polygala tenuifolia extract*	PTE inhibits lipid accumulation by reducing lipid formation and triglyceride content, increasing lipase activity, and modulating the expression of the master transcription factor PPAR- α. It also alters gut microbiota profiles.	1 to 500	
14	*Cornus officinalis* and *Ribes fasciculatum*	Combination treatment of CO and RF inhibits adipocyte differentiation by downregulating adipogenesis-associated genes (Srebp1, PPAR-α, C/EBP-α, FABP4, SREBP-1c, FAS) in 3T3-L1 cells.	10 to 50	(Park et al., 2020a)
15	*Eriobotrya japonica (EJ)*	The treatment of EJ, NN, and MIX in 3T3-L1 adipocytes effectively inhibited lipid accumulation, significantly decreased expression of PPAR-α, SREBP1c, AP2 and significantly increased phosphorylation of AMP activated protein kinase (AMPK).	EJ(1000), NN(100) & MIX(100)	(Sharma et al., 2015)
16	*Garcinia cambogia and Pear Pomace*	MIX shows greater inhibition of lipid accumulation compared to PE or GE alone, reducing the expression of adipogenesis-related factors (C/EBP-α, PPAR- α, FAS) and enhancing lipolysis in 3T3-L1 pre-adipocytes.	PE(500), GE (1 mg/ml) & MIX(250 PE & 500 GE)	(Sharma et al., 2018)
17	*Soshiho-tang*	SST inhibits lipid accumulation in 3T3-L1 adipocytes by decreasing triglyceride content, leptin concentration, and the expression of adipogenesis-related genes (LPL, FABP4, C/EBP- α, PPAR- α).	50 to 200	(Yoo et al., 2016)
18	*Jasonia glutinosa (L.)*	RT extract inhibited lipase, α-glucosidase and fatty acid amide hydrolase. Furthermore, the extract displayed anti-adipogenic properties in a dose-dependent manner as it significantly reduced TG accumulation during adipocyte differentiation	1 to 50	(Les et al., 2020)
19	*Ginseng saponin fraction (RGS) and Glycyrrhiza glabra L.(GG)*	The combination of RGS and GG extracts in different ratios (SG31, SG11, and SG13) efficiently inhibits triglyceride accumulation without cytotoxicity in 3T3-L1 adipocytes. It decreases the expression of adipogenic and lipogenic genes such as C/EBP- α, and SREBP-1c.	100 to 300	(Zheng et al., 2020)
20	*Raphanus sativus* L.	Water Extract of *Raphanus Sativus* (WERG) reduces weight gain, hepatic lipid accumulation, and improves serum lipid biomarkers. WERG treatment also improves intestinal permeability and suppresses harmful intestinal enzyme activities in feces, contributing to improved gut health.	100	(Sim et al., 2019)
21	*Ipomoea alba* L., *Convolvulaceae*	Ethanolic Extract of *Ipomoea Alba* (Iwong) significantly reduces lipid accumulation and glycerol-3-phosphate dehydrogenase (GPDH) activity, as well as down-regulates PPAR-α and C/EBP-α mRNA levels in 3T3-L1 mouse embryo fibroblasts.	100 to 300	(N'dille et al., 2019)
22	*Fermented Platycodon grandiflorum*	FPG significantly inhibited fat accumulation during 3T3-L1 adipogenesis through downregulating adipogenic transcript factors.	PG(100 to 200) FPG (100–200)	(Huang et al., 2016)

improved serum lipid profiles attributed to the downregulation of adipogenic/lipogenic genes and up-regulation of adiponectin and carnitine palmitoyltransferase-1 (CPT-1) in high-fat diet (HFD)-induced obesity. *Corchorus olitorius* L leaves administration in mice significantly lowers body weights, gut permeability, and hepatic lipid accumulation in the HFD group. *Artemisia annua* L leaves, administered orally in Sprague–Dawley male rats, exhibit notable reductions in body weight gain, adipose tissue mass, adipocyte cell size, serum triglycerides, and total cholesterol levels in HFD-induced obesity. *Cynara scolymus* leaves co-administered in Wistar female rats on an HFD demonstrate reductions in serum lipid profiles and hepatic disorders, alleviating hepatic dysfunction and oxidative stress. *Cyclocarya paliurus* leaves dose-dependently block increases in body mass, decrease food utilization, visceral fat mass, and serum lipids in Sprague–Dawley rats on an HFD. *Gynostemma pentaphyllum* leaves reduce serum triglycerides, total cholesterol, and LDL-cholesterol in male C57BL/6 N mice, activating AMPK and suppressing adipogenesis. *Salvia plebeia R. Br* aerial part reduces body weight, serum lipids, and adipocyte size in HFD-induced

Table 5
Anti-obesity potential of selected plants flower, root, fruit, seed, and rhizome parts on HFD induced mice.

Sr no	Plant name	Part of plant	Mechanism	Method	Conc. (mg/kg)	Ref
1	*Polygonum multiflorum Thunb*	Root	Supplementation in male C57BL/6 N mice reduces visceral fat mass, size, and body weight, upregulating PPAR-α, CPT1, CPT2, UCP1, and HSL mRNA levels and downregulating PPAR-γ and DGAT2 genes.	Male C57BL/6 N mice	5	(Choi et al., 2018)
2	*Adenophora triphylla*	Root	ATE treatment significantly decreases body weight gain, white adipose tissues (WATs) weight, and plasma triglyceride levels while increasing plasma high-density lipoprotein cholesterol in male C57BL/6J mice on an HFD.	Male C57BL/6J mice	200 to 400	(Lee et al., 2015)
3	*Allium hookeri*	Root	Oral administration of AHR in male C57BL/6J mice suppresses body weight gain, adipose tissue weight, serum leptin levels, and adipocyte cell size in HFD-induced obesity by modifying the expression of genes involved in adipogenesis, lipogenesis, and lipolysis in white adipose tissue and liver, including those related to cholesterol and fatty acid synthesis	Male C57BL/6J mice	100 to 500	(Kim et al., 2019)
4	*Capparis spinosa* L. *(AFBECS)*	flower buds	Treatment results in a significant reduction in body weight, fat-pad and organ weights, and normalization of glucose, insulin, leptin, lipid profiles, and antioxidant status in Wistar strain of male albino rats.	Wistar strain of male albino rats	100 to 300	(Athesh and Brindha, 2022)
5	Lotus	seeds	Bound phenolics extracted from lotus seeds (LBP) oral administration retards body weight gain, improves plasma lipid profile, increases phosphorylation of AMPK, and down-regulates adipogenic/lipogenic genes while up-regulating lipolytic genes in male mice.	Male mice	250 to 500	(Lee et al., 2019)
6	*Ramulus mori*	Twig	Administration to male C57BL/6 mice with HFD-induced obesity reduces body weight, liver weight, and epididymal adipose tissue weight, along with decreased serum lipid levels and reduced lipid accumulation	Male C57BL/6 mice	150 to 400	(Park et al., 2020c)
7	*Allium cepa* L	peels	OPE treatment in C57BL/6J mice on an HFD significantly decreases body weight, fat coefficient, serum triglyceride, total cholesterol, and low-density lipoprotein cholesterol, along with down-regulation of adipogenesis genes.	C57BL/6J mice	36 to 144	(Yu et al., 2021)
8	*Aronia melanocarpa*	Berries	Extract-treated HFD-induced obese male C57BL/6J mice exhibit significant decreases in body weight, serum triglyceride, and low-density lipoprotein cholesterol levels, along with improved insulin sensitivity.	Male C57BL/6J mice	100 to 200	(Baum et al., 2016)
9	*Blueberry (Vaccinium ashei) anthocyanin (BA)*	Berries	BA supplementation in high-fat diet-induced obese male C57BL/6 mice decreases serum glucose, attenuates epididymal adipocytes, improves lipid profiles, and down-regulates expression levels of TNFα, IL-6, PPAR γ, and FAS genes, altering body weight by suppressing fatty acid synthesis and alleviating inflammation.	Male C57BL/6 mice.	50 to 200	(Wu et al., 2016)
10	*ginger extract (GE)*	Rhizome	GE in C57BL/6 J mice improves running endurance capacity, up-regulates PPAR-α targeted gene expression in skeletal muscle and the liver, and acts as a specific PPAR-α ligand.	C57BL/6 J mice	500	(Wang et al., 2019)
11	*Roselle (Hibiscus sabdariffa)*	calyx	Reduces body weight, food intake, lipid profiles, and inflammatory cytokines in male Sprague Dawley rats on an HFD, while increasing glucose uptake in adipose tissue and muscle.	Male Sprague Dawley rats,	250	(Janson et al., 2021)

obese mice by suppressing adipogenesis and lipogenesis-related genes. These findings collectively underscore the potential of plant extracts, particularly from leaves and aerial parts, as effective interventions against obesity, offering diverse mechanisms that merit further exploration for therapeutic applications. (Table 6).

Table 6
Anti-obesity potential of selected plants Leaves on HFD induced mice.

Sr. no	Plant name	Part	Mechanism	Animals	Conc. (mg/kg)	Ref
1	*C. setidens Nakai*	Leaves	Treatment in C57BL/6J mice reduces body weights and adipose tissue weights, improving serum lipid profiles through the down-regulation of adipogenic/lipogenic genes and upregulation of adiponectin and carnitine palmitoyltransferase-1 (CPT-1) in HFD-induced obesity.	C57BL/6J mice	25 to 200	Cho et al. (2017)
2	*Corchorus olitorius* L	Leaves	Mice treated with 100 mg/kg WM experience significantly lower body weights, gut permeability, and hepatic lipid accumulation compared to those in the HFD group.	C57BL/6J mice	100	(Lee et al., 2019)
3	*Artemisia annua* L	Leaves	Oral administration of AWL extracts in Sprague–Dawley male rats significantly decreases body weight gain, adipose tissue mass, adipocyte cell size, serum triglyceride, and total cholesterol levels in HFD-induced obesity	Sprague–Dawley male rats	150	(Song et al., 2017)
4	*Cynara scolymus*	Leaves	Co-administration in Wistar female rats on an HFD reduces serum lipid profile and hepatic disorders, alleviating hepatic dysfunction and oxidative stress.	Wistar female rats	200 to 400	(Ben Salem et al., 2019)
5	*Cyclocarya paliurus*	Leaves	CPE dose-dependently blocks increases in body mass, decreases food utilization, visceral fat mass, serum total cholesterol, triglycerides, and low-density lipoprotein cholesterol, and elevates high-density lipoprotein cholesterol levels in Sprague–Dawley rats on an HFD.	Sprague–Dawley rats	2 to 8gm/kg	(Yao et al., 2015)
6	*Gynostemma pentaphyllum*	Leaves	GPE reduces serum levels of triglyceride, total cholesterol, and LDL-cholesterol in male C57BL/6 N mice, activating AMPK and suppressing adipogenesis by regulating the expression of genes involved in lipid metabolism.	Male C57BL/6 N mice	100 & 300	(Lee et al., 2019)
7	*Salvia plebeia R. Br*	Leaves	Reduces body weight, serum lipids, and adipocyte size in HFD-induced obese mice by suppressing adipogenesis and lipogenesis-related genes.	Mice C57BL/6 N	200 & 400	(Choi et al., 2016)
8	*Raphanus sativus* L.	Leaves	100 μg/ml WERG reduces lipid accumulation in 3T3-L1 adipocytes and male C57BL/6J mice on an HFD.	Male C57BL/6J mice	50 to 100	(Sim et al., 2019)

4.3. Anti-obesity potential of selected whole plant part on HFD induced mice

The diverse plant extracts examined in this study demonstrate significant anti-obesity effects through various mechanisms, providing a valuable array of potential interventions. *Akebia quinata, Solidago virgaurea* var. *gigantean, Sanguisorba officinalis* L., *Gentiana lutea* L., and *Valeriana dageletiana Nakai* exhibit anti-obesity properties by regulating adipogenesis-related genes, particularly involving PPAR-α and C/EBP-α, leading to reduced body weight and adipose tissue mass in different mouse models fed a high-fat diet. Additionally, *Spergularia marina Griseb, Buginawa (Bugi), Polygala tenuifolia extract, Cornus officinalis (CO)* and *Ribes fasciculatum (RF), Eriobotrya japonica (EJ), Nelumbo nucifera (NN)* and MIX, *Soshiho-tang, Ginseng saponin fraction (RGS) and Glycyrrhiza glabra* L. *(GG), Raphanus sativus* L., *fermented Platycodon grandiflorum, Garcinia cambogia, and Sargassum thunbergii* demonstrate their efficacy in preventing HFD-induced obesity, influencing body weight, adipose tissue weight, and lipid profiles in different experimental settings. These findings collectively highlight the potential of these plant extracts as promising natural agents for combating obesity through diverse molecular pathways, offering a foundation for further exploration and development of therapeutic strategies. Table 7.

5. Gold nano particles for both 3T3-L1 adipocytes and HFD induced mice

The presented study explores the potential anti-obesity and metabolic-regulating properties of various plant-derived nanoparticles. The findings provide valuable insights into the effects of these nanoparticles on adipocytes and related molecular pathways, shedding light on their therapeutic potential in managing obesity and associated complications. The nano particles derived from plants notably diminished lipid accumulation in 3T3-L1 obese cells and decreased nitric oxide (NO) production in Raw 264.7 macrophage cells. Additionally, they down-regulated the expression of adipogenic genes PPAR-γ and C/EBP-α, indicating potential antiadipogenic and anti-inflammatory

Table 7
Anti-obesity potential of selected whole plant part on HFD induced mice.

Sr. no	Plant name	Part of plant	Mechanism	Method	Conc. (mg/kg)	Ref
1	*Akebia quinate*	Whole Plant	Anti-obesity mechanism involves AMPK activation in white adipose tissue, mitigating excessive body and adipose tissue weight gains in male mice consuming a high-fat diet (HFD).	Male C57BL/6 N mice	400	(Sung et al., 2015)
2	*Solidago virgaurea* var. *gigantean*	Whole Plant	Prevents obesity by reducing lipid accumulation in adipose and hepatic tissues of male C57BL/6 N mice, modulating adipogenesis and lipogenesis-related genes.	Male C57BL/6 N mice	10	(Wang et al., 2017)
3	*Sanguisorba officinalis* L.	Whole Plant	50 % Ethanolic extract exhibits anti-obesity effects in obese C57BL/6J mice by inhibiting adipogenesis through PPAR-α and C/EBPα regulation, potentially involving AMPK activation.	C57BL/6J mice	50 to 200	(Jung et al., 2016)
4	*Gentiana lutea* L.	Whole Plant	Extract prevents HFD-induced weight gain, fatty hepatocyte deposition, and adipocyte size increase in male C57BL/6J mice by decreasing leptin and insulin secretion.	Male C57BL/6J mice.	100 to 200	(Park et al., 2020a)
5	*Valeriana dageletiana Nakai*	Whole Plant	Reduces body weight gain, food intake, and hepatic lipid metabolites in C57BL/6 N mice on an HFD by decreasing adipogenesis-related mRNA expression of PPAR-γ, C/EBP-α, and aP2.	C57BL/6 N mice	100	(Wang et al., 2017)
6	*Spergularia marina Griseb*	Whole Plant	Attenuates fat accumulation in HFD-induced obese rats, improving lipid profiles in serum and tissues.	Sprague–Dawley male rats	30 to 50	(Park et al., 2020a)
7	*Vigna nakashimae*	Whole Plant	Extract suppresses HFD-induced increases in body weight, epididymal fat tissue weight, and hepatic lipid levels, while decreasing plasma triacylglycerols, fatty acid, total cholesterol, and inflammatory cytokines in male C57BL/6 mice.	Male C57BL/6 mice (HFD)	300 to 500	(Son et al., 2013)
8	*Buginawa (Bugi) contains twelve medicinal herbs*	Whole Plant	Administration reduces body weight gain, white adipose tissue (WAT) weight, and prevents lipid droplet accumulation in epididymal white adipose tissue and liver in male C57BL/6 N mice.	Male C57BL/6 N mice	50	Park et al. (2019)
9	*Polygala tenuifolia extract*	Whole Plant	Reduces increased body weight, elevated serum triglyceride content, and liver steatosis in C57BL/6J mice with high-fat diet–induced obesity, altering the expression of genes involved in lipid and cholesterol metabolism.	C57BL/6J mice	250	(Wang et al., 2017)
10	*Cornus officinalis (CO) and Ribes fasciculatum (RF)*	Whole Plant	Mixture inhibits HFD-induced weight gain, decreases abdominal visceral fat tissues, and prevents adipocyte differentiation and lipid accumulation in female C57BL/6J mice.	Female C57BL/6J mice	75 to 300	(Park et al., 2020a)
11	*Eriobotrya japonica (EJ), Nelumbo nucifera (NN) and MIX*	Whole Plant	Mix of EJ and NN extract more strongly decreases body weight, fat weight, and liver weight in male C57BL/6J mice with high-fat diet-induced obesity compared to EJ and NN extract alone.	Male mice (C57BL/6J)	200 to 400	(Sharma et al., 2015)
12	*Soshiho-tang*	Whole Plant	Administration to C57BL/6J mice with HFD-fed obesity significantly reduces body weight and fat accumulation in adipose tissue	C57BL/6J mice	200 to 600	(Yoo et al., 2016)
13	*Ginseng saponin fraction (RGS) and Glycyrrhiza glabra* L.*(GG)*	Whole Plant	SG31, a mixture of RGS and GG extracts in male C57BL/6J obese mice on an HFD, significantly reduces white adipose tissue weight and body weight, improves dyslipidemia, and decreases serum triglyceride levels by activating the AMPK pathway and stimulating adiponectin secretion in adipose tissue.	Male C57BL/6J obese mice	100 to 300	(Zheng et al., 2020)
14	*fermented Platycodon grandiflorum*	Whole Plant	FPG markedly reduces final body weight, epididymal adipose tissue mass, and adipocyte size in male C57BL/6J mice, inhibiting adipogenesis and regulating lipid metabolism.	Male C57BL/6J mice	100 to 200	(Huang et al., 2016)
15	*Garcinia cambogia*	Whole Plant	Extract lowers body weight gain, visceral fat accumulation, blood and hepatic lipid concentrations, plasma insulin, and leptin levels in HFD-induced obesity in C57BL/6J mice, reversing the expression pattern of adipose tissue genes (AP2, SREBP1c, PPAR-γ, C/EBPα).	C57BL/6J mice	500	(Heo et al., 2016)
16	*Sargassum thunbergia*	Whole Plant	Treatment decreases body weight and fat accumulation in HFD-induced obese mice, along with reduced insulin and cardiovascular disease-related factors in serum.	Male C57BL/6 mice	100 to 300	(Kang et al., 2020)

activities.

In a study involving different plants, Korean *Curcuma longa* extracted from rhizomes demonstrated promising effects in reducing body weight, fat mass, and improving serum lipid profiles in high-fat diet-induced obese mice. It also exhibited benefits such as lowered fasting blood glucose and increased insulin sensitivity, along with stimulation of lipolysis and improved glycolipid metabolism in adipose tissue (Lee YS et al., 2023). *Salacia chinensis*, particularly its leaves in the form of SCNPS (*Salacia chinensis* nanoparticles), showed potential in decreasing body weight, BMI, adipose index, and various metabolic markers in male albino Wistar animals, accompanied by increased levels of adiponectin, HDL-C, and PAMPK-α1(Gao L et al., 2020). Additionally, *Smilax glabra* nanoparticles from rhizomes displayed interactions with adipocytes, influencing adipokine secretion and providing a protective effect against diabetes-induced damage in liver cells and heart vessels in male Wister rats (Ansari S et al., 2019). Table 8 highlight the diverse mechanisms and positive outcomes associated with these plant-derived compounds in addressing obesity-related and metabolic issues in animal models.

In obesity treatment, mTOR inhibition reduces adipogenesis and lipid synthesis, improving metabolic balance. Concurrently, activation of FOXO1 enhances insulin sensitivity and promotes lipid catabolism by upregulating genes involved in energy expenditure. Together, modulating mTOR and FOXO1 pathways helps suppress fat accumulation and supports weight management.

6. Discussion

The studies investigating the anti-obesity potential of various plant parts on 3T3-L1 adipocytes present a comprehensive view of the multifaceted approaches plant extracts can offer in combating obesity. The detailed analysis of these extracts' effects on key adipogenic and lipogenic transcription factors, activation of lipolysis, metabolic enzymes and overall implications for obesity management is promising. A pivotal aspect of the research is the focus on how plant extracts downregulate critical transcription factors such as PPAR-α, C/EBP-α, SREBP-1 and PPAR-γ which are fundamental in the process of adipocyte differentiation and lipid accumulation (Ranade SD et al., 2024; Gharge S et al., 2025). For instance, extracts like *Cydonia oblonga* and *Polygonum multiflorum* have demonstrated the capability to inhibit these transcription factors, thereby preventing the maturation of pre-adipocytes into adipocytes and reducing the lipid accumulation within cells (Lee et al., 2022; Choi et al., 2018). This suggests that targeting these transcription pathways could be an effective strategy in preventing or reducing obesity. Several extracts like those from *Polygonum multiflorum* and *Heracleum mollendorffii* roots have shown promising results in inhibiting pre-adipocyte differentiation (Geum et al., 2021). This effect is critical as it prevents the early-stage conversion of pre-adipocytes into fully mature adipocytes, thus reducing the overall capacity for lipid storage within fat tissue. Many extracts were noted to down-regulate key transcription factors such as PPAR-α, C/EBP-α, and SREBP-1c, which are pivotal in the transcriptional regulation of genes necessary for adipogenesis and lipogenesis. PPAR-γ and C/EBP-α are key transcription factors regulating adipocyte differentiation and fat storage. Inhibiting their expression disrupts adipogenesis, reducing the formation of new fat cells and lipid accumulation. This suppression helps decrease adipose tissue mass, making PPAR-γ/C/EBP-α inhibition a crucial mechanism in the treatment of obesity (Choi et al., 2018). For instance, *Chrysanthemum morifolium Ramat* extract affects these pathways by modulating AMPK phosphorylation, a central regulator of cellular energy (Lee Y et al., 2021). Some extracts, like *Myrica nagi* fruit extract, demonstrate inhibitory activity against lipase, α-amylase, and α-glucosidase, thus promoting the breakdown of fats and preventing their accumulation (Prashar and Patel, 2020). Activation of AMPK by Lotus seeds also points to enhanced fatty acid oxidation, further contributing to reduced lipid levels in cells. The diversity in mechanisms through which these plant extracts operate suggests a multifaceted approach to managing and potentially treating obesity (Lin et al., 2019). Plant extracts offer promising multi-targeted approaches for obesity management by modulating adipocyte function and fat metabolism. For instance, Lotus seed extract activates AMPK, a key energy regulator, promoting fat breakdown and preventing new fat accumulation. These natural compounds modulate key metabolic pathways such as lipogenesis, lipolysis, and energy homeostasis, presenting a safer alternative to conventional pharmacological treatments. For instance, inhibition of the mTOR pathway suppresses adipogenesis and lipid synthesis, thereby enhancing metabolic balance. Simultaneously, activation of FOXO1 improves insulin sensitivity and stimulates lipid breakdown by upregulating genes associated with energy expenditure. Collectively, the coordinated regulation of mTOR and FOXO1 pathways by these compounds contributes to reduced fat accumulation and offers effective support for weight management (Nagai S et al., 2018; Cao Y et al., 2022). Their diverse mechanisms suggest potential for personalized treatment based on individual metabolic profiles. While *in vitro* results are encouraging, further *in vivo* and clinical studies are essential to confirm efficacy,

Table 8
Anti-obesity potential of selected plants gold nano particles on 3T3-L1 pre adipocytes and HFD induced mice.

Sr. no	Plant name	Part of plant	Mechanism	Method	Ref
1	*Gynostemma pentaphyllum*	Whole Plant	GP-aunps significantly decreased lipid accumulation in 3T3-L1 obese cells and reduced NO production in Raw 264.7 macrophage cells.	3T3-L1 Pre-adipocytes	(Akter et al., 2022)
2	*Curcuma longa*	Rhizomes	CLE treatment activates AMPK phosphorylation, a key regulator of energy homeostasis. This activation inhibits adipogenesis and enhances lipolysis by modulating related proteins. Consequently, lipid accumulation is reduced in adipose and liver tissues, improving metabolic function.	3T3-L1 Pre-adipocytes	(Lee et al., 2023)
3	*Panax ginseng*	Leaves	P.g aunps (*Panax ginseng* nanoparticles) exhibited anti-adipogenic effects by downregulating PPAR-γ, C/EBPα signaling in 3T3-L1 mature adipocytes.	3T3-L1 fibroblast preadipocytes	(Simu et al., 2019)
4	*Plocamium telfairiae*	Whole plant	PT-AuNS reduced lipid accumulation by downregulating the mRNA and protein expression of key adipogenic markers such as C/EBPα, PPARγ, SREBP1, FAS, and aP2. Additionally, it upregulated the expression of UCP1, PRDM16, and PGC1α, promoting mitochondrial biogenesis and effectively stimulating brown adipocyte differentiation in mature adipocytes.	3T3-L1 preadipocytes	(Park et al., 2022)
5	*Marsila quadrifolia*	Whole plant	Gnps (Gold nanoparticles) did not cause significant toxicity at 100 μm concentration. Enhanced glucose utilization in 3T3-L1 cells, surpassing the effects of insulin and metformin.	3T3-L1 adipocytes	(Chowdhury et al., 2017)
6	*Vicenin 2*	Flavonoid	VN-aunps (Vicenin 2 nanoparticles) increased glucose uptake in 3T3-L1 adipocytes. Docking data analysis suggested interactions with PTP1B and AMPK, potentially enhancing insulin sensitivity.	3T3-L1 adipocytes	(Chockalingam et al., 2015)
7	*Dendropanax morbifera Léveille*	Whole plant	D-aunps downregulate adipogenic genes (PPAR-γ, C/EBP-α, ap2, Jak2, STAT3), upregulate PPAR-α, and decrease ACC and FAS expression, indicating potential anti-obesity effects and cholesterol regulation.	3T3-L1 adipocytes	(Yu et al., 2020)

safety, and pharmacokinetics. Overall, plant-based interventions could serve as effective adjunct therapies in obesity management.

The recent study on the potential anti-obesity and metabolic-regulating properties of various plant-derived nanoparticles offers intriguing insights into the application of nanotechnology in the field of metabolic health and obesity management. This research advances our understanding by demonstrating the effects of nanoparticles on molecular pathways relevant to obesity, specifically focusing on adipocyte behavior and systemic metabolic functions in animal models. the activation of lipolysis and metabolic enzymes, the broader implications for obesity management, the significance of *in vivo* studies, and the mechanisms of action underlying these effects. A significant aspect of the study highlights how nanoparticles derived from plants such as *curcuma longa* and *Salacia chinensis* can regulate critical transcription factors like PPAR-γ and C/EBP-α. (Lee et al., 2023). These factors are central to the process of adipogenesis, influencing the differentiation and maturation of preadipocytes into adipocytes. By down-regulating these genes, nanoparticles effectively inhibit the formation of new fat cells, contributing to reduced fat mass and combating obesity at a molecular level. The nanoparticles were shown to enhance lipolysis and stimulate the activity of key metabolic enzymes. For example, *curcuma longa* nanoparticles improved glycolipid metabolism and increased insulin sensitivity, which are crucial for enhancing the breakdown of fats and sugars within the body. Similarly, *Salacia chinensis* nanoparticles increased the levels of adiponectin and activated AMPK, a pivotal enzyme in cellular energy homeostasis that promotes the catabolism of fatty acids and glucose. These findings underscore the potential of nanoparticles to serve as powerful tools in managing obesity and related metabolic disorders. By targeting fundamental biological pathways that govern fat metabolism and energy regulation, nanoparticles offer a novel approach that could complement or enhance existing therapies. Their ability to be engineered to specific target sites potentially allows for reduced side effects and improved efficacy compared to traditional pharmacological agents. The use of *in vivo* models, such as HFD-induced obese mice and Wistar rats, is vital for assessing the practical applications and effects of these nanoparticles. These studies provide essential data on the efficacy, pharmacokinetics, and safety of the nanoparticles, offering a closer approximation to how these interventions might perform in human clinical scenarios. They also allow for the observation of systemic effects and long-term outcomes, which are crucial for any new therapeutic approach. The cytotoxicity of the synthesized gold nanoparticles (GNPs) was evaluated using 3T3-L1 preadipocytes to assess their biocompatibility. Consistent with previous reports (Akter et al., 2022; Lee et al., 2023; Yi et al., 2020; Chowdhury et al., 2017; Chockalingam et al., 2017), no significant cytotoxic effects were observed across a wide concentration range of 3.125–200 μg/mL, indicating excellent cellular compatibility. Specifically, mediated gold nanoparticles (MQ-GNPs) demonstrated a cellular viability of 71.23 ± 1.56 % in 3T3-L1 adipocyte cells, further supporting their low cytotoxic potential and suitability for biological applications. The study provides compelling evidence that plant-derived nanoparticles act through diverse mechanisms to exert their anti-obesity effects. These include direct interactions with adipocytes to prevent lipid accumulation, modulation of inflammation within adipose tissues, enhancement of insulin signaling pathways, and regulation of genes involved in fat metabolism. Such multifaceted actions highlight the complex interactions of nanoparticles with cellular and molecular pathways.

7. Conclusion

This study highlights the potential of plant-derived compounds, particularly when encapsulated in gold nanoparticles, in combating obesity by targeting key proteins involved in adipogenesis and lipid metabolism. These compounds demonstrate significant anti-adipogenic effects through the modulation of adipocyte signaling pathways, reduction of lipid accumulation, and enhancement of lipolytic gene expression. Various plant parts, including roots, leaves, flowers, fruits, seeds, and rhizomes, exert their anti-obesity effects by inhibiting adipocyte differentiation, down-regulating adipogenic transcription factors, and improving insulin sensitivity. Additionally, some plant extracts enhance glucose uptake, activate AMPK, and suppress lipid accumulation without causing cytotoxicity. Gold nanoparticles, in particular, show promise in both 3T3-L1 adipocytes and HFD-induced mice. While these findings underscore the therapeutic potential of natural remedies for obesity and related metabolic disorders, further research is required to validate these effects and explore their clinical applicability for safer and more effective anti-obesity treatments.

CRediT authorship contribution statement

Sachin Gudasi: Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation. **Mrityunjaya B. Patil:** Writing – review & editing, Validation, Investigation.

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Declaration of competing interest

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

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Abbreviations:

PPAR	Peroxisome proliferator activated receptor
SREB-1C	Sterol regulatory element binding protein
AP2	Adipocyte lipid-binding protein
AMPK	adenosine monophosphate-activated protein kinase
ACC	Acetyl-CoA carboxylase
FAS	Fatty acid synthase
FAT	Fatty acid translocase
C/EBPα	CCAAT/enhancer binding protein α
FABP4	Fatty acid binding protein 4
CPT1	Carnitine palmitoyl transferase
HSL	Hormone-sensitive lipase HSL
SIRT1	Sirtuin 1
LPL	Lipoprotein lipase
PGC-1α	Peroxisome proliferator activated receptor gamma coactivator 1-alpha
HFD	High fat diet
GNP	Gold nano particle
FOXO	Forkhead box O

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