iMedPub Journals
http://www.imedpub.com

Translational Biomedicine
ISSN 2172-0479

2015
Vol. 6 No. 3:21

Review of Medicinal Plants for Anti-Obesity Activity

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Abstract

Obesity is a complex health issue to address, it is a serious and chronic disease that can have a negative effect on many systems in your body. Overweight and obesity may increase the risk of many health problems, including diabetes, heart disease, osteoarthritis and certain cancers. Obesity is increasing at an alarming rate throughout the world. Today it is estimated that there are more than 300 million obese people world-wide. Obesity is regarded as a disorder of lipid metabolism and the enzymes involved in this process could be targeted selectively for the development of antiobesity drugs. However, most of the anti-obesity drugs that were approved and marketed have now been withdrawn due to serious adverse effects. The naturopathic treatment for obesity has been explored extensively since ancient times and gaining momentum in the present scenario. Traditional medicinal plants and their active phytoconstituents have been used for the treatment of obesity and their associated secondary complications. Some active medicinal plants and their respective bioactive compounds were also tested by clinical trials and are effective in traemnet of obesity. This review focus on natural phytoextracts with their mechanism of action and their preclinical experimental model for further scientific research.

Keywords: Obesity; Antiobesity drugs; Medicinal plants

Introduction

In the present scenario, obesity is the major public health problem with about 1.9 billion adults (18 years and older) worldwide are overweight and about 600 million of them are clinically obese [1]. Obesity is characterized by increase in adipose cell size which is determined by amount of fat accumulated in the cytoplasm of adipocytes [2]. This change in the metabolism in the adipocytes is regulated by various enzymes such as fatty acid synthase, lipoprotein lipase and adipocyte fatty acid-binding protein [3].

Obesity results from an imbalance between energy intake and expenditure. It is caused by altered lipid metabolic processes including lipogenesis and lipolysis [4]. Lipogenesis is the process that stores free fatty acids in the form of triglyceride (TG) [5]; similarly, lipolysis is the process whereby the TG stored is metabolized to free fatty acids and glycerol [6]. Obesity accompanied by hyperlipidemia which is indicated by abnormally high concentration of lipids in blood [7]. The adipose tissue, an endocrine organ, has a major role in the regulation of metabolism and homeostasis, through the secretion of several biologically active adipokines [8]. During adipose tissue development, three major transcription factors, peroxisome proliferator-activated receptor (PPAR) γ, CCAAT/enhancer binding protein (C/EBP) α, and sterol regulatory element-binding protein (SREBP) 1c, regulate the expression of these lipid-metabolizing enzymes [9]. 5' AMP-activated protein kinase (AMPK) plays a major role in glucose and lipid metabolism by inactivating acetyl-CoA carboxylase (ACC) and stimulates fatty acid oxidation by up-regulating the expression of carnitine palmitoyltransferase-1 (CPT-1), PPARα, and uncoupling protein [10].

Nowadays, changes in human lifestyle and high energy diet have increased the incidence of obesity and even have become a risk factor to the population of children [11,12]. There are several pharmacologic substances available as antiobesity drugs, however they have hazardous side effects and hence natural products have been used for treating obesity in many Asian countries [13]. The potential of natural products for the treatment of obesity is still largely unexplored and can be an excellent alternative for the safe and effective development of antiobesity drugs [14].

Currently drugs available in the market for treatment of obesity can be divided into two major classes one being orlistat, which reduces fat absorption through inhibition of pancreatic lipase and the second is subutramine which is an anorectic or appetite suppressant. Both drugs have adverse effects including increased blood pressure, headache, drymouth, insomnia, and constipation [15,16]. In 1990 Fenfluramine and Dexfenfluramine were withdrawn from the market because of heart valve damage [17].

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The US FDA in 1997 approved subutramine drug as a treatment for obesity. But later in October 2010 the drug was withdrawn from the market due to increased cardiovascular events and strokes [18,19]. In February 2011 the US FDA rejected approval of contrive which is a combination of bupropion/naltrexone due to concerns over potential cardiovascular risks [20]. Certain drugs have potential for abuse such as phentermine and diethylpropion and hence are approved for short term use [21].

At present, because of high cost and potentially hazardous side effects, the need for natural products against obesity is under exploration which may be an alternative strategy for developing effective, safe antiobesity drugs [22]. In 2000, Moro and Basile reported the use of certain well known medicinal plants that had claimed to be useful in treating obesity. The antiobesity effects of natural products from more diverse sources [23]. The aim of the present review was to update data on potential antiobesity herbal plants.

Methods

Databases used for this study to search include PubMed, Scopus, Google Scholar, Web of Science, and IranMedex with information reported between September 2, 2006 to September 22, 2014. Search of literatures was focused on human or animals investigating the benefits and harms of herbal medicines to treat obesity. The search terms were "obesity" and ("herbal medicine" or "plant", "plant medicinal" or "medicine traditional") without narrowing or limiting search items. Publications with abstract from the mentioned databases were used to prepare this review. The main outcome measures were defined as body weight, body fat, including fat mass/fat weight or fat percentage/visceral adipose tissue weight, waist or hip circumference, triceps thickness and appetite, and the amount of food/energy intake. Abstracts of publications on plants used to evaluate the activity on human, animals, cell lines studies with the main outcome as mentioned above were included. In vitro studies, review articles and letters to the editor were excluded. Two reviewers reviewed the articles for abstracts and title. Due to our inclusion and exclusion criteria, the duplicate articles were eliminated. The review includes active components and mechanism of action against obesity in animals and presented in **Table 1**. Some of the plants are tested for their activity against obesity in cell lines listed in **Table 2** and plants that were tested on human volunteers or clinical trails are listed in **Table 3**. In some instances scientist have evaluated the anti-obesity activity in isolated cell organelles, isolated cellular enzymes specifically pancreatic lipase are listed in **Tables 3** and **4** respectively. **Table 4** present the plant which was studied for its activity against obesity in an *in silico* model.

Discussion

In this review, we have report the antiobesity effects of different herbal plants or compounds containing minerals or chemical extracts of plants. Plants having reported antiobesity effects are listed in **Table 1** with information about their active components and their effects. From the review it was suggested that, plant showing anti-obesity potential mainly belongs to the family Leguminoseae, Lamiaceae, Liliaceae, Cucurbitaceae, Asteraceae, Moraceae, Rosaceae and Araliaceae. Majority of the studies indicates decrease in body weight or body weight gain in animals and humans with or without changes in body fat indicating antiobesity effects. The antiobesity effects such as body weight reduction, decrease in the levels of triglycerides, total cholesterol, and low density lipoprotein cholesterol with simultaneous increase in high density lipoprotein cholesterol was observed in the animals treated with the plants [1,15,29,31,39,54,60,78,79,83,85,98,100,101,133,145,152,165,190,196,201]. In one study [41], it has been reported that a compound chakasaponin II, suppressed mRNA levels of neuropeptide Y (NPY) and enhanced the release of serotonin (5-HT) that suppressed the appetite signals in the hypothalamus of the mice. Clinical trials were conducted on humans for various plant extracts [45,49,135] which showed a significant decrease in body weight and body fat reduction. There was an increase in metabolic rate and energy expenditure. It was also reported that the clinical trials performed on humans for the plant extracts [151,165,226] showed an excess fat elimination, body mass index, fat percentage and blood glucose lowering effects. In another clinical trial study [148] the fenugreek seed extract decreased the fat consumption and also insulin/glucose ratio. The essential oil from the plants [124,227] suppressed fat

Table 1. Anti-obesity effect of natural occurring plants with mechanism of action studied on animal models

	Plant name	Part(s)	Mechanism	Experimental model	Reference
1	*Achyranthes aspera* Linn (Amaranthaceae)	Seed	The plant lowers total cholesterol, total triglyceride, and LDL-cholesterol, and increases HDL cholesterol level.	High-fat-fed male Swiss albino mice	[24]
2	*Acorus calamus* Linn (Araceae)	Rhizome, roots and leaves	Ethyl acetate extarct of *A. calamus* inhibits α-glucosidase activity.	Glucose challenged mice.	[25]
3	*Achyranthes bidentata* Blume (Amaranthaceae)	Root	The drug affects on differentiation of adipocyte and decrease of phospho-Akt expression.	Male Sprague-Dawley fed with a high-fat diet	[26]
4	*Actinidia polygama* Max (Actinidiaceae)	Fruits	Serum levels of aspartate decreased in the mice treated with the extract without changes in serum levels of alanine transaminase blood urea nitrogen and creatinine.	Mice with high-fat diet induced obesity	[27]
5	*Adenophora triphylla* Hara (Campanulaceae)	Root	Anti-obesity effect of *A. triphylla* is mediated by increasing adipocytes adiponectin and activating pathway like AMPK, and PPAR-α, and decreasing adipokines TNF-α, GPDH, and PPAR-α. It also actively expresses low-density lipoprotein [LDL] receptor and cholestorl 7α- hydroxylase (CYA7A1) and inhibits expression of 3 hydroxy-3 methyl glutaryl - CoA (HMG-CoA) reductase.	High fat diet (HFD)-C57B2/6 mice	[28,29]

6	*Aegle marmelos* Linn (Rutaceae)	Leaves	The active chemical constituents of *A. marmelos* for anti-adipogenic activity are halfordinol, ethyl ether aegeline and esculetin were responsible for the decrease in adipocyte accumulation. Active compounds umbelliferone and esculetin depletes lipid content in the adipocytes and by decreasing the hyperlipidemia.	High fat diet induced obese male Sprague Drawly rat	[30,31]
7	*Allium cepa* Linn (Amaryllidaceae)	Peel	The mRNA levels of activating protein (AP2) is down-regulated by *A.cepa* and those of carnitine palmitoyl transferase-1 α (CPT-1α) and fatty acid binding protein 4 (FABP4) are up-regulated. It is also proposed that *A. cepa* increases level of PPAR-γ2 mRNA (mesenteric fats) and IL-6 mRNA levels (perirenal and mesenteric fats).	High fat-fed rats, Diet-induced obese Male Sprague-Dawley rats	[32,33]
8	*Allium fistulosum* Linn (Liliaceae)	Root	Significant reduction in body weight and adipose tissue weight as well as adipocyte size. Genes involved in lipogenesis are down-regulated by *A. fistulosum*.	High fat diet- induced mice	[34]
9	*Allium nigrum* Linn (Amaryllidaceae)	Bulb	Extract of *A. nigrum* upregulates AMPK, FOXO1, Sirt1, ATGL, HSL, perilipin, ACO, CPT-1, and UCP1 in the adipose tissues, whereas it downregulates CD36.	High-fat diet induced obese mice	[35]
10	*Allium sativum* Linn (Amaryllidaceae)	Stem, Bulb and Roots	It increases antioxidant enzymes and suppresses glutathione depletion and lipid peroxidation in hepatic tissue. Oil isolated from *A. sativum* down regulates sterol regulatory element binding protein-1c, acetyl-coA carboxylase, fatty acid synthase, and 3-hydroxy-3-methylglutaryl-coenzyme A reductase.	High-fat diet-induced obese C57BL/6J mice	[36,37]
11	*Alpinia galanga* Linn (Zingiberaceae)	Rhizome	Galangin, the principal compontent of *A. galangal* decreases serum lipids, liver weight, lipid peroxidation and accumulation of hepatic TGs.	Obesity induced in female rats by feeding cafeteria diet	[38]
12	*Alpinia officinarum* Hance (Zingiberaceae)	Root	The drug controls and improves lipid profile in animals by lowering serum Total-C, TG, and LDL-C concentrations, leptin content.	Obesity in mice fed a high-fat diet	[39,40]
13	*Angelica gigas* Nakai (Apiaceae)	Roots	Decursin, the active constituent of *A.gigas* improves glucose tolerance. Decursin along with the HFD significantly reduces secretion adipocytokines such as leptin, resistin, IL-6 and MCP-1.	Mice fed a high-fat diet	[41]
14	*Argyreia nervosa* Bojer (Convolvulaceae)	Root	Serum contents of leptin, total cholestrol, LDL, and triglycerides are reduced by *A. speciosa*.	Diet- induced obesity rats	[42]
15	*Artemisia iwayomogi* (Compositae)	Whole Plant	It downregulates adipogenic transcription factors PPARγ2 and C/EBPα and their target genes CD36, aP2, and FAS. The extract decreases gene expression of proinflammatory cytokines including TNFα, MCP1, IL-6, IFNα, and INFβ in epididymal adipose tissue and reduces plasma levels of TNFα and MCP1.	Mice fed a high-fat diet.	[43]
16	*Atractylodes lancea* (Thunb.) DC (Compositae)	Rhizome	It inhibits human pancreatic lipase. A new polyacetylene, *syn*-(5*E*,11*E*)-3-acetoxy-4-O-(3-methylbutanoyl)-1,5,11-tridecatriene-7,9-diyne-3,4-diol has been isolated and identified and exhibits lipase inhibitory activity.	High-fat diet-induced obesity mice	[44]
17	*Aster pseudoglehni Lim, Hyun & Shin (Asteraceae)*	Leaves	It suppresses expression of adipogenesis-related genes including PPARγ, C/EBPα, and SREBP1c.	High fat diet induced-male C57BL/6J mice	[45]
18	*Bauhinia variegata* Linn (Leguminosae)	Stem and root barks	Extract of *E. variegata* increases brain serotonin level and high-density lipoprotein with a concomitant decrease in total cholesterol, triglycerides and low-density lipo protein.	Hypercaloric diet - induced mice	[46]
19	*Bergenia crassifolia* (L.) Fritsch (Saxifragaceae)	Leaves	Galloylbergenin derivatives 3,11-Di-O-galloylbergenin and 4,11- di-O-galloylbergenin are found to be present in *B. crassifolia* moderates anti-lipid accumulation activities.	Rats with high-calorie diet-induced obesity	[47]

20	*Boehmeria nivea* (L.) Gaudich (Urticaceae)	Leaf	The extracts reduces adipose tissue weight serum alkaline aminotransferase and lactate dehydrogenase activities. Serum triglyceride, total cholesterol, LDL-cholesterol level, atherogenic index and cardiac risk factors are decreased in animals fed with leaf powder and serum HDL -cholestrol levels are increased.	High fat/ cholestrol diet-induced Male Sprague-Dawley rats.	[48]
21	*Boerhaavia diffusa* L. (Nyctaginaceae)	Root	The phytoconstituents compounds sitosterol found in this plant which is structurally similar to cholesterol has been suggested to reduce cholesterol by lowering the level of LDL-cholesterol and cholesterol level decreased significantly in plasma without any side effects.	High fat diet in female Sprague-Dawley rats	[49]
22	*Bombax ceiba* L. (Malvaceae)	Stem bark	The extract and active constituent gemfibrozil reverses the effects of HFD treatment on serum parameters. This activity may be due to the inactivation of acetyl-coA carboxylase, as a result of AMPK activation that mediates thermogenesis and FAS inhibition.	Male, Wistar albino rats	[50]
23	*Anredera cordifolia* (Ten.) Steenis (Basellaceae)	Leaves	The extract suppresses lipid accumulation and down-regulates PPARγ, CCAAT/enhancer binding protein α, SREBP, and their target genes. It also increases phosphorylation of AMPK.	High-fat diet-induced obese rats	[51]
24	*Brassica rapa* L. (Brassicaceae)	Root	Lipolysis-related genes including β_3-adrenergic receptor, hormone-sensitive lipase, adipose triglyceride lipase, and uncoupling protein are induced in white adipocytes of animals treated with extract of *B. campestris*.	High fat diet induced mice	[52]
25	*Buddleja officinalis* Maxim (Scrophulariaceae)	Whole Plant	The extract reduces body weight gain induced through adipocyte differentiation.	High-fat diet to C57BL/6 mice	[53]
26	*Bursera grandiflora* (Schltdl.) Engl (Burseraceae)	Roots	*B. grandiflora* exerts anti-obesity activity by decreasing in the plasma-triglyceride levels.	Mice of the C57B1/6 strain with hypercaloric diet.	[54]
27	*Calanus finmarchicus* (Calanidae)	Wax	*C. finmarchicus* reduces macrophage infiltration and downregulates expression of proinflammatory genes including tumor necrosis factor-α, interleukin–6, and monocyte chemoattractant protein–1, whereas up-regulates adiponectin expression.	C57BL/6J mice with high-fat diet	[55]
28	*Camellia japonica* L. (Theaceae)	Leaves	*C. japonica* control insulin which is a modulator of lipid synthesis via sterol regulatory element binding protein-1c (SREBP-1c), decreased levels of insulin affects hepatic triglyceride synthesis.	High fat diet induced Sprague–Dawley rats	[56]
29	*Camellia oleifera Abel (Theaceae)*	Fruit hull	*Serum levels of total cholesterol and triacylglycerols are decreased but high-density lipoprotein cholesterol increased.Activity of fatty acid in animal liver is lowered by.*	Male ICR mice were fed a HFD	[57]
30	*Camellia sinensis* (L.) Kuntze (Theaceae)	Leaves, twigs and stems, flower buds	*C. sinesis* attenuates the gene expression of (SREBP-1c), fatty acid synthase and CCAAT/enhancer binding protein α. Extract found to reduce sICAM-1 release followed by nonpharmacological HGTE supplementation in db/db mice causing no adiponectin-inducing or antiadipogenic effects, reduced sICAM-1 release. Chakasaponin II from flower bud, suppresses mRNA levels of neuropeptide Y (NPY). The mRNA levels of adipogenic genes such as PPAR-γ, C/EBP-α, SREBP-1c, adipocyte fatty acid-binding protein, lipoprotein lipase and fatty acid synthase are decreased in *C. Sinensis* treated animals.	Albino rats fed on high-fat diet, diet-induced obesity in Female ddY mice, high fat induced- C57BL/6J-Lepob/ob mice, high fat diet- induced C57BL/6J mice	[58-64]
31	*Cheilanthes albomarginata* C.B. Clarke (Pteridaceae)	Rhizome	Extract of *C. albomarginata* lowers plasma triglyceride activity as well as reduces weight of adipose tissue.	High fat diet induced obese male Sprague Dawleyrats	[65]

32	*Chenopodium quinoa* Willd (Amaranthaceae)	Seeds	*C. quinoa* extract attenuate mRNA levels of several inflammation markers including monocyte chemotactic protein-1, CD68 and insulin resistance osteopontin, plasminogen activator inhibitor-1 and it also reverses the effects of HF-induced downregulation of the uncoupling protein(s) mRNA levels in muscle.	Mice fed with standard low-fat or a high-fat diet	[66]
33	*Cirsium brevicaule* A. Gray (Compositae)	Leaves	*C. brevicaule* inhibits fatty acid synthase and suppress the differentiation and lipid accumulation and affecting transcription factors such as SREBP-1c, C/EBPα, and PPARγ known to control the fatty acid synthase expression.	C57BL/6 mice that were fed a high-fat diet	[67]
34	*Citrus reticulata* Blanco (Rutaceae)	Peel	mRNA expression levels of lipogenesis rrelated genes such as SREBP1c, FAS and ACC1 in the liver are lowered and the size of adipocytes are reduced.	High fat diet induced mice	[68]
35	*Citrus sunki* (Hayata) Yu.Tanaka (Rutaceae)	Peel	Phosphorylation levels of AMPK and acetyl-CoA carboxylase are decreased.	High-fat diet induced obese C57BL/6 mice	[69]
36	*Clerodendrum phlomidis* L. f. (Lamiaceae)	Roots	It nhibits pancreatic lipase activity. The extract contains β-sitosterol.	High fat diet induced obesity in C57BL/6J mice	[70]
37	*Coccinia grandis* (L.) Voigt (Cucurbitaceae)	Fruit	Reduces body weight, food intake, organ and fat pads weight and serum GLU, CHO, TRG, LDL and VLDL cholesterol levels and increases HDL levels.	Cafeteria diet and Atherogenic diet induced obesity in female rats.	[71]
38	*Codonopsis lanceolata* (Siebold & Zucc.) Benth. & Hook.f. ex Trautv (Campanulaceae)	Roots	Reduces weight of adipose pads and the serum levels of triglycerides, total cholesterol, and low density lipoprotein cholesterol.	High-calorie/high-fat-diet induced obesity Sprague-Dawley male rats	[72]
39	*Coffea arabica* L. (Rubiaceae)	Seed	*C. arabica* diet supplementation can impair glucose tolerance, hypertension, cardiovascular remodeling, and nonalcoholic fatty liver disease.	High-carbohydrate, high-fat diet-fed Wistar male rats	[73]
40	*Coleus forskohlii* (Willd.) Briq. (Lamiaceae).	Root	*C. forskohlii* act as anti-obesisity drug by inhibiting dyslipidemia.	Diet-induced obesity in rats	[74,75]
41	*Corchorus olitorius* L. (Malvaceae)	Leaves	Liver tissue gene expression of gp91phox (NOX2) involved in oxidative stress is down-regulated by *C. olitorius* and genes related to the activation of β-oxidation like PPARα and CPT1A are up-regulated by the plant.	High fat diet - induced LDL receptor deficient mice	[76]
42	*Cordia ecalyculata* Vell (Boraginaceae)	Whole plant	Anti-obesity activity of the *C. ecalyculata* is medicated by anorectic central action, facilitating binding to adenosine receptors, thereby promoting an extension of adrenalin.	Mice (albino, swiss strain) treated with cyclophosphamide	[77]
43	*Cornus officinalis* Siebold & Zucc. (Cornaceae)	Rhizome	Platycodin D is the major component effective to activate AMPK-α. The extract reduces serum levels of aspartate transaminase and alanine transaminase.	C57BL/6J mice were fed a HF diet	[78]
44	*Cucumis melo* L. (Cucurbitaceae)	Fruit peel	*C. melo* reduces gain in body weight, serum lipid profile like total cholesterol, triglyceride, LDL-C level, atherogenic index and increases serum HDL-C levels.	High cholesterol diet induced in rats	[79]
45	*Cyamopsis tetragonoloba* (L.) Taub (Leguminosae)	Beans	It decreases adipose triglyceride accompanied by enhancing activity of hormone-sensitive lipase-facilitating mobilization of depot fat.	High-fat-fed Wistar rats	[80]
46	*Dimocarpus longans* Leenh (Sapindaceae)	Flower	By combined effect of decreased exogenous lipid absorption, normalization of hepatic PPAR-γ gene expression, suppression of pancreatic activity and SREBP-1c and FAS gene expression, and higher fecal triglyceride output.	Hyper caloric diet- male Sprague-Dawley rats.	[81]
47	*Dioscoreae tokoronis* Linn (Dioscoreaceae)	Root	It decreases triglyceride, total plasma cholesterol, and low-density lipoprotein-cholesterol. It suppresses the expression of SREBP-1 as well as that of fatty acid synthase in adipose and liver tissues.	High fat diet - induced mice	[82]

48	*Eucommia ulmoides* Oliv (Eucommiaceae)	Leaves, Bark	Asperuloside increases adenosine 5'-triphosphate production in WAT and increases use of ketone bodies/ glucose in skeletal muscle.	Obesity induced by ovariectomy in female Wistar rats, rats fed a high-fat diet.	[83,84]
49	*Fraxinus excelsior* L. (Oleaceae)	Seed	Secoiridoids present enhances fat metabolism through β-oxidation, inhibit adipocyte differentiation during animal growth and limit fat accumulation.	High fat diet induced mice	[85]
50	*Garcinia cowa* Roxb. ex Choisy (Clusiaceae)	Fruit, commercially available tablet	Inhibits the enzyme ATP-dependent citrate lyase, which catalyzes the cleavage of citrate to oxaloacetate and acetyl-CoA.Serum apo A1 levels are increased by the plant and the serum total cholesterol levels.	Female Sprague-Dawley rats fed atherogenic diet	[86,87]
51	*Geranium thunbergii* Siebold ex Lindl. & Paxton (Geraniaceae)	Leaf	The extract ameliorates high-fat diet-induced obesity by altering the adipokine levels and downregulates expression of transcription factors and lipogenic enzymes involved in lipid metabolism.	High fat diet - induced mice	[88]
52	*Glycine max* (L.)Merr. (Leguminosae)	Bean	Reductions glucose-6-phosphate dehydrogenase, malic enzyme, fatty acid synthetase, as well as acetyl-CoA carboxylase. The extract decreases appetite and HF diet-induced body weight gain through leptin-like STAT3 phosphorylation and AMPK activation.	Diet-induced obese mice	[89,90]
53	*Gymnema sylvestre* (Retz.) R.Br. ex Sm (Apocynaceae)	Leaves	Inhibits serum lipids, leptin, insulin, glucose, apolipoprotein B and LDH levels while it increases the HDL-cholesterol, apolipoprotein A1 and antioxidant enzymes levels.	High fat diet-induced obesity in wistar rats	[91-93]
54	*Hibiscus cannabinus* L. (Malvaceae)	Leaves	It decreases serum cholesterol, triglycerides, LDL-C, SGOT and SGPT activities.	High cholesterol diet induced obesity in female albino rats	[94]
55	*Hibiscus sabdariffa* L. (Malvaceae)	Leaf	Promotes LXRα/ABCA1 pathway, stimulating cholesterol removal from macrophages, delaying atherosclerosis. Also, the extract treatment attenuated liver steatosis, downregulated SREBP-1c and PPAR-γ, blocked the increase of IL-1, TNF-α mRNA and lipoperoxidation and increased catalase mRNA.	High fat diet-induced obese C57BL/6NHsd mice	[95,96]
56	*Holoptelea integrifolia* (Roxb.) Planch. (Ulmaceae)	Bark	HMG-CoA reductase activity is reduced and cholesterol biosynthesis and increase in lecithin, cholesterolacyltransferase activity.	Diet-induced obese rat	[97]
57	*Humulus lupulus* L. (Cannabaceae)	Female inflorescence	Hepatic fatty acid synthesis is reduced through the reduction of hepatic SREBP1c mRNA expression in the rats fed a high-fat diet.	High-fat diet induced obese rat, male C57BL/6J mice fed a HF diet	[98,99]
58	*Hunteria umbellata* (K.Schum.) Hallier f. (Apocynaceae)	Seed	The extract reduces weight gain pattern and causes dose related reductions in the serum lipids, Coronary artery risk index. Also, pre-treatment significantly improves triton-induced hepatic histological lesions.	High fat diet- induced rats	[100]
59	*Hypericum philonotis* Schltdl. & Cham. (Hypericaceae)	Leaves	Decreases body weight and serum glucose levels. It also decreases total cholesterol, triglycerides and high-density lipoprotein-cholesterol without changing low-density lipoprotein-cholesterol, AI, AST and ALT level.	Male Wistar rats fed with high fat diet	[101]
60	*Hypericum silenoides* Juss. (Hypericaceae)	Leaves	Body weight and serum glucose levels of the rats decreased. The drug also has effect on total cholesterol, triglycerides and high-density lipoprotein-cholesterol.	Male Wistar rats fed with high fat diet	[101]
61	*Ilex paraguariensis* A.St.-Hil. (Aquifoliaceae)	Leaves and unripe fruits	Down-regulates expression of Creb-1 and C/EBPa, and up-regulates expression of Dlk1, Gata2, Gata3, Klf2, Lrp5, $Pparc_2$, Sfrp1, Tcf7l2, Wnt10b, and Wnt3a. The mRNA levels of PPAR-γ2 were downregulated.	High fat diet- induced mice, male Wistar rats fed diet	[102-105]
62	*Ipomoea batatas* (L.) Lam (Convolvulaceae)	Fruit	Expression of SREBP-l, Acyl-CoA Synthase, Glycerol-3-Phosphate Acyltransferase, HMG-CoA Reductase and Fatty Acid Synthase in liver tissue in mice is altered.	Mice fed with high-fat diet	[106]
63	*Saccharina japonica* (Phaeophyceae)	Whole Plant	Expression of the fat intake-related gene ACC2 and lipogenesis-related genes are reduced. It increases phosphorylation of AMPK and its direct downstream protein, acetyl coenzyme A carboxylase.	High-fat-diet-induced obese male Sprague-Dawley rats	[107,108]

64	*Larix laricina* (Du Roi) K.Koch (Pinaceae)	Whole Plant	Stimulates glucose uptake, potentiated adipogenesis, activated AMPK, and acted as mitochondrial uncoupler/ inhibitor (on normal isolated mitochondria).	Diet-induced obese C57BL/6 mice	[109]
65	*Ligularia fischeri* (Ledeb.) Turcz. (Compositae)	Leaves	Polyphenols present in the extract exhibits antiobesity effects by inhibiting pancreatic lipase.	C57BL/6 mice	[110]
66	*Ligustrum lucidum* W.T.Aiton (Oleaceae)	Fruits	Treatment with the extract decreases HFD-induced obesity, mainly by improving metabolic parameters, such as fats and triglycerides.	High fat-diet-induced C58BL/6J obese mice	[111]
67	*Lithocarpus polystachyus* (Wall. ex A.DC.) Rehder (Fagaceae).	Leaves	Decreases levels of serum lipids, attenuates body weight gain and lowers circulatingleptin and insulin levels, ameliorate the state of oxidative stress, raise serum adiponectin, reduce circulating CRP and resistin levels, and depresses expression of PPARγ and C/EBPα.	High fat diet-induced obese rats	[112]
68	*Lithospermum erythrorhizon* Siebold & Zucc. (Boraginaceae)	Roots	Reduces high-fat diet-induced increases in body weight, white adipose tissue mass, serum triglyceride and total cholesterol levels, and hepatic lipid levels and decreases lipogenic and adipogenic gene expression. Acetylshikonin, active constituent of *L. erythrorhizon* suppresses adipocyte differentiation and attenuates adipogenic transcription factor expression.	C57BL/6J mice were fed a normal or high-fat diet	[113,114]
69	*Morinda citrifolia* L. (Rubiaceae)	Fruit	Reduces body weight and fat mass. It increases glucose tolerance and reduced plasma triglycerides level.	High-fat diet-induced obesity in mice	[115]
70	*Morus alba* L. (Moraceae)	Fruit, leaves	The hepatic peroxisome PPAR-R and carnitine palmitoyltransferase-1 are elevated, while fatty acid synthase and 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase are reduced. It decreases hepatic lipids, fatty acid synthase and 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase and elevates hepatic peroxisome PPAR-α and carnitine palmitoyltransferase-1.	High fat diet- induced mice, 6-week-old male hamsters.	[116]
71	*Morus australis* Poir (Moraceae)	Fruit	Reduces resistance to insulin, associated with leptin.	Male C57BL/6 mice fed with high-fat diet	[117]
72	*Morus nigra* L. (Moraceae)	Fruit, leaves,	Proinflammatory cytokines MCP-1 and TNF-α, plasma triglyceride, liver lipid peroxidation levels and adipocyte size are decreased. Inflammatory markers (monocyte chemoattractant protein-1, inducible nitric oxide synthase, C-reactive protein, tumour necrosis factor-α and interleukin-1) in liver and adipose tissue are increased.	Adenovirus 36-induced obesity in mice, high-fat (HF) diet-induced obese mice.	[116-120]
73	*Murraya koenigii* (L.) Spreng. (Rutaceae)	Leaves	Reduces body weight gain, plasma total cholesterol and triglyceride levels in mice.	High fat diet -induced mice	[121]
74	*Myrciaria dubia (Kunth) McVaugh (Myrtaceae)*	Fruit	Reduces animal body weights of the fat in white adipose tissues, glucose, total cholesterol, triglycerides, and LDL-c and insulin blood levels. An increase in HDL-c levels also seen.	Wistar rats with obesity induced by subcutaneous injection of monosodium glutamate	[122]
75	*Myrtus communis* L. (Myrtaceae)	Leaves	The body weight reduced by 32 % when administered with sibutramine, while it was reduced by 21 % and 24 % when administered with the methanolic extract of *M. communis*/kg body weight.	High-fat diet induced obese mice	[123]
76	*Nelumbo nucifera* Gaertn. (Nelumbonaceae)	Seed epicarp, leaves, seed, petals	The extracts effective in inhibiting preadipocyte differentiation. The flavonoids inhibits effect on both adipocyte differentiation and pancreatic lipase activity, accumulation and decreases expression PPARγ, GLUT4, and leptin in cultured human adipocytes, indicating that it inhibits the differentiation of pre-adipocytes into adipocytes. The methanol extract inhibits lipase activity and suppresses the expression of fatty acid synthase, acetyl-CoA carboxylase, and HMGCoA reductase and increases the phosphorylation of AMP-activated protein kinase in the liver.	High fat diet- induced mice Male Sprague-Dawley rats were fed with a normal diet and a high-fat diet, High fat diet - induced C57BL/6 mice.	[124-127]

77	*Nephelium lappaceum* L. (Sapindaceae)	Fruit	The expression of Igf-1 and Igf-1R were reduced on obese rat model treated with extract of *N. lappaceum*.	Rat fed with high calorie diet and treated with ellagic acid	[128]
78	*Nitraria retusa* (Forssk.) Asch. (Nitrariaceae)	Shoot	The extract supresses increase in body and fat mass weight, and decreases triglycerides and LDL-cholesterol levels and enhances gene expression related to lipid homeostasis in liver showing anti-obesity actions.	BKS.Cg-Dock7^{m}+/+ Lepr$^{db/}$J mice model	[129]
79	*Olea europaea* L. (Oleaceae)	Leaves	The extract reverses HFD-induced upregulation of WNT10b- and galanin-mediated signaling molecules and key adipogenic genes (PPARγ, C/EBPα, CD36, FAS, and leptin). It also induces downregulation of thermogenic genes involved in uncoupled respiration (SIRT1, PGC1α, and UCP1) and mitochondrial biogenesis (TFAM, NRF-1, and COX2).	High-fat diet-induced obesity in mice	[130,131]
80	*Orthosiphon aristatus* (Blume) Miq (Lamiaceae)	Whole plant	Betulinic acid, the active constituent suppresses hypothalamic protein tyrosine phosphatase 1B in mice and enhances the antiobesity effect of leptin in obese rats	High-fat-fed mice	[132]
81	*Panax ginseng* C.A.Mey. (Araliaceae)	Root	Ginsam increases PPAR- γ expression and AMP-activated protein kinase phosphorylation in liver and muscle. The extracts strongly activates Hormone Specific Lipase via Protein Kinase A.	Insulin - resistant rat, high fat diet induced obese C57BL6/J mice	[133,134]
82	*Perilla frutescens* (L.) Britton (Lamiaceae)	Leaf	It decreases body weight gain, food efficiency ratio, and relative liver and epididymal fat mass.	High fat diet - induced rats	[135]
83	*Petasites japonicus* (Siebold & Zucc.) Maxim. (Compositae)	Flower buds	The extracts attenuate three adipogenetic transcription factors, peroxisome PPAR-γ2, CCAAT/ enhancer- binding protein and sterol regulatory element- binding protein 1c.	Diet- induced obesity-prone mice.	[136]
84	*Phaseolus vulgaris* L. (Leguminosae)	Bean	It reduces food intake and body weight in an animal model of obesity resulting in suppression of glycaemia.	Genetically obese adult male Zucker fa/fa rats.	[137]
85	*Phyllostachys edulis* (Carrière) J.Houz. (Poaceae)	Leaves	The extract ameliorates elevated MCP-1 concentration in the blood.	High fat diet - induced C57BL/6J mice	[138]
86	*Pinus koraiensis* Siebold & Zucc (Pinaceae)	Leaves	Suppresses fat accumulation and intracellular triglyceride associated with downregulation of adipogenic transcription factor expression, including PPARγ and CEBPα in the differentiated 3T3-L1 adipocytes. It attenuates expression of FABP and GPDH as target genes of PPARγ during adipocyte differentiation.	High fat diet Male Sprague-Dawley rats	[139]
87	*Piper fragile* Benth (Piperaceae)	Seed	*P. fragile* rude oil shows significant reduction in body weight.	Male Sprague dawley mice were treated with high cholesterol diet	[140]
88	*Piper sarmentosum* Roxb. (Piperaceae)	leaves	*P. sarmentosum* group shows reduction in enzyme activity. Aqueous extract of *P. fragile* have the ability to reduce 11β-HSD1 enzyme activity.	Ovariectomy-Induced Obese Rats	[141]
89	*Platycodon grandiflorum* (Campanulaceae)	Roots	Platycodin feeding increases cholesterol absorption up to 60%, but not cholesterol synthesis. Platycodin-enriched diets can lower circulating and whole body cholesterol contents.	Golden Syrian hamsters	[142]
90	*Polygonum aviculare* L. (Polygonaceae)	Aerial Parts	Extract of *P. aviculare* suppresses the elevated mRNA expression levels of sterol regulatory element-binding protein-1c, peroxisome PPAR-γ, fatty acid synthase, and adipocyte protein 2 in the white adipose tissue of obese mice.	High-fat diet induced obese mice	[143]
91	*Populus balsamifera* L. (Salicaceae)	Whole Plant	Salicortin reduces whole body and retroperitoneal fat pad weights, as well as hepatic triglyceride accumulation. It also modulates key components in signaling pathways involved with glucose regulation and lipid oxidation in the liver, muscle, and adipose tissue.	C57Bl/6 mice subjected to high fat diet	[144]

92	*Premna integrifolia* Linn (Verbenaceae)	Roots	A significant decrease in the levels of serum glucose, triglyceride, total cholesterol, LDL and VLDL observed in the animals treated with the extract of *P. integrifolia.*	Female Swiss Albino mice, fed with cafetaria diet	[145]
93	*Prunus mume* (Siebold) Siebold & Zucc (Rosaceae)	Fruit	Increases CPT-1 expression and decreases FAS, ACC, and SREBP-1c in the liver and quadriceps muscles to resulting in reducing triglyceride accumulation. It also improves insulin sensitivity in OVX rats and prevents the impairment of energy, lipid, and glucose metabolism by OVX through potentiating hypothalamic leptin and insulin signaling.	High fat diet, ovariectomized rats	[114]
94	*Pueraria montana* var. chinensis (Ohwi) Sanjappa & Pradeep (Leguminosae)	Flower	It downregulates acetyl-CoA carboxylase expression. For adipose tissue, the expressions of hormone-sensitive lipase in white adipose tissue and uncoupling protein 1 in brown adipose tissue are upregulated.	Male C57BL/6J mice were fed a high-fat diet	[146]
95	*Punica granatum* L (Lythraceae)	Leaves, seed	Punicic acid binds and activates PPAR-α and γ, thus upregulating PPAR α and its responsive genes (Stearoyl-CoA desaturase-1, SCD1; Carnitine palmitoyltransferase 1, Cpt-1; and acyl-coenzyme A dehydrogenase) as well as PPAR γ-responsive genes expression (CD36 and Fatty Acid Binding Protein4, FABP4) in intra-abdominal white adipose tissue while suppressing expression of the inflammatory cytokine TNF-α and NF-κB activation.	High-fat diet induced obese mice	[147,148]
96	*Rheum palmatum* L. (Polygonaceae)	Root	It inhibits peroxisome PPAR-γ transactivity and the expression of its target genes, suggesting that rhein acts as a PPARγ antagonist.	Diet-induced obese female C57BL/6 mice	[108,149, 150]
97	*Rosmarinus officinalis* L. (Lamiaceae)	Leaves	It decreases circulating tumor necrosis factor alpha, IL-1β, and leptin, and upregulated adiponectin. The extract also induces phase I and phase II gene expression and the peroxisome PPAR-γ coactivator 1-alpha. Serum triglycerides, cholesterol and insulin levels are also decreased in the lean animals.	Lean (Le, *fa*/+) and obese (Ob, *fa*/*fa*) female Zucker rats	[151]
98	*Rubus fruticosus* L. (Rosaceae)	Fruit	Purified blueberry anthocyanins have been shown to improve body weight and body composition and reduce obesity in mice.	C57BL/6J mice fed a high-fat diet	[152]
99	*Sapindus emarginatus* Vahl (Sapindaceae)	Pericarp of flower	Methanolic extract decreases body weight, BMI, Blood glucose levels, total cholesterol, LDL-C, HDL-C, Triglycerides, SGOT, and SGPT.	Monosodium glutamate induced obesity in wistar albino rats	[153]
100	*Sasa quelpaertensis* Nakai (Poaceae)	Leaves	Adipogenesis is inhibited by this drug by downregulating the expression of CCAAT/enhancer-binding protein α, peroxisome PPAR-γ, SREBP-1c, and aP2. It also decreases the expression of fatty acid synthase and adiponectin mRNAs in differentiating adipocytes. It increases AMPK and acetyl-CoA carboxylase phosphorylation.	High-fat diet-induced obese C57BL/6 mice	[154,155]
101	*Schisandra chinensis* (Turcz.) Baill. (Schisandraceae)	Peel	It decreases expression of C/EBPβ, C/EBPα or PPARγ, and resultant down-regulation of the terminal marker gene, aP2 during differentiation of 3T3-L1 preadipocytes into adipocytes. Akt and GSK3β phosphorylation are down-regulated blocking adipogenesis and adipocyte differentiation.	HFD-induced obese rats	[156]
102	*Senna siamea (Lam.) H.S.Irwin & Barneby (Leguminosae)*	Roots	Active constituents includes chrysophanol, physcion, emodin, cassiamin A, friedelin and cycloart-25-en-3,24-diol exhibits pancreatic lipase inhibitory activity.	Alloxan induced diabetes rats.	[157]
103	*Shorea robusta* Gaertn (Diptercarpaceae)	Leaves	It decreasesserum glucose, triglyceride, cholesterol, LDL-C, HDL-C, VLDL-C, atherogenic index, SGPT and SGOT.	Monosodium glutamate induced obesity in albino rats	[158]
104	*Sida rhombifolia* L. (Malvaceae)	Leaf	Up-regulation of PPARγ 2 and SREBP-1c expression in the epididymal adipose tissue, leading to attenuation of adipogenesis.	High fat diet- induced C57BL/6J mice	[159]
105	*Solanum lycopersicum* L. (Solanaceae)	Fruit	AMP-activated protein kinase and acetyl-CoA carboxylase phosphorylation in liver is elevated, and HMG-CoA reductase expression is decreased. It strongly decreases expression of peroxisome PPAR-γ, CCAAT/enhancer-binding protein alpha and perilipin in the adipose tissue.	High-fat-diet-induced obesity in C57BL/6 mice	[160,161]

106	*Syzygium aromaticum* (L.) Merr. & L.M.Perry (Myrtaceae)	Flower buds	The extract suppresses expression of lipid metabolism-related proteins, including SREBP-1, FAS, CD36 and PPARγ in the liver and WAT, in addition to downregulates mRNA levels of transcription factors including SREBP and PPAR-γ.	High fat diet fed mice	[162]
107	*Tamarindus indica* L. (Leguminosae)	Fruit pulp, pulp, seed coat	Levels of plasma total cholesterol, lowdensity lipoprotein, and triglyceride is decreased and it increases high-density lipoprotein, with the concomitant reduction of body weight.	Diet-induced obese Sprague-Dawley rats	[163-165]
108	*Tecomella undulata* (Sm.) Seem.	Bark	The extract shows a significant increase in SIRT1 and adiponectin levels and decrease in PPAR, C/EBP, E2F1, leptin and LPL levels in preadipocytes and adipocytes and shows improvement in lipid profile and glucose levels.	High Fat Diet obese mice.	[166]
109	*Vaccinium corymbosum* L. (Ericaceae)	Peel	It inhibits lipid accumulation and decreases expression of C/EBPβ, as well as the C/EBPα and PPARγ genes during the differentiation of preadipocytes into adipocytes. It down-regulates adipocyte-specific genes such as aP2 and FAS.	High-fat diet-induced obese rats	[167]
110	*Veratrum nigrum* L. (Melanthiaceae)	Whole plant	It reduces weight gain and the fat pad weight in high fat diet-induced obese mice.	High-fat diet-induced obese mice	[134]
111	*Vigna angularis* (Willd.) Ohwi & H. Ohashi (Leguminosae)	Seed	It reduces total hepatic lipid accumulation and lipid secretion into the feces. Incubation of adipocytes with the extract significantly decreases triglyceride accumulation, glycerol phosphate dehydrogenase activity and inflammatory responses without affecting cell viability.	High fat diet-induced obesity in rats	[168]
112	*Vigna nakashimae* (Ohwi) Ohwi & H. Ohashi (Leguminosae)	Seeds	It decreases expression of peroxisome proliferator activated receptorγ and its target genes. It enhances the phosphorylation of AMP-activated protein kinase (AMPK) and acetyl CoA carboxylase (ACC), and increases the expression of fatty acid oxidation genes.	High-fat diet fed mice	[169]
113	*Viscum album* L. (Santalaceae)	Leaves, stems, and fruits	Body and epididymal fat pad weights are, and histological examination indicates an amelioration of fatty liver. It potently induces mitochondrial activity by activating thermogenesis and improving endurance capacity and also inhibited adipogenic factors in vitro.	Male C57Bl/6 mice fed a high-fat diet	[170]
114	*Vitis thunbergii* Siebold & Zucc (Vitaceae)	Roots	Activation of AMPK activating glucose and lipid metabolism.	High-fat diet-fed C57BL/6JNarl mice	[171]
115	*Vitis vinifera* L. (Vitaceae)	Seed flours, peel, roots, fruit	By up-regulating hepatic genes related to cholesterol (CYP51) and bile acid (CYP7A1) synthesis as well as LDL-cholesterol uptake. Lipid metabolism-associated genes Mlxp1, Stat5a, Hsl, Plin1, and Vdr were down-regulated. The extract treatment decreases expression of aP2, Fas, and Tnfa, known markers of adipogenesis, as measured by real-time polymerase reaction. Expression of PPAR-γ in liver and adipose tissue is lowered by regulating the lipid metabolism and suppressed obesity.	Male Golden Syrian hamsters fed high-fat (HF) diets, high fat diet - induced C57BL/6J mice	[54,171-178]
116	*Zanthoxylum bungeanum* Maxim. (Rutaceae)	Fruit	It reduces weight gain, white adipose tissue mass, and serum triglyceride and cholesterol levels. It also decreased lipid accumulation and PPARγ, C/EBPα, SREBP-1, and FAS protein and mRNA levels in the liver.	Obese C57BL/6 mice fed a high-fat diet	[179]
117	*Ziziphus mauritiana* Lam (Rhamnaceae)	Bark	It reduces body weight, fat mass and pancreatic lipase activity.	High Fat Diet induced obesity in Wistar rats	[180]
118	*Dohaekseunggi-tang* traditional plant-based medicine (Taohe Chengqi Tang: Chinese)	Commercial formula	*Dohaekseunggi-tang* consists of five herbs including *Glycyrrhizae uralensis* Fischer (40 g), *Rheum undulatum*Linne (80 g), *Prunus persica* Linne (60 g), *Cinnamomum cassia* Presl (40 g), and Natrii Sulfas (40 g) mixed. The extract decreased serum total cholesterol, LDL-cholesterol, triglyceride, glucose, and leptin concentrations, and increased HDL-cholesterol and adiponectin levels and increased mRNA expression of peroxisome proliferator activated receptor-γ, uncoupling protein-2, and adiponectin in visceral adipose tissue of HFD mice	High-fat diet induced obese mice	[181]

Table 2. Anti-obesity effect of plants with mechanism of action studied on cell line as model.

1	*Acorus calamus* Linn (Araceae)	Rhizome, roots and leaves	Ethyl acetate extract of *A. calamus* inhibits α-glucosidase activity.	HTT-T15 cell line	[25]
2	*Aegle marmelos* Linn (Rutaceae)	Leaves	Active compounds umbelliferone and esculetin depletes lipid content in the adipocytes and by decreasing the hyperlipidemia in obese rats fed with high-fat diet.	3T3-L1 preadipocytes	[30,31]
3	*Agrimonia pilosa* Ledeb (Rosaceae)	Aerial parts	Active constituent 1beta-hydroxy-2-oxopomolic acid inhibits adipocyte differentiation and expression of adipogenic marker genes, such as PPAR-γ, C/EBPalpha, GLUT4, adiponectin, aP2, ADD1/SREBP1c, resistin, and fatty acid synthase. It also inhibits adipocyte differentiation through downregulation of various adipocytokines by blocking PPAR-γ and C/EBPalpha expression.	3T3-L1 preadipocytes	[182]
4	*Alnus hirsuta* (Spach) Rupr. (Betulaceae)	Leaves	Platyphyllonol-5-O-β-d-xylopyranoside suppresses the induction of PPARγ and C/EBPα protein expression, and inhibits adipocyte differentiation.	3T3-L1 preadipocyte cells	[183]
5	*Amomum cardamomum* L. (Zingiberaceae)	Seeds	By regulating the C/EBPα, C/EBPβ and PPARγ gene and protein expressions.	3T3-L1 Cell lines.	[184]
6	*Bauhinia variegate* L. (Fabaceae)	Flowers, flower buds, stem, roots, stem bark, seeds, leaves	it reduces increased level of total cholesterol, triglycerides, LDLP and increases the level of HDLP, brain serotonin level. β -sitosterol in the stem induces secretion of serotonin in brain and in turn exhibits anti-obesity activity.	Human neutrophils.	[185]
7	*Brassica rapa* L. (Brassicaceae)	Root	Lipolysis-related genes including β_3-adrenergic receptor, hormone-sensitive lipase, adipose triglyceride lipase, and uncoupling protein are induced in white adipocytes of animals treated with extract of *B. campestris*. Activation of cyclic AMPK, HSL, and extracellular signal-regulated kinase are induced in EBR-treated 3T3-L1 cells.	3T3 adipocytes.	[52]
8	*Caesalpinia sappan* L. (Leguminosae)	Heartwood	Brazilein inhibits intracellular lipid accumulation during adipocyte differentiation in 3T3-L1 cells and suppresses the induction of peroxisome PPAR-γ (PPARγ).	Postconfluent 3T3-L1 preadipocytes	[186]
9	*Citrus aurantium* L. (Rutaceae)	Fruits, leaves	It inhibits Akt activation and GSK3β phosphorylation, which induces the down-regulation of lipid accumulation and lipid metabolizing genes, ultimately inhibiting adipocyte differentiation.	3T3-L1 preadipocytes	[22,187,188]
10	*Coptis chinensis* Franch. (Ranunculaceae)	Rhizome	It inhibits lipid accumulation in 3T3-L1 cells. The five alkaloids present in this plant significantly reduces expression levels of several adipocyte marker genes including proliferator activated receptor and CCAAT/enhancer- binding protein. Isolated alkaloids found to inhibit adipogenesis.	3T3-L1 adipocytes cells	[189]
11	*Cucurbita moschata* Duchesne (Cucurbitaceae)	Stems	Reduces expression of peroxisome PPAR-γ, CCAAT/enhancer-binding protein α, fatty acid-binding protein 4, sterol response element-binding protein-1c and stearoyl-coenzyme A desaturase-1, and decreases lipid accumulation.	Primary mouse embryonic fibroblasts	[190]
12	*Curcuma longa* L. (Zingiberaceae)	Rhizomes	Increase hormone-sensitive lipase and adipose triglyceride lipase mRNA levels and decreases perilipin mRNA level via AMPK, resulting in lipolysis. In adipose tissue, curcumin inhibits macrophage infiltration and nuclear factor κB activation induced by inflammatory agents.	3T3-L1 adipocytes	[191,192]
13	*Cyclopia falcata* (Harv.) Kies (Leguminosae)	Stem	Flavonoid, phloretin-3',5'-di-C-glucoside inhibits intracellular triglyceride and down regulates PPAR2 expression and in *in vitro* condition it can inhibit adipogenesis.	3T3-L1 mouse pre-adipocytes	[193]
14	*Cyclopia maculata* (Andrews) Kies (Leguminosae)	Stems	Mangiferin, hesperidin inhibits intracellular triglyceride and fat accumulation, and decreases PPAR2 expression and in *in vitro* it can inhibit adipogenesis.	3T3-L1 mouse pre-adipocytes	[193]

15	*Dalbergia sissoo* DC. (Leguminosae)	Leaves	Inhibits pancreatic lipase and can be used as an anti-obesity agent in suitable form.	Chicken pancreas	[194]
16	*Dioscorea oppositifolia* L. (Dioscoreaceae)	Rhizome	Decreases expression of PPAR-γ. Batatasin I compound from the extract was found to increase p-AMPK and CPT-1 in 3T3-L1 adipocytes, resulting in inhibiting adipogenesis.	Mouse embryo preadipocyte (3T3-L1) cell lines	[195]
17	*Eremochloa ophiuroides* (Munro) Hack (Poaceae)	Whole Plant	Expression of C/EBP and PPAR, the central transcriptional regulators of adipogenesis. Moreover, this plant down-regulates phosphorylation levels of Akt and GSK3.	Mouse 3T3-L1 preadipocytes	[196]
18	*Glycine max* (L.)Merr. (Leguminosae)	Bean	It inhibits adipocyte differentiation in 3T3-L1 preadipocyte cells. Accumulation of triglycerides is inhibited and activation of AMPK.	3T3-L1 preadipocyte cells	[89,90]
19	*Houttuynia cordata* Thunb. (Saururaceae)	Leaf	Attenuates expression of fatty acid synthase, sterol regulatory element-binding protein-1 and glycerol 3-phosphate acyltransferases. The extract inhibits the elevation of plasma TG levels in mice. The extracts possibly suppress the uptake of NEFA and glycerol by blocking FAT/CD 36 and also suppress aquaproin-7.	Human HepG2 hepatocytes	[197,198]
20	*Ilex paraguariensis* A.St.-Hil. (Aquifoliaceae)	Leaves and unripe fruits	A modulatory effect on the expression of genes related to the adipogenesis as PPAR2, leptin, TNF and C/EBP are also seen.	3T3-L1 cell line	[102-105]
21	*Ipomoea batatas* (L.) Lam (Convlvulaceae)	Fruit	Expression of SREBP-I, Acyl-CoA Synthase, Glycerol-3-Phosphate Acyltransferase, HMG-CoA Reductase and Fatty Acid Synthase in liver tissue.	Murine 3T3-LI adipocytes	[106]
22	*Irvingia gabonensis* (Aubry-Lecomte ex O'Rorke) Baill. (Irvingiaceae)	Seed	Inhibits adipogenesis in adipocytes. The effect appears to be mediated through the down regulated expression of adipogenic transcription factors (PPAR-γ) and adipocyte-specific proteins (leptin), and by upregulated expression of adiponectin.	Murine 3T3-LI adipocytes	[199]
23	*Morus australis* Poir. (Moraceae)	Root	Increases lipolytic effects such as decreased intracellular triglyceride and the release of glycerol.	3T3-L1 adipocytes	[200]
24	*Nelumbo nucifera* Gaertn. (Nelumbnaceae)	Seed epicarp, leaves, seed, petals	The extracts effective in inhibiting preadipocyte differentiation. The flavonoids inhibits effect on both adipocyte differentiation and pancreatic lipase activity, accumulation and decreases expression PPARγ, GLUT4, and leptin in cultured human adipocytes, indicating that it inhibits the differentiation of pre-adipocytes into adipocytes.	3T3-L1 (adipocyte), NIH3T3 (mouse fibroblast, embryo), L-02 (normal hepatocyte) cells CHO-K1, and U2OS cells,	[124-127]
25	*Nepeta tenuifolia* Benth. (Lamiaceae)	Whole plant	Inhibits triglyceride accumulation in 3T3-L1 adipocytes, suggesting anti-obesity activity.	3T3-L1 cells	[201]
26	*Pericarpium zanthoxyli* (Rutaceae)	Seed	Decreases expression of the adipogenesis-related transcription factor, PPAR-γ and PPAR-γ-target genes, such as adipocyte protein 2 (aP2), fatty acid synthase (FAS) and other adipocyte markers and also decreases levels of CCAAT/enhancer-binding protein β (C/EBPβ) in a dose-dependent manner.	OP9 cells	[202]
27	*Petasites japonicus* (Siebold & Zucc.)	Flower buds	The extracts attenuate three adipogenetic transcription factors, peroxisome PPAR-γ2, CCAAT/enhancer- binding protein and sterol regulatory element- binding protein 1c.	3T3-L1 murine preadipocytes	[136]
28	*Peucedanum japonicum* Thunb. (Apiaceae)	Leaves	Pteryxin down regulates genes SREBP-1c, fatty acid synthase, and acetyl-coenzyme A carboxylase-1 in treated 3T3-L1 adipocytes and HepG2 hepatocytes and up-regulates lipid catabolizing genes. In aother study it was proved that the extract down-regulates a key lipogenic activator, SREBP1 c and adipocyte size marker gene, paternally expressed gene 1/mesoderm-specific transcript (PEG1/MEST) in adipose tissue in vivo.	Both 3T3-L1 and HepG2 cell lines, 3T3-L1 and HepG2 cells	[203,204]
29	*Rubus chingii* var. suavissimus (S.K.Lee) L.T.Lu (Rosaceae).	Leaves	The extract increases adipogenesis and increases expression of adiponectin and leptin. In the early phase of adipogenesis, extract increases the mRNA expression of adipogenic transcription factors CCAAT/enhancer binding protein α and PPAR-γ.	3T3-L1 preadipocytes	[205]

30	*Salicornia herbacea* L. (Amaranthaceae)	Whole plant	Isorhamnetin 3-O-β-D-glucopyranoside suppresses adipogenic differentiation by downregulation of peroxisome proliferator-activated receptor-γ, CCAAT/enhancer-binding proteins, SREBP1, and the adipocyte-specific proteins. Specific mechanism mediating the effects of isorhamnetin 3-O-β-D-glucopyranoside confirmed by activation of AMPK.	3T3-L1 preadipocytes	[206]
31	*Siegesbeckia pubescens*L. (Amaranthaceae)	Whole plant	The anti-obesity effect is modulated by cytidine-cytidine-adenosine-adenosine-thymidine/enhancer binding proteins, and peroxisome proliferator-activated receptor, gene and protein expressions.	3T3-L1 preadipocytes	[207]
32	*Smilax china* L. (Smilacaceae)	Leaves	Polyphenol and flavonoid, exhibits α-glucosidase and lipid accumulation inhibition properties.	3T3-L1 adipocytes	[208]
33	*Tetrapanax papyriferus* (Hook.) K.Koch (Araliaceae)	Whole plant	The anti-obesity effect is modulated by cytidine-cytidine-adenosine-adenosine-thymidine/enhancer binding proteins, and peroxisome proliferator-activated receptor, gene and protein expressions.	3T3-L1 preadipocytes	[207]
34	*Veratrum nigrum* L. (Melanthiaceae)	Whole plant	It decreases lipid accumulation and the expressions of two major adipogenesis factors, PPAR and C/EBP, in 3T3-L1 cells.	3T3-L1 cells	[134]
35	*Vitis labrusca* L. (Vitaceae)	Seed	The extract of *V. labrusca* inhibits lipid accumulation of C3H10T1/2 and 3T3-L1 cells in a dose-dependent manner. Inhibition is associated with reduced expression of PPAR-γ.	C3H10T1/2 and 3T3-L1 cells	[177]
36	*Vitis vinifera* L. (Vitaceae)	Seed flours, peel, roots, fruit	By up-regulating hepatic genes related to cholesterol (CYP51) and bile acid (CYP7A1) synthesis as well as LDL-cholesterol uptake. Lipid metabolism-associated genes Mlxp1, Stat5a, Hsl, Plin1, and Vdr were down-regulated. The extract treatment decreases expression of aP2, Fas, and Tnfa, known markers of adipogenesis, as measured by real-time polymerase reaction. Expression of PPAR-γ in liver and adipose tissue is lowered by regulating the lipid metabolism and suppressed obesity.	3T3-L1 preadipocytes, high fat diet- induced mice, murine 3T3-LI adipocytes,	[54,171-178]
37	*Ziziphus jujube* Mill. (Rhamnaceae)	Fruit	Suppresses lipid accumulation and glycerol-3-phosphate dehydrogenase. Elicits the most inhibitory effect with attenuation of the expression of key adipogenic transcription factors, including PPAR-γ and CCAAT enhancer binding proteins (C/EBPs) at the protein level.	3T3-L1 preadiocytes	[209-211]
38	Germinated brown rice, germinated waxy brown rice, germinated black rice, and germinated waxy black rice	Seed	Extract of these seeds decreases body weight gain and lipid accumulation in the liver and epididymal adipose tissue. The mRNA levels of adipogenic transcriptional factors, such as CCAAT enhancer binding protein (C/EBP)-α, SREBP(SREBP)-1c, and peroxisome proliferator activated receptors (PPAR)-γ, and related genes (aP2, FAS) are decreased by the seed extract.	3T3-L1 murine adipocytes	[212]

Table 3 List of plants exhibiting anti-obesity activity studied on human volunteers.

1	*Carum carvi* L. (Apiaceae)	Seed	Reduces weight, body mass index, body fat percentage, and waist-to-hip ratio.	Human clinical trials	[213]
2	*Cissus quadrangularis* L. (Vitaceae)	Cylaris a formula contains a *C. quadrangular*extract	Phytosterols and fiber extracts have anti-lipase, and anorexiant properties that reduce the absorption of dietary fats and enhance satiation by increasing serum serotonin levels.	Human clinical trials	[214]
3	*Citrus aurantium* L. (Rutaceae)	Fruits, leaves	The active constituent p-synephrine increases metabolic rate, energy expenditure and increase in weight loss. The leaf extract down-regulates the expression of C/EBPβ and subsequently inhibits the activation of PPARγ and C/EBPα. The anti-adipogenic activity of is mediated by the inhibition of Akt activation and GSK3β phosphorylation, which induces the down-regulation of lipid accumulation and lipid metabolizing genes, ultimately inhibiting adipocyte differentiation.	Human clinical trials	[22,187,188]

4	*Garcinia cowa* Roxb. ex Choisy (Clusiaceae)	Fruit, commercially available tablet	Inhibits the enzyme ATP-dependent citrate lyase, which catalyzes the cleavage of citrate to oxaloacetate and acetyl-CoA.Serum apo A1 levels are increased by the plant and the serum total cholesterol levels.	Human clinical trials	[86,87]
5	*Gynostemma pentaphyllum* (Thunb.) Makino (Cucurbitaceae)	Leaves	Activation of AMPK by 5-aminoimidazole-4-carboxamide- 1-b-D-ribofuranoside (AICAR) inhibits adipogenesis by downregulating PPARc and CEBP1a as well as lipogenic factors including fatty acid binding protein 4 and lipoprotein lipase. AMPK activation directly inactivates ACC through Ser79 phosphorylation, leading to decreased fat synthesis by reducing the production of malonyl-CoA from acetyl-CoA.	Human clinical trials	[215]
6	*Nigella sativa* L. (Ranunculaceae)	Commercial *Nigella sativa* oil prepared by steam distillation.	*N. sativa* reduces total cholesterol, low density lipoprotein (LDL) and fasting blood glucose. The oil is effective as an add-on therapy in patients with metabolic syndrome.	Human Volunteer	[216,217]
7	*Salacia reticulata* wight (Celastraceae)	Root	Significant weight and body-fat reduction was observed in *S. reticulata* treated animals and also BMI reduction is seen.	Human clinical trials	[218]
8	*Trigonella foenum-graecum* L. (Leguminosae)	Seed	Daily fat consumption, expressed as the ratio fat reported energy intake/total energy expenditure (fat-REI/ TEE), is decreased in overweight subjects administered the fenugreek seed extract. Significant decrease in the insulin/glucose ratio in subjects treated with fenugreek seed extract.	Clinical trials	[219]
9	*Turnera diffusa* Willd. ex Schult. (Passifloraceae)	Leaves	The herbal preparation capsules delays gastric emptying, reducing the time to perceived gastric fullness and induces weight loss.	Healthy volunteers	[220,221]
10	*Vernonia amygdalina* Delile (Compositae)	Leaf	Fat elimination usually occurred within 2 sec, 2 min of extract intake. The blood glucose lowers effects of *V. amygdalina* leaf extract were usually exerted in 2 sec, 2 min of extract intake by the patient.	Clinical trials	[222]
11	*Ziziphus jujube* Mill. (Rhamnaceae)	Fruit	The extract suppresses lipid accumulation and glycerol-3-phosphate dehydrogenase. *Z. jujuba* extract elicits the most inhibitory effect with attenuation of the expression of key adipogenic transcription factors, including PPAR-γ and CCAAT enhancer binding proteins (C/EBPs) at the protein level.	Human clinical trials	[209-211]

Table 4. Anti-obesity effect of plants with mechanism of action studied on isolated cell organelles.

1	*Verbesina persicifolia* DC (Compositae)	Aerial parts	4β-cinnamoyloxy,1β,3α-dihydroxyeudesm-7,8-ene is the active constituent present in *V. persicifolia* induces bioenergetic collapse in rat liver mitochondria, demonstrating typical uncoupling agent. It acts as a mild uncoupler droping Δψ and increases respiratory state 4. The energy collapse, mild uncoupling, and the fact that *V. persicifolia* is largely used in folk medicines, this plant may be viewed as a potentially effective anti-obesity drug.	Rat liver mitochondria	[223]

Table 5. Anti-obesity effect of plants with mechanism of action studied on isolated cell enzymes.

1	*Fraxinus chinensis* subsp. rhynchophylla (Hance) A.E.Murray (Oleaceae)	Stems and barks	Major active components are secoiridoids ligstroside, oleuropein, 2"-hydroxyoleuropein and hydroxyframoside B. These compounds significantly inhibit pancreatic lipase and hydroxyframoside B being the most active inhibitor in a mixed mechanism of competitive and noncompetitive manner.	Porcine pancreatic lipase	[224]
2	*Vitis vinifera* L. (Vitaceae)	Seed flours, peel, roots, fruit	By up-regulating hepatic genes related to cholesterol (CYP51) and bile acid (CYP7A1) synthesis as well as LDL-cholesterol uptake. Lipid metabolism-associated genes Mlxp1, Stat5a, Hsl, Plin1, and Vdr were down-regulated. The extract treatment decreases expression of aP2, Fas, and Tnfa, known markers of adipogenesis, as measured by real-time polymerase reaction. Expression of PPAR-γ in liver and adipose tissue is lowered by regulating the lipid metabolism and suppressed obesity.	Pure pancreatic lipase	[54,171-178]

accumulation, intracellular triglyceride and decrease in body weight. Ginseng which is a popular Chinese herbal medicine significantly decreased the weight gain and improved glucose tolerance [115,120]. *P. granatum* exhibits potential antiobesity mechanism including inhibition of pancreatic lipase activity and suppression of energy intake. Its effect on energy intake was similar to subutramine but with a different mechanism.

A study reported that Green tea possessed higher antioxidant activity than antiobesity activity due to its high concentration of catechins, including epicatechins, ECG and EGCG. It was proved that antiobesity activity of catechins resulted from the combined actions of appetite reduction, greater lipolytic activity, energy expenditure and adipocyte differentiation.

The active compounds umbelliferone and esculetin from the plant *Aegle marmelos* have shown marked effect by depleting the lipid content in the adipocytes and by decreasing the hyperlipidemia. Similarly, galangin a compound from *Alpinia galangal* showed a significant decrease in serum lipids, liver weight, lipid peroxidation and accumulation of hepatic Triglycerides. Decursin a compound from *Angelica gigas* significantly improved glucose tolerance and reduced the secretion of HFD-induced adipocytokines. The phytoconstituent compound sitosterol found in *Boerhaavia diffusa* is structurally similar to cholesterol has been suggested to reduce cholesterol by lowering the level of LDL-cholesterol. p-synephrine compound from the plant *Citrus aurantium* showed increased metabolic rate, energy expenditure and increase in weight loss. In *Nelumbo nucifera* flavonoids showed mild inhibitory effect on both adipocyte differentiation and pancreatic lipase activity. Among the flavonoids, flavones without glucose inhibited pancreatic lipase activity, whereas flavone glycosides did not show inhibition. The presence of ephedrine and pseudo-ephedrine in the plant *Sida rhomboidea* induced appetite suppression that inhibits body weight gain.

Conclusion

Natural products identified from traditional medicinal plants have always paved the way for development of new types of therapeutics. Generally most of the compounds were isolated from natural sources despite which orlistat a semi-synthetic derivative of lipstatin have been approved by the US food and drug administration for the treatment of obesity. Orlistat is a potent inhibitor of pancreatic lipase (PL) which is a lipolytic enzyme which hydrolyses dietary fats in the initial step of lipid metabolism. There have been many reports on other effects such as anti-oxidative stress effects which may be important in the management of other diseases like cardiovascular diseases and diabetes. The antiobesity drugs are generally preferred based on high efficacy and effectiveness. The active exploration of natural sources has provided new developments based on the understanding of complex and redundant physiological mechanisms. Such exploration will lead to a safe and effective pharmacological treatment.

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