Medicinal Plants with Anti-Obesity Effects: A Special Emphasis on Their Mode of Action

Ali Esmail Al-Snafi* Narjes Alfuraiji**

ABSTRACT

Objective: Obesity is a major public health issue in developed and developing countries. An individual with a body mass index equal to or higher than 30 is considered obese. The pathophysiology of obesity included alterations in neuropeptides, hormones, and adipokines in the brain, gut, and adipose tissue. This review was designed to investigate the plants with anti-obesity effects as alternative weight loss remedies with minimal adverse effects.

Materials and Methods: PubMed, Science Direct, Web Science, and Scopus were searched to investigate the plants which possessed anti-obesity effects.

Results: Many medicinal plants possess anti-obesity activity via different mechanisms, including pancreatic lipase activity inhibition, thermogenesis enhancement, adipocyte differentiation prevention, boosting lipid metabolism, and lowering appetite.

Conclusion: Plants contain many pharmacologically active ingredients that possess anti-obesity by many mechanisms. Further investigations were required to determine the molecular mechanism and the clinical efficacy of the natural anti-obesity agents.

Keywords: Obesity, Anti-obesity, Medicinal Plants, Bodyweight, Appetite, Lipase activity, Thermogenesis Anti-obesity

INTRODUCTION

Obesity is a major public health issue in both developed and developing countries. An individual with a body mass index equal to or higher than 30 is considered obese. The pathophysiology of obesity included alterations in neuropeptides, hormones, and adipokines in the brain, gut, and adipose tissue. There are two factors linked to overweight and obesity: an increased intake of high energy foods, decreased physical activity due to changes in the nature of many forms of work, increasing urbanization, and changing modes of transportation[1].

The typical anti-obesity drug is a drug that sustains weight loss with minimal adverse effects. Many medications have been used to manage obesity over the years. However, most anti-obesity drugs were withdrawn from the markets due to serious adverse effects[2].

Improved knowledge in understanding the peptidergic signaling of hunger and satiety from the gastrointestinal tract, mediated by cholecystokinin, ghrelin, glucagon-like peptide-1, peptide YY, and homeostatic mechanisms associated with leptin and its upstream pathways in the hypothalamus, revealed novel targets for discovering new anti-obesity drugs[3]. Many medicinal plants possess anti-obesity activity with different mechanisms, as shown in table 1 and figure 1[4-9]. The use of natural remedies for weight loss is increased based on availability, safety, and cheapness compared with synthetic drugs or surgical procedures[10,11]. The current review was designed to improve knowledge on the use of anti-obesity medicinal preparations and encourage obese patients to consume them along with physical exercises.

MEDICINAL PLANTS WITH ANTI- OBESITY EFFECT

Avena sativa: To investigate the oat β-glucan's n effect on the metabolic parameters in obese mice, they were fed three doses of oat β-glucan. Energy intake, lipid profile, glycemic state, and appetite-related hormones were investigated. β-glucan decreased average energy intake and body weight and decreased HDL, total cholesterol, plasma peptide Y, arcuate peptide Y mRNA, and arcuate peptide Y receptor two mRNA. However, an increment of peptide Y-Y expression and plasma peptide Y-Yoat β-were noticed in obese mice[12,13].

In a clinical trial conducted to investigate the oat anti-obesity effect, participants were given either beta glucan-containing oat cereal or a placebo for 12 consecutive weeks. A reduction in body weight, body fat, BMI, and the waist-to-hip ratio was observed in the oat group with a decrement in AST and ALT. However, ultrasonic image analysis did not reveal any anatomic changes. Oat administration did not cause any adverse effects, and it was well tolerated during the trial[14].

***Bauhinia variegata*:** The methanolic extract of *Bauhinia variegata* stem and root bark anti-obesity potential were studied using hypercaloric diet-fed female rats. A significant hypolipidemic effect, feed intake, and bodyweight reduction were observed with methanolic plant extract at 200 and 400 mg/kg, respectively. There was an increment in serotonin level and serum HDL, while total cholesterol, LDL and triglycerides were decreased[15,16].

Brassica campestris: The anti-obesity effect of *Brassica campestris* Rapa roots (EBR) ethanolic extracts was investigated in

* Department of Pharmacology
College of Medicine
University of Thi-Qar, Thi-Qar, Nasiriyah, B O Box 42, Iraq.
** Department of Pharmacology
College of Medicine
University of Karbala, Karbala, Iraq.
E-mail: Narjesalfuraiji@gmail.com

Table 1: The probable mechanisms of anti-obesity effects of the medicinal plants

Medicinal plants	Active extract/ or compound	Model	Probable Mechanisms	Reference
Avena sativa	β-glucan	Obese mice	β-glucan affected satiety perception, gastric emptying, gut hormones, and short chain fatty acids in the complex interplay of appetite and energy regulation	12,13
Bauhinia variegata	Methanolic extract of stem and root barks	Female rats fed with hypercaloric diet	Decreased appetite by increasing brain serotonin level	15,16
Brassica campestris	Ethanolic extracts of the roots	High fat diet- fed mice	Extract induced the expression of lipolysis-related genes, including $beta_3$-adrenergic receptor ($beta_3$-AR), hormone-sensitive lipase (HSL), adipose triglyceride lipase, and uncoupling protein 2	17,18
Capsicum annuum	Aqueous extracts of the fruit after removing internal seeds	The expression of lipoprotein lipase (LPL) mRNA in 3T3-L1 cells	Decreased LPL mRNA expression level in 3T3-L1 cells	19,20
Citrullus colocynthis	Seeds fixed oil and hydro-alcoholic extract	Obese rats and Mice	Increased feces output, and lipid in Feces significantly Decreased food intake by 3.52%, body weight by 4.02%	21-23
Citrus aurantifolia	Essential oils	Mice model of increasing the food intake and body weight by Ketotifen	Promotes anorexia, resulting in reducing food consumption and body weight	24,25
Crotalaria juncea	leaf extracts	High fat induced obesity in rats	Inhibited lipoprotein lipase	26,27
Echinochloa crus-galli	Grains hydro-alcoholic extract and methanolic Extract	Obese rats	Decreased food consumption and weight gain, and increased fecal fat excretion	28-30
Foeniculum vulgare	Fruit extracts	High fat fed rats	Inhibited lipase activity	31,32
Helianthus annuus	Methanolic extract of seeds	Mice received cafeteria diet	Decrease food consumption	33,34
Hibiscus sabdariffa	Aqueous extract of the calyces	High-fat fed mice	Reduced food intake Reduced fat tissue accumulation Increased fatty acids excreted in feces	35-41
Jasminum sambac	Ethanolic extract of flowers	High -fat fed mice	Inhibited pancreatic lipase activity	42,43
Kochia scoparia	Ethanol extract of fruit	High -fat fed mice	Inhibited pancreatic lipase activity	44,45
Lagerstroemia speciosa	Hot water leaves extract	Genetically obese diabetic mice	Inhibited lipogenesis in the liver	46-48
Mangifera indica	Leaves tea	High –fat fed rats	controls the expression of adipogenesis-related transcription factors and enzymes	49,50
Momordica charantia	Aqueous and methanolic extracts of the fruits	High -fat fed mice	Suppressed leptin and resistin levels in adipose tissues and plasma	51-53
Morus alba	Leaves extract	High -fat fed mice	ameliorated LXRα-mediated lipogenesis. Up-regulation of lipolysis associated markers (lipoprotein lipase)	54-58
Morus nigra	Leaves	Leaves-feed Pigs	A significantly increased leptin receptor, phosphorylated signal transducer and activator of transcription 3	59
Ocimum basilicum	leaves extracts	*In vitro*	Inhibited pancreatic lipase activity	60,61
Olea europaea	Leaf extract	High -fat fed mice	Decreased expression of thermogenesis- and adipogenesis- related molecules	62
Plantago lanceolata	Leaves powder	High -fat fed mice	Boosts visceral fat metabolism via activation of lipolysis, increasing fatty acid oxidation, and suppression of fatty acid synthase	63,64
Plantago ovata	20 g of seed	Women	Appetite suppression, significantly increased feelings of fullness	65
Polygonum aviculare	Ethanolic and methanolic extract of the whole herb	High -fat fed mice	Inhibits pancreatic lipase activity suppressing mRNA expression of sterol regulatory element-binding protein-1c, adipocyte protein 2, fatty acid synthase, peroxisome proliferator-activated receptor γ, and inhibiting adipocyte differentiation and fat accumulation	66-68

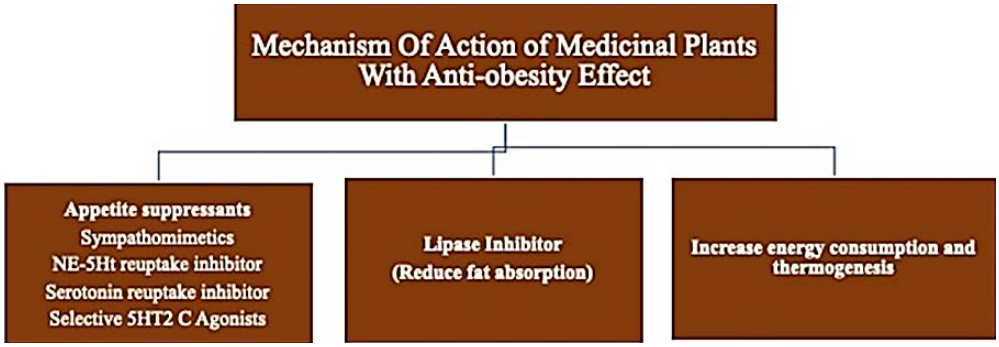

Figure 1: Mechanism of action of medicinal plants with anti-obesity effect

3T3-L1 adipocytes and HFD-fed mice. A high decrement in weight gain and epididymal fat accumulation in the obese mice were obtained by administrating 50 mg/kg/day EBR orally for eight weeks; however, no effect in the amount of food consumed was observed. The extract induced the expression of lipolysis-related genes, including hormone-sensitive lipase (HSL), beta3-adrenergic receptor (beta3-AR), adipose triglyceride lipase, and uncoupling protein 2. The cAMP-dependent protein kinase and extracellular signal-regulated kinase in 3T3-L1 cells were also induced. EBR's lipolytic effects included beta3-AR regulation, as indicated by the inhibition of propranolol, a beta3-AR antagonist. Consequently, by inhibiting lipid accumulation and stimulating beta3 AR-dependent lipolysis, EBR may constitute a promising, safe, and effective anti-obesity agent[17,18].

Capsicum annuum: The aqueous extracts' anti-obesity effects of Seven *Capsicum annuum* varieties, including [Cheongyang gochu (Cca), Green pepper (Gca), Kwari putgochu (Kca), Oyee gochu (Oca), Putgochu (Pca), Red paprika (Rca), and Yellow paprika (Yca)] were studied by evaluating the expression of lipoprotein lipase (LPL) mRNA in 3T3-L1 cells. To determine the anti-obesity effects of the primary fractions, only proven ones underwent secondary and tertiary re-fractionating. A significant decrease was recorded from seven different *Capsicum annuum* in the LPL mRNA expression level of 50.9% in Cheongyang gochu aqueous extract treatment compared to the control group. The primary fractions (Fr) 56 of Cheongyang gochu aqueous extracts resulted in a significant reduction in the LPL mRNA expression (30.5% decrease) and (36.2% decrease, respectively. To determine the LPL mRNA expression, Fr 5 and 6 were re-fractionated. Treatment with Fr 5-6 and Fr 6-6 significantly decreased LPL mRNA expression (53.8 and 35.3%, respectively)[19,20].

Citrullus colocynthis: The effects of a fixed oil extracted from *Citrullus colocynthis* seeds on blood homeostasis, and body weight was investigated in rats. Daily treatment with 4% of the oil of *Citrullus colocynthis* for eight weeks exhibited a substantial decrease in the body weight compared to the rats that were given 4% sunflower oil. The treatment significantly increased feces output and lipid in feces[21].

The *Citrullus colocynthis* extract's inhibitory effect on inflammatory cytokines secreted in obesity was investigated in mice. Body weight and food consumed were recorded weekly, while the expression of TNF-α, IL-6, and IL-10 in serum was recorded bi-monthly. The food intake was decreased by 3.52%, body weight by 4.02% and reduced expression of IL-6 30.23 ($p< 0.001$) and TNF-α 44.83 ($p< 0.001$), and elevated IL-10 5.31 ($p> 0.05$) in stout mice[22,23].

Citrus aurantifolia: The anti-obesity effect of Citrus *aurantifolia* essential oil, combined with Ketotifen (the antihistaminic drug that caused weight gain), has been studied using the mouse model. Reducing body weight and food consumption was obtained with *Citrus aurantifolia* essential oil treatment, probably by promoting anorexia. Administration of essential oil with Ketotifen significantly decreased the body weights of mice[24,25].

Crotalaria juncea: In high fat-diet-induced obesity in rats, the anti-obesity efficacy of *Crotalaria juncea* leaves extract was proven[26,27].

Echinochloa crus-galli: The anti-obesity activity of the hydroalcoholic extracts was assessed in albino rats using a high-fat diet to induce obesity. The obese rats were treated with hydroalcoholic extracts at 200, 400 and 600 mg/kg, bw orally for 4 weeks. A significant decrement was observed in adipose tissue, body weights, SGPT, SGOT, blood glucose, triglyceride, total cholesterol, VLDL, LDL, and the atherogenic index, with a substantial elevation of HDL.

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The antihypercholesterolemic effect of *Echinochloa crus-galli* extract was assessed *in vivo* to identify its effects on weight gain, food consumption, fecal fat excretion, biochemical profiles, and serum lipid. The methanolic extract decreased TC, LDL, VLDL, SGOT, and SGPT and increased HDL considerably ($P< 0.01$ and $P< 0.05$) in a dose-dependent manner. Food intake and body weight were substantially less in the treated groups than in the control group[29,30].

Foeniculum vulgare: The effect and role of *Foeniculum vulgare* fruit extracts in obesity and associated cardiovascular disorders were investigated experimentally in rats fed a high-fat diet. A successive solvent technique was used to separate three fractions from the methanol extract of *Foeniculum vulgare*. Then, the female albino rats were fed a high-fat diet combined with fruits at a dose of 300 mg/bw by oral gavage and volatile oil (produced by hydrodistillation) at a dose of 0.2 ml/bw intraperitoneally once daily for six weeks. Results showed a decrement in the body and fat pad weights in animals fed with extracts, with the highest effect observed for the extracts' methanolic fraction, which contained the maximum amount of flavonoidal contents (21.44 mg/g) and phenolic (48.37 mg/g)[31,32].

***Helianthus annuus*:** The anti-obesity effect of the *Helianthus annuus* seeds methanolic extract was studied in mice. The mice received a cafeteria diet and Helianthus *annuus* extract (200 mg/kg) / day for 6 weeks. The methanolic extract of *Helianthus annuus* seeds significantly increased locomotor activity (grooming, ambulation, rearing) with HDL and significantly decreased f triglyceride, total

cholesterol, glucose, body weight, food consumption, body mass index, and lee index of obesity[33,34].

Hibiscus sabdariffa: The standardized aqueous extract of *Hibiscus sabdariffa* calyces' effect on body weight was investigated in obese mice administered monosodium glutamate. *Hibiscus sabdariffa* aqueous extract was orally administered (120 mg/kg/day) for 60 days to obese and healthy mice. The extract substantially decreased body weight in obese mice while liquid intake increased in both groups, with no nonsignificant reductions observed with cholesterol and triglyceride in animals treated with *Hibiscus sabdariffa*[35].

The aqueous extract of *Hibiscus sabdariffa* (Hs) effect on body weight gain and its protective effects on the liver by improving lipid metabolism were studied in high fat diet-induced obese C57BL/6NHsd mice. The extract decreased body weight gain, fat tissue accumulation, normalized glucose level, and minimized dyslipidemia compared with the untreated obese mice group. Also, it attenuated liver steatosis, blocked the increase of IL-1, TNF-α mRNA, lipoperoxidation and down-regulated SREBP-1c and PPAR-γ, and increased catalase mRNA[36].

Hibiscus sabdariffa water extract (HSE) treatment showed a concentration-dependent reduction in fat accumulation in the hamster's liver fed with a fat diet (HFD). Also, it decreased liver triglycerides and cholesterol, which HFD elevated. The HSE seems to regulate lipid peroxides and protect organs from oxidation-produced damage. HSE treatment also reduces the levels of aspartate aminotransferase and serum alanine aminotransferase (liver damage markers) elevated by HFD. The HSE was as effective as anthocyanin, which indicated that the anthocyanins content of the HSE may represent the biologically active compound against HFD-induced obesity[37,38].

The effects of the calyx of *Hibiscus sabdariffa* (Hs) extract on weight gain, fat absorption, and excretion were investigated experimentally. Rats were given either a basal diet (SDC) or supplemented with Hs extracts (5%, 10%, and 15%, SD5, SD10, and SD15). SD5 did not significantly increase food consumption and weight compared to SDC. However, in the SD15 group, there was a significant decrement in the parameters mentioned above. The response in the SD10 group was similar to SD15, except for food consumption. SD5 and SDC groups did not affect body weight; only SD5 caused significantly greater fatty acids in feces[39,40].

To prove the metabolic-regulating and liver-protecting effect of *Hibiscus sabdariffa* extracts (HSE), a clinical trial was conducted for this purpose. Individuals aged 18–65 with a BMI of 27 were divided into two groups (control and HSE-treated groups). HSE consumption decreases body weight, body fat, BMI, and the waist-to-hip ratio and lowers serum-free fatty acids. Anatomical changes showed that HSE improved liver steatosis. HSE was well tolerated, with no unfavorable effect observed during the study period[41].

Jasminum sambac: The anti-obesity effect of the ethanolic extract of *Jasminum sambac* flowers was studied *in vivo* in high-fat-fed mice and *in vitro* using pancreatic lipase enzyme. The ethanolic extract of *Jasminum sambac* flowers at a dose of 100 and 300 mg/kg bw resulted in a substantial reduction in mice's food intake, body weight, and fat index. Inhibition of pancreatic lipase enzyme activity was observed *in vitro* assay, using *Jasminum sambac* flowers ethanolic extract[42,43].

Kochia scoparia: The effect of *Kochia scoparia* fruit ethanol extract in preventing high-fat diet-induced obesity in mice was evaluated for nine weeks. The increment in body and adipose tissue weight that induced the high-fat diet was prevented by administering the ethanolic extract of *Kochia scoparia* fruit. A significant increment in fecal triacylglycerol level was observed upon administering a high-fat diet supplemented with 1% or 3% of *Kochia scoparia* extract compared to the high-fat diet group. The plasma triacylglycerol elevation after oral administration of the lipid emulsion was inhibited by the ethanol extract and total saponins of *Kochia scoparia.* Furthermore, the pancreatic lipase activity was inhibited in vitro by the total saponins, 2'-O-beta-d-glucopyranosyl momordin IIc, and momordin Ic, 2'-O-beta-d-glucopyranosyl momordin Ic, which were isolated from *Kochia scoparia* fruit[44,45].

Lagerstroemia speciose: In female mice with a considerable body weight gain, the anti-obesity effect of dietary Lagerstroemia speciosa leaves extract was investigated. A placebo or test diet supplemented with 5% of a hot-water leaves extract was used to feed the mice for 12 weeks. There was a significant reduction in body weight gain and parametrial adipose tissue weight in *Lagerstroemia speciosa* diet group. There was no decrement in blood glucose level; however, a suppression in hemoglobin A1C was observed at the end of the study. Serum lipids did not affect, but *Lagerstroemia speciosa* extract caused a significant reduction in hepatic lipid contents[46].
A well-controlled study for 14 weeks (including a 2-week run-in phase) was conducted to study the efficacy and safety of IQP-GC-101 (a standardized extract of *Lagerstroemia speciosa, Camellia sinensis, Garcinia cambogia*, and unroasted *Coffea arabica*) in decreasing body weight and body fat mass in obese Caucasian adults. IQP-GC-101 resulted in 2.26 ± 2.37 kg weight loss compared to placebo (0.56 ± 2.34 kg), ($p <= 0.002$) after 12- week. More significant decrement in hip circumference, waist circumference, and body fat mass in the IQPGC-group. No serious adverse events were reported[47,48].

Mangifera indica: *Mangifera indica* tea's anti-obesity effect was investigated by employing obese mice fed on *a* high-fat diet (HFD). Consumption of 24.7±2.1ml/day showed anti-inflammatory and antioxidant effects, increment in total antioxidant capacity and interleukin-1 serum concentrations, down-regulated FAS expression, up-regulated PPAR-γ and LPL, and reduced abdominal fat accumulation. According to the results, *Mangifera indica* tea can treat obesity and related diseases by regulating transcriptional factors expression and adipogenesis-associated enzymes[49,50].

Momordica charantia: *Momordica charantia* extracts revealed beneficial effects on obesity and related insulin resistance in mice and rats. Leptin and resistin levels in adipose tissues and plasma were suppressed, and anti-inflammatory mediators and adiponectin were elevated in high fat-fed animals[51-53].

Morus alba: Mice Matrigel plug assay was used to determine the effect of Ob-X (contained: *Artemisia capillaries, Morus alba*, and *Melissa officinalis*) on angiogenesis. Ob-X showed a dose-dependent decrement in angiogenesis. Five weeks of treatment of Ob-X resulted in a 27% decrement in body weight gain and 46 and 15% decrement in the visceral adipose tissue and the size of adipocytes in visceral adipose. Furthermore, there was a significant decrement in the hepatic accumulation of lipids, and blood glucose levels[54].

The effect of the leaf extract of *Morus alba* on obesity-induced lipogenesis, oxidative stress, and fibrosis in the liver was investigated in obese mice fed on a high-fat diet (HFD). A significant improvement in LXRα-mediated lipogenesis and hepatic fibrosis markers such as α-smooth muscle actin was obtained, while lipolysis-associated markers such as lipoprotein lipase in the HFD-fed mice were up-regulated.

Additionally, the activities of antioxidant enzymes, including heme oxygenase-1 and glutathione peroxidase, normalized[55].

The effect of *Morus alba* flavonoid standardized extract on food intake and weight reduction was evaluated in mice fed a high-fat diet. Dose-dependent significant food intake reduction was recorded in acute and long-term studies. Reductions in food intake of 58.6% and 44.8% at 250 mg/kg and 50.1% and 44.3% at 500 mg/kg were observed at 1 and 2 h post food provision. A daily calorie intake was reduced by 20% in the long-term study. Obese mice treated with a high dose of root bark extract lost 10.4 g (22.5%) and 7.1 g (16.5%) of their body weight from baseline to week seven, respectively. A statistically significant decrease in visceral fat deposit and biochemical markers was also recorded[56].

UP601 effect (*Morus alba, Magnolia Officinalis, and Yerba mate* extracts) was investigated in obesity-related parameters, and biochemical markers in high-fructose (HFF) induced obesity in mice. A 1.8-times increment in lipolysis was observed upon administering UP601at (250 mcg/ml). Administering 300mg, 450mg, and 600 mg/kg of UP601 for seven weeks resulted in 9.1, 19.6, and 25.6% decrement in rat body weight. The total cholesterol decreased by 9.1, 16.9, and 18.6%; triglycerides decreased by 45.0, 55.0, and 63.6%; LDL decreased by 34.8, 37.1, and 41.6%; and serum glucose by 3.2, 21.6 and 33.7%, respectively. UP601 also resulted in a 31.6% decrease in the distribution of body fat, and decrement in the mesenteric fat reached 89.1%[57].

The effect of oral UP601 at 1.3 g/kg/day on appetite suppression and management of metabolic disorders in mice models weeks was studied for seven weeks, and a remarkable reduction was observed in food intake. Furthermore, body weight gain decreased by 21.5% VS 8.2% at seven weeks compared to the untreated group (high fat diet-mice), calorie intake decreased by 40.5% in the first week, insulin and leptin by 75.9% and 46.8%, respectively, ghrelin level increased by 4.2 times, with a significant decrement in cholesterol and LDL.UP601 treatment in Mice resulted in body fat and less mesenteric fat pad reduction, while there was an enhancement in non-alcoholic steatohepatitis scores[58].

Morus nigra: Mulberry leaves effects on fat deposition were studied in pigs. A significantly higher leptin receptor, activator of transcription 3, and phosphorylated signal transducer were observed in pigs fed a diet supplemented with Mulberry leaf, which proposes the enhancement of leptin signaling in the subcutaneous fat[59].

Ocimum basilicum: The inhibitory effect of the leaves extracts of *Ocimum basilicum* on pancreatic lipase (PL) involved in obesity was studied *in vitro*. Extracts inhibited PL (IC50: 64.99µg/ml) and scavenged DPPH in a dose-dependent manner[60,61].

Olea europaea: The anti-obesity activity of the leaf extract of *Olea europaea* was studied in high-fat-induced mouse models. In high-fat diet-induced mice, the extract significantly decreased food efficiency ratio, weight gain, visceral fat accumulation, and serum lipid composition. In the extract-treated group, expression of thermogenesis- and adipogenesis- related molecules was decreased[62].

***Plantago lanceolate*:** Supplementation of lambs' diet with 5% fresh *Plantago lanceolata* increased growth hormone and insulin concentrations in plasma level, whereas decreased carcass fat by 32.7%[63].

The anti-obesity effects of *P. lanceolate* leaves powder were investigated in male mice. The combination of a high-fat diet and *P. lanceolate* significantly decreased body weight and serum free-fatty acid and reduced visceral fat accumulation. Mice fed on *P. lanceolata*-revealed a substantial increment in HSL, Cpt2 mRNA, and Adrd3 levels and decrement in epididymal white adipose tissue Fas transcripts[64].

Plantago ovata: The appetite suppressive effect of administering 20 g of *Plantago ovata* seed 3 h before and immediately after meal for three days was studied in 17 women. A significant feeling of fullness 1 h after meals with a significantly lower fat intake was reported[65].

Polygonum aviculare: The anti-atherosclerosis properties of *Polygonum aviculare* ethanolic extract (PAE) were studied in mice fed a Western diet (WD) for 12 weeks. 50 and 100 mg/kg *Polygonum aviculare* ethanol extract or statin (10 mg/kg) lowered serum lipids and decreased blood pressure, and the treated mice showed less adipose tissue and gained less body weight than untreated animals. The extract results in a dose dose-dependent decrement in aorta VCAM-1, ICAM-1, and NF-κB levels. The extract also reduced adipocyte size and atherosclerotic plaque. In addition, it decreased phosphorylation of MAPK pathway components in the aorta of mice treated with the extract, indicating that the anti-atherosclerotic activity of the extract was mediated by MAPK pathway-dependent mechanism[66]. The inhibitory properties of the methanolic crude extracts of *Polygonum aviculare* on pancreatic lipase were studied. The extract possessed high inhibitory activity on pancreatic lipase (63.97 ± 0.05% inhibition). The chemical analysis identified flavonol-3-O-(2″-galloyl)-glycosides, flavonol-3-O-glycosides, and flavonol aglycones as active ingredients. The inhibitory activity of these ingredients was closely related to changing pancreatic lipase[67]. The anti-obesity effects of the ethanol extract of *Polygonum aviculare* (400 mg/kg, for 6.5 wks) were investigated in high-fat diet- (HFD-) induced obese mice. In the extract-treated (HFD-induced obesity) mice, body weights, adipose tissue weight, and adipocyte area were increased, while leptin, total serum triglyceride, and malondialdehyde concentrations were decreased compared to the untreated group. Also, significant suppression of the elevated mRNA expression levels of peroxisome proliferator-activated receptor γ, sterol regulatory element-binding protein-1c, adipocyte protein 2, and fatty acid synthase, and fat accumulation and adipocyte differentiation inhibition in a dose-dependent manner were observed[68].

CONCLUSION AND RECOMMENDATIONS

The complications of untreated obesity are life-threatening. The current review focused on the therapeutic potential of natural anti-obesity agents. Plants contain many natural ingredients which act as anti-obesity by many mechanisms. Further investigations were required to determine the molecular mechanism and the clinical efficacy of the natural anti-obesity agents. It was an interesting and attention-grabbing subject for future research.

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