Medicinal plants for the treatment of obesity and overweight: A review

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Abstract

Obesity and overweight have increased and became a major public health problem in the world during the last decades. Obesity and overweight increased the risk of diabetes, heart disease, osteoarthritis, bile diseases and certain cancers. In the current review, PubMed, Web Science, Science Direct, Researchgate, Academia.edu and Scopus were searched to highlight the anti-obesity activities of medicinal plants.

Keywords: Obesity; Overweight; Anti-Obesity; Medicinal Plants

1. Introduction

Obesity is a metabolic disease characterized by an increase in fat stores in the body. It is a major public health problem which is not only confined to developed countries but has now become an important public health problem in developing countries. Excessive caloric intake due to increased consumption of refined sugars, sugar-sweetened beverages and vegetable oils, fast food, lack of physical activity, lack of playgrounds (outdoors), and a sedentary lifestyle all play a role in the development of obesity. It is an important risk factor for osteoarthritis, many types of cancer, cardiovascular disorders, and respiratory and metabolic diseases [1-2]. Behavioral interventions and lifestyle changes aimed to increase energy expenditure and reduce the caloric intake showed limited efficacy because of complex etiology (hormonal, metabolic, and neurochemical). Current therapies have shown modest effects on weight loss in the general obese population. Drug combinations that target multiple, complementary pathways in the treatment of obesity look promising [3-4]. Recent reviews showed that many medicinal plants possess anti-obesity effect [5-9]. In the current review, PubMed, Web Science, Science Direct, Researchgate, Academia.edu and Scopus were searched to verify the anti-obesity activities of medicinal plants.

2. Medicinal plants with anti-obesity activity

2.1. Avena sativa

A clinical trial was carried out to confirm the anti-obesity effect of oat. Subjects with BMI ≥27 and aged 18-65, were randomly divided into a control (n=18) and an oat-treated (n=16) group, taking a placebo or beta glucan-containing oat cereal, respectively, for 12 weeks. The result showed that consumption of oat reduced body weight, BMI, body fat and the waist-to-hip ratio. Profiles of hepatic function, including AST and ALT showed decrements in patients with oat consumption. Nevertheless, anatomic changes were not observed by ultrasonic image analysis. Ingestion of oat was well tolerated and there was no adverse effect during the trial [10].
To explored the dose-dependent effect of oat cereal β-glucan on improving metabolic indexes of obesity mice, C57-B1 mice were randomized to chow diet (N) group and high fat diet group and other three doses of oat β-glucan groups (low β-glucan, medium β-glucan, and high β-glucan). Energy intake, glucose, lipids, and appetite related hormones were tested. Dose-dependent relation was observed on oat β-glucan doses and body weight change, average energy intake, total cholesterol, HDL cholesterol, plasma neural peptide Y, arcuate neural peptide Y mRNA, and arcuate neural peptide Y receptor 2 mRNA level. Oat β-glucan helped to increase plasma peptide Y-Y and intestine peptide Y-Y expression in obesity mice [11-12].

2.2. Bauhinia variegata

The antiobesity effect of methanolic extract of stem and root barks of Bauhinia variegata was examined in female rats fed with hypercaloric diet. The methanolic plant extract (200 and 400 mg/kg) exhibited a significant hypolipidemic effect with a reduction in the feed intake and body weight. Treatment of obese animals with the methanolic extract of B. variegata exhibited an increased brain serotonin level and high density lipoprotein with a concomitant decrease in total cholesterol, triglycerides and low density lipoprotein. Thus the antiobesity activity of methanolic extract of B. variegata could be attributed to tendency of the extract to reduce lipid profile and elicit the brain serotonin level [13-14].

2.3. Brassica species

The influence of ethanolic extracts of Brassica campestris spp. rapa roots (EBR) on obesity was examined in imprinting control region (ICR) mice fed a high-fat diet (HFD) and in 3T3-L1 adipocytes. The molecular mechanism of the antiobesity effect of EBR was investigated in 3T3-L1 adipocytes as well as in HFD-fed ICR mice. In the obese mouse model, both weight gain and epidymal fat accumulation were highly suppressed by the daily oral administration of 50 mg/kg EBR for 8 weeks, whereas the overall amount of food intake was not affected. EBR treatment induced the expression in white adipocytes of lipolysis-related genes, including beta3-adrenergic receptor (beta3-AR), hormone-sensitive lipase (HSL), adipose triglyceride lipase, and uncoupling protein 2. Furthermore, the activation of cyclic AMP-dependent protein kinase, HSL, and extracellular signal-regulated kinase was induced in EBR-treated 3T3-L1 cells. The lipolytic effect of EBR involved beta3-AR modulation, as inferred from the inhibition by the beta3-AR antagonist propranolol. Accordingly, EBR may have potential as a safe and effective antiobesity agent via the inhibition of adipocyte lipid accumulation and the stimulation of beta3-AR-dependent lipolysis [15-16].

2.4. Capsicum species

The anti-obesity effects of water extracts of seven Capsicum annuum L. varieties, Putgochu (Pca), Oyeegochu (Oca), Kwariputgochu (Kca), Green pepper (Gca), Yellow paprika (Yca), Red paprika (Rca) and Cheongyanggochu (Cca), were examined through the evaluation of lipoprotein lipase (LPL) mRNA expression level in 3T3-L1 cells (mouse pre-adipocytes). After capsaicin elimination by chloroform defatting, freeze-dried powder of Cca was treated to 3T3-L1 cells and anti-obesity effects were examined by determining the LPL mRNA level using the RT-PCR method. Of the primary fractions, only proven fractions underwent secondary and tertiary re-fractionating to determine anti-obesity effects. From seven different Capsicum annuum, there was a significant decrease of the LPL mRNA expression level of 50.9% in Cca treatment compared to the control group. A significant decrease of the LPL mRNA expression level was shown in primary fractions (Fr) 5 (36.2% decrease) and 6 (30.5% decrease) of the Cca water extracts. Due to the impurities checked by UPLC chromatography, Fr 5 and 6 were re-fractionated to determine the LPL mRNA expression level. Treatment of Fr 6-6 (35.8% decrease) and Fr 5-6 (35.3% decrease) showed a significant decrease in the LPL mRNA expression level. When analyzed using UPLC, major compounds of Fr 6-6 and Fr 5-6 were very similar. Subsequently, Fr 6-6 and Fr 5-6 were re-fractionated to isolate the major peak for structure elucidation. Treatment of Fr 5-6-1 (26.6% decrease) and Fr 6-6-1 (29.7% decrease) showed a significant decrease in the LPL mRNA expression level [17-18].

2.5. Citrullus colocynthis

The effects of the fixed oil extracted from the seeds of Citrullus colocynthis on blood homeostasis and body weight were studied in rats. Animals were given daily 4% of dietary regimen of the Citrullus colocynthis oil for 8 weeks, they showed significant slowdown of the body weight evolution comparatively to the animal in control group received 4% of sunflower oil. Furthermore, Colocynth oil treatment had a tendency to increase food intake feces output, and lipid in feces significantly. In parallel, the serum cholesterol, triglycerides, ALP levels and the count of erythrocytes and haematocrit level decreased significantly by 15.38, 22.22,46.29, 14.97 and 14.17%, respectively compared to control values; while AST level increased significantly by 21.71%. These results support the suggestion of using Citrullus colocynthis oil as a treatment for dyslipidemia and hyperglycemia, and related abnormalities [19].
The inhibitory effect of *Citrus colocynthis* (CCT) on inflammatory cytokines secreted in obesity conditions was studied in mice. Control group was fed with normal diet (N-D) for 42 days alone or plus 50 mg/kg hydro-alcoholic (H-A) extract of CCT. The obese mice were given high fat diet (H-F-D) for 42 days alone or plus CCT extract. Food intake and body weight were recorded each week and expression of TNF-α, IL-6 and IL-10 in serum were assayed after every two weeks. CCT extract reduced body weight by 4.02% (p> 0.05) and food intake by 3.52% (p> 0.05), but dramatically decreased expression of TNF-α 44.83 (p< 0.001), IL-6 30.23 (p< 0.001) and marginally increased IL-10 5.31 (p> 0.05) in obese mice. Accordingly, CCT extract did not show anti-obesity effects, it could have an anti-inflammatory effect through down regulation of obesity-associated pro-inflammatory cytokines [20-21].

2.6. *Citrus species*

Eriocitrin (eriodictyol 7-rutinoside), a powerful antioxidative flavonoid in lemon with lipid-lowering effects was evaluated in a rat model of high-fat diet to investigate its mechanism of action. A feeding experiments was conducted in zebrafish with diet-induced obesity. Oral administration of eriocitrin (32 mg/kg/day for 28 days) improved dyslipidaemia and decreased lipid droplets in the liver. DNA microarray analysis revealed that eriocitrin increased mRNA of mitochondrial biogenesis genes, such as mitochondria transcription factor, nuclear respiratory factor 1, cytochrome c oxidase subunit 4, and ATP synthase. In HepG2 cells, eriocitrin also induced the corresponding orthologues, and reduced lipid accumulation under conditions of lipid loading. Eriocitrin increased mitochondrial size and mtDNA content, which resulted in ATP production in HepG2 cells and zebrafish [22-23].

2.7. *Crotalaria juncea*

Anti-obesity effect of *Crotalaria juncea* leaves extract was documented in high fat induced obesity in rats [24-25].

2.8. *Cuminum cyminum*

The effect of cumin powder on body composition and lipid profile was studied in overweight and obese women in a randomized clinical trial.88 overweight/obese women were randomly assigned into two groups. The experimental group was given 3 g/day cumin powder with yogurt at two meals for 3 months. The same amount of yogurt without cumin powder was prescribed for the control group. All patients received nutrition counseling for weight loss in a similar manner. Anthropometric and biochemical parameters were determined before and after the intervention. Cumin powder reduced serum levels of fasting cholesterol, triglyceride, and LDL and increased HDL. Weight, BMI, waist circumference, and fat mass were also significantly reduced. However, it exerted no effect on FBS and fat-free mass [26].

The effects of *Cuminum cyminum* intake on weight loss and metabolic profiles among overweight subjects was studied by a randomized double-blind placebo-controlled clinical trial which conducted among 78 overweight subjects (male, n = 18; female, n = 60) aged 18-60 years old. Participants were randomly assigned into three groups to receive: (1) *Cuminum cyminum* capsule (n = 26); (2) orlistat 120 capsule (n = 26) and (3) placebo (n = 26) three times a day for 8 weeks. Anthropometric measures and fasting blood samples were taken at baseline and after 8 weeks of intervention. Consumption of the *Cuminum cyminum* and orlistat120 resulted in a similar significant decrease in weight (-1.1 ± 1.2 and -0.9 ± 1.5 compared with placebo 0.2 ± 1.5 kg, respectively, p = 0.002) and BMI (-0.4 ± 0.5 and -0.4 ± 0.6 compared with placebo 0.1 ± 0.6 kg/m(2), respectively, p = 0.003). In addition, *Cuminum cyminum*, compared with orlistat and placebo, led to a significant reduction in serum insulin levels (-1.4 ± 4.5 vs. 1.3 ± 3.3 and 0.3 ± 2.2 µU/ml, respectively, p = 0.02), HOMA-B (-5.4 ± 18.9 vs. 5.8 ± 13.3 and 1.0 ± 11.0, respectively, p = 0.02) and a significant rise in QUICKI (0.01 ± 0.01 vs. -0.005 ± 0.01 and -0.004 ± 0.01, respectively, p = 0.02) [27-28].

2.9. *Cyperus rotundus*

The biological efficacy of *Cyperus rotundus* tubers extract was studied on weight control in obese Zucker rats. Administration of 45 or 220 mg/kg/day of *Cyperus rotundus* tubers hexane extract for 60 days in Zucker rats induced a significant reduction in weight gain without affecting food consumption or inducing toxicity. *In vitro*, 250 microg/ml of this extract was able to stimulate lipolysis in 3T3-F442 adipocytes suggesting that this medicinal plant contained activators of beta-adrenoceptors (AR). The binding assay performed on the rat beta3-AR isoform, known to induce thermogenesis, demonstrated that *Cyperus rotundus* tubers extract can consistently and effectively bind to this receptor. The data suggest that the effect on weight gain exerted by *Cyperus rotundus* tubers extract may be mediated, at least partially, through the activation of the beta3-AR [29-30].

2.10. *Echinochloa crus-galli*

The anti-obesity effect of hydroalcoholic extracts of *Echinochloa crus-galli* grains was evaluated in high fat diet induced obesity in albino rats. Obesity was induced by administration of high fat diet for 4 weeks, the obtained obese rats were
treated with hydroalcoholic extracts of *Echinochloa crus-galli* grains in a dose of 200, 400 and 600 mg/kg, bw orally for next 4 weeks. *Echinochloa crus-galli* caused significant decrease in body weights, adipose tissue weight, SGOT and SGPT levels, blood glucose levels, LDL-C, VLDL-C, total cholesterol, triglyceride levels, atherogenic index, with a significant increase in HDL-C levels compared with high fat diet control group[31].

The effect of *Echinochloa crus-galli* extract as antihypercholesterolemic therapy was evaluated by performing in vivo studies and identifying its effects on food consumption, weight gain, fecal fat excretion, and serum lipid and biochemical profiles. The animal group administered methanolic extract of the plant showed decreased levels of TC, LDL, VLDL, TG, HDL+VLDL, VLDL+LDL, LDL/TC, AI, SGOT, SGPT and elevated levels of HDL, HDL/TC significantly (P < 0.01 and P < 0.05) in a dose dependent manner. Body weight and food intake in treated groups were significantly lower than that in model control [[32-33]].

### 2.11. Ephedra species

Several studies have found that ephedrine/caffeine combinations were modestly effective for short- and long-term weight loss [34-38].

### 2.12. Ficus carica

The hypolipidemic and preventive effects of *Ficus carica* leaf extract(50 or 100 mg/kg for 6 weeks) were studied in hyperlipidemia in high fat diet-induced obese male rats. *Ficus carica* leaf extract significantly lowered TG and IL-6 levels and elevated HDL cholesterol (p < 0.05). The effects of *Ficus carica* leaf extract on lipid parameters were more pronounced than those of the positive control pioglitazone. *Ficus carica* leaf extract significantly lowered atherogenic index and coronary risk index (p < 0.01) while it had no effect on adiponectin and leptin levels [39-40].

### 2.13. Foeniculum vulgare

The effect of *Foeniculum vulgare* fruit extracts in high fat diet and their possible role in obesity and associated cardiovascular disorders were studied in rats. Three fractions prepared by successive solvent technique from methanol extract of *Foeniculum vulgare*. Fruits were administered at a dose of 300 mg/body weight by oral gavage and volatile oil obtained by hydro-distillation at a dose of 0.2 ml/bw intraperitoneally once daily along with high fat diet to the female albino rats for six weeks. Results revealed that body weight and fat pad weights were reduced in extracts fed animals in a variable pattern. Cholesterol and triglycerides levels, which were elevated in high fat diet fed animals, improved in a significant manner. Maximum activity was observed with methanol fraction of the extracts which contained maximum amount of phenolic (48.37 mg/g) and flavonoidal contents (21.44 mg/g) [41-42].

### 2.14. Helianthus annuus

The anti-obesity activity of the methanolic extract of *Helianthus annuus* seeds was studied in mice model. The mice received cafeteria diet, atorvastatin (10 mg/kg) and *Helianthus annuus* 200 mg/kg daily for 6 weeks. Parameters such as food consumption, locomotor activity, body weight, body mass index (BMI), lee index of obesity (LIO), total cholesterol, triglyceride, LDL and HDL glucose were studied. The methanolic extract of *Helianthus annuus* seeds significantly increased locomotor activity (rearing, grooming, ambulation) with HDL and significantly decrease food consumption, body weight, BMI, LIO, total cholesterol, triglyceride, LDL and glucose [43-44].

### 2.15. Hibiscus sabdariffa

The effect of a standardized *Hibiscus sabdariffa* calyx’s aqueous extract on body weight was evaluated in an obese mice model induced by the administration of monosodium glutamate. *Hibiscus sabdariffa* aqueous extract was orally administered (120 mg/kg/day) for 60 days to healthy and obese mice. *Hibiscus sabdariffa* administration significantly reduced body weight gain in obese mice and increased liquid intake in healthy and obese mice. ALT levels were significantly increased on the 15th and 45th days in obese mice, but AST levels did not show significant changes. Triglycerides and cholesterol levels showed non-significant reductions in animals treated with *Hibiscus sabdariffa* [45].

*Hibiscus sabdariffa* water extract (HSE) treatment reduced fat accumulation in the livers of hamsters fed with fat diet (HFD) in a concentration-dependent manner. Administration of HSE reduced the levels of liver cholesterol and triglycerides, which were elevated by HFD. Analysis of the effect of HSE on paraoxonase 1, an antioxidant liver enzyme, revealed that HSE potentially regulated lipid peroxides and protects organs from oxidation-associated damage. The markers of liver damage such as serum alanine aminotransferase and aspartate aminotransferase levels that were elevated by HFD were also reduced on HSE treatment. The effects of HSE were as effective as treatment with...
anthocyanin; which indicated that anthocyanins present in the HSE may play a crucial role in the protection established against HFD-induced obesity [46-47].

The effect of Hibiscus sabdariffa L. (Hs) calyx extract on fat absorption-excretion and body weight was studied in rats. Rats were fed with either a basal diet (SDC = Control diet) or the same diet supplemented with Hs extracts at 5%, 10% and 15% (SD5, SD10 and SD15). Only SD5 did not show significant increases in weight, food consumption and efficiency compared to SDC. The opposite occurred in SD15 group which showed a significant decrease for these parameters. The SD10 responses were similar to SD15, with the exception of food consumption. In both SDC and SD5 groups, no body weight loss was observed; however, only in the latter group was there a significantly greater amount of fatty acids found in feces [48].

A clinical trial was carried out to confirm the metabolic-regulating and liver-protecting effect of Hibiscus sabdariffa extracts (HSE). Subjects with a BMI ≥ 27 and aged 18–65, were randomly divided into control and HSE-treated groups, for 12 weeks. The results revealed that consumption of HSE reduced body weight, BMI, body fat and the waist-to-hip ratio. Serum free fatty acids were also lowered by HSE. Anatomic changes revealed that HSE improved the illness of liver steatosis. Ingestion of HSE was well tolerated and there was no adverse effect during the trial [49-50].

2.16. Jasminum sambac

The anti-lipid peroxidation effect of Jasminum sambac was evaluated using the standard antioxidants BHT, Vitamin C, Vitamin E and Rutin. The methanolic extract of the Jasminum sambac flowers shows anti-lipid peroxidative effect which was similar to that of all standards [51].

The ethanolic extract of Jasminum sambac flowers was evaluated as the anti-obesity in an in vitro assay using pancreatic lipase enzyme and in vivo on high-fat diet-induced mice. The ethanolic extract of Jasminum sambac flowers at a dose 100 mg/kg and 300 mg/kg bw caused significant decrease of mice body weight, fat index, and food intake. In in vitro assay, the ethanolic extract of Jasminum sambac flowers inhibited pancreatic lipase enzyme activity [52-53].

2.17. Kochia scoparia

The effect of ethanol extract of Kochia scoparia fruit was evaluated for prevention of obesity induced in mice by a high-fat diet for 9 weeks. The ethanol extract of K. scoparia fruit prevented the increases in body weight and parametrial adipose tissue weight induced by the high-fat diet. Consumption of a high-fat diet containing 1% or 3% K. scoparia extract significantly increased the fecal content and the fecal triacylglycerol level at day 3 compared with those in the high-fat diet group. The ethanol extract (250 mg/kg) and total saponins (100 mg/kg) of K. scoparia inhibited the elevation of the plasma triacylglycerol level 2 or 3 h after the oral administration of the lipid emulsion. Total saponins, momordinic, 2'-O-beta-d-glucopyranosyl momordin Ic and 2'-O-beta-d-glucopyranosyl momordin Iic isolated from K. scoparia fruit inhibited the pancreatic lipase activity (in vitro) [54-55].

2.18. Lagerstroemia speciosa

The antiobesity effect of dietary Lagerstroemia speciosa leaves extract was studied in female mice with remarkable body weight gain. Mice were fed a control diet or test diet containing 5% of a hot-water leaves extract instead of cellulose for 12 wk. Neither group showed any changes in diet intake during the experimental period. Body weight gain and adipose tissue weight were lowered significantly in Lagerstroemia speciosa diet group. Blood glucose levels were not suppressed in the Lagerstroemia speciosa diet group, but hemoglobin A1C was found to be suppressed at the end of the experiment. No effects on the serum lipids were observed, but the mice fed Lagerstroemia speciosa extract showed a significant decrease (to 65% of the control level) in total hepatic lipid contents [56].

A randomized, placebo-controlled, double-blind, parallel group study conducted over 14 weeks (including a 2-week run-in phase) was designed to investigate the efficacy and safety of IQP-GC-101 (a standardized extracts of Garcinia cambogia, Camellia sinensis; unroasted Coffea arabica, and Lagerstroemia speciosa) in reducing body weight and body fat mass in overweight Caucasian adults. Subjects took three IQP-GC-101 or placebo tablets, twice a day, 30 min before main meals. All subjects also adhered to a 500 kcal/day energy deficit diet with 30% of energy from fat. After 12-week intervention, IQP-GC-101 resulted in a mean (±SD) weight loss of 2.26 ± 2.37 kg compared with 0.56 ± 2.34 kg for placebo (p < 0.002). There was also significantly more reduction in body fat mass, waist circumference, and hip circumference in the IQP-GC-101 group. No serious adverse events were reported [57].

DLBS3233, a combined bioactive fraction of Cinnamomum burmanii and Lagerstroemia speciosa, possessed beneficial effects on glucose and lipid metabolism through the up regulation of insulin-signal transduction. The clinical efficacy of
DLBS3233 was evaluated in type-2 diabetes mellitus subjects inadequately controlled by metformin and other oral anti-diabetic drugs. DLBS3233 was given orally at the dose of 100 mg once daily for 12 weeks of therapy in addition to their baseline oral anti-diabetic medication. After 12 weeks of treatment, the HbA1c level was reduced by 0.65±1.58 % (p=0.001) from baseline (9.67±2.11 %); while the 1h- postprandial glucose level was reduced by -1.45±3.89 mmol/l (p=0.021) from baseline (15.29±4.49 mmol/l). Insulin sensitivity, lipid profile and adiponectin level were improved to a considerable extent. DLBS3233 did not adversely affect body weight, liver, and renal function. Most adverse events observed were mild and they all had been resolved by the end of the study [58-59].

2.19. Mangifera indica
Mangiferin (10 and 20 mg/kg, ip) showed significant antihyperlipidemic and antiatherogenic activities as evidenced by significant decrease in plasma total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C) levels, together with elevation of high-density lipoprotein cholesterol (HDL-C) level and diminution of atherogenic index in diabetic rats[60].

The anti-obesity effects of tea from Mangifera indica were studied in obese rats fed a high-fat diet (HFD). The consumption of Mangifera indica tea (24.7±2.1ml/day) exerted antioxidant and anti-inflammatory effects, increasing total antioxidant capacity and interleukin-1 serum concentrations, reduced abdominal fat accumulation, up regulated PPAR-γ and LPL and down regulated FAS expression. According to the results, Mangifera indica tea has therapeutic potential in treating obesity and related diseases through regulating the expression of transcriptional factors and enzymes associated with adipogenesis[61-62].

2.20. Momordica charantia
Many studies showed that Momordica charantia extracts possessed hipolipidemic effects (decreased cholesterol, LDL, VLDL, and increased HDL) in rats and mice. Momordica charantia extracts also revealed beneficial effects on obesity and obesity-associated insulin resistance in mice and rats [63-78].

Momordica charantia (bitter melon) or its constituents enhanced insulin signals, AMP-associated protein kinase (AMPK) and peroxisome proliferator activating receptors (PPARs), reduce lipogenic gene expression and increase lipid oxidation in adipose tissues. It also suppressed the pro-inflammatory mediators in obesity associated inflammation. It suppressed leptin and resistin levels in adipose tissues and plasma, elevate system levels of anti-inflammatory mediator, adiponectin and improved system and brain inflammation in animals fed with high fat diets [66-67, 79-85].

3. Conclusion
Obesity and overweight are the most prevalent health problem affecting all age groups, and leads to many complications. The investigation of natural sources has provided new developments lead to a safe and effective pharmacological treatment. The current review highlighted the anti-obesity effects of medicinal plants as natural and safe source for the treatment of obesity and its complications

Compliance with ethical standards

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