

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

Ali Esmail Al-Snafi ^{1,*}, Muayad Hussein Amer ², Kareema Helal Shnawa ²

¹ Department of Pharmacology, College of Medicine, University of Thi Qar, Iraq.

² Thi Qar Health directorate, Iraq.

World Journal of Biology Pharmacy and Health Sciences, 2022, 10(02), 001-010

Publication history: Received on 23 March 2022; revised on 28 April 2022; accepted on 30 April 2022

Article DOI: <https://doi.org/10.30574/wjbphs.2022.10.2.0075>

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].

*Corresponding author: Ali Esmail Al-Snafi
Department of Pharmacology, College of Medicine, University of Thi Qar, Iraq.

To explore the dose-dependent effect of oat cereal β -glucan on improving metabolic indexes of obesity mice, C57-BL 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 anti-obesity 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 epididymal 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 β ₃-adrenergic receptor (β ₃-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 β ₃-AR modulation, as inferred from the inhibition by the β ₃-AR antagonist propranolol. Accordingly, EBR may have potential as a safe and effective anti-obesity agent via the inhibition of adipocyte lipid accumulation and the stimulation of β ₃-AR-dependent lipolysis [15-16].

2.4. *Capsicum species*

The anti-obesity effects of water extracts of seven *Capsicum annum* 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 annum*, 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 *Citrullus 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 orlistat 120 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/m²), 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 μ IU/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-adrenoreceptors (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, HDL and 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 14weeks (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 (\pm 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 $0.65 \pm 1.58\%$ ($p=0.001$) from baseline ($9.67 \pm 2.11\%$); 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 ± 2.1 ml/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 hypolipidemic 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

Acknowledgments

The authors acknowledged the College of Medicine, University of Thi-Qar for support.

References

- [1] Fitzgerald FT. The problem of obesity. *Annu Rev Med* 1981;32:221-231.
- [2] Sarnali TT, Moyenuddin PK. Obesity and disease association: A review. *AKMMC J* 2010;1(2):21-24.
- [3] Jackson VM, Breen DM, Fortin JP, Liou A, Kuzmiski JB, Loomis AK, Rives ML, Shah B, Carpino PA. Latest approaches for the treatment of obesity. *Expert Opin Drug Discov* 2015;10(8):825-839.
- [4] Haywood C, Sumithran P. Treatment of obesity in older persons-A systematic review. *Obes Rev* 2019; 20(4): 588-598.

- [5] Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with hypolipidemic, hemostatic, fibrinolytic and anticoagulant effects (part 1). *Asian Journal of Pharmaceutical Science & Technology* 2015; 5(4): 271-284.
- [6] Al-Snafi AE. Cardiovascular effects of *Carthamus tinctorius*: A mini-review. *Asian Journal of Pharmaceutical Research* 2015; 5(3): 199-209.
- [7] Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with cardiovascular effects (part 1). *Int J of Pharmacology & Toxicology* 2015; 5(3): 163-176.
- [8] Al-Snafi AE. Medicinal plants with cardiovascular effects (part 2): plant based review. *IOSR Journal of Pharmacy* 2016; 6(7): 43-62.
- [9] Al-Snafi AE. Medicinal plants for prevention and treatment of cardiovascular diseases - A review. *IOSR Journal of Pharmacy* 2017; 7(4):103-163.
- [10] Chang HC, Huang CN, Yeh DM, Wang SJ, Peng CH and Wang CJ. Oat prevents obesity and abdominal fat distribution, and improves liver function in humans. *Plant Foods Hum Nutr* 2013;68(1):18-23.
- [11] Lin N, Li Y, Tang L, Shi J and Chen Y. In vivo effect of oat cereal β -glucan on metabolic indexes and satiety-related hormones in diet-induced obesity C57-BL mice. *Mol Nutr Food Res* 2013 ;57(7):1291-1294.
- [12] Al-Snafi AE. The nutritional and therapeutic importance of *Avena sativa* - An Overview. *IntJof Phytother* 2015;5:48-56.
- [13] Balamurugan G and Muralidharan P. Antiobesity effect of *Bauhinia variegata* bark extract on female rats fed on hypercaloric diet. *Bangladesh J Pharmacol* 2010; 5: 8-12.
- [14] Al-Snafi AE. The pharmacological importance of *Bauhinia variegata*. A review. *J Pharma Sci Res* 2013;4:160-164.
- [15] An S, Han JI, Kim MJ, Park JS, Han JM, Baek NI, Chung HG, Choi MS, Lee KT and Jeong TS. Ethanolic extracts of *Brassica campestris* spp. rapa roots prevent high-fat diet-induced obesity via β_3 -adrenergic regulation of white adipocyte lipolytic activity. *J Med Food* 2010; 13(2): 406-414.
- [16] Al-Snafi AE. The pharmacological importance of *Brassica nigra* and *Brassica rapa* grown in Iraq. *J of Pharmceutical Biol* 2015;5:240-253.
- [17] Baek J, Lee J, Kim K, Kim T, Kim D, Kim C, Tsutomu K, Ochir S, Lee K, Ho Park C, Lee Y and Choe M. Inhibitory effects of *Capsicum annuum* L. water extracts on lipoprotein lipase activity in 3T3-L1 cells. *Nutrition Research and Practice* 2013; 7(2): 96-102.
- [18] Al-Snafi AE. The pharmacological importance of *Capsicum* species (*C. annuum* and *C. frutescens*) grown in Iraq. *J Pharmaceut Biol* 2015;5: 124-142.
- [19] Amamou F, Bouafia M, Chabane-Sari D, Meziane RK and Nani A. *Citrullus colocynthis*: a desert plant native in Algeria, effects of fixed oil on blood homeostasis in Wistar rat. *J Nat Prod Plant Resour* 2011; 1 (3):1-7.
- [20] Sanadgo N, Najafi S, Ghasemi LV, Motalleb G and Estakhr J. A study of the inhibitory effects of *Citrullus colocynthis* (CCT) using hydro-alcoholic extract on the expression of cytokines: TNF- α and IL-6 in high fat diet-fed mice towards a cure for diabetes mellitus. *Journal of Pharmacognosy and Phytotherapy* 2011; 3(6): 81-88.
- [21] Al-Snafi AE. Chemical constituents and pharmacological effects of *Citrullus colocynthis*- A review. *IOSR Journal of Pharmacy* 2016; 6: 57-67.
- [22] Hiramitsu M, Shimada Y, Kuroyanagi J, Inoue T, Katagiri T, Zang L, Nishimura Y, Nishimura N and Tanaka T. Eriocitrin ameliorates diet-induced hepatic steatosis with activation of mitochondrial biogenesis. *Sci Rep* 2014; 4: 3708.
- [23] Al-Snafi AE. Nutritional value and pharmacological importance of citrus species grown in Iraq. *IOSR Journal of Pharmacy* 2016; 6(8): 76-108.
- [24] Sreedhar KS. Evaluation of Anti-obesity activities of *Crotalaria juncea* L. in albino rats. MSc thesis, Gautham College of Pharmacy 2011.
- [25] Al-Snafi AE. The contents and pharmacology of *Crotalaria juncea*- A review. *IOSR Journal of Pharmacy* 2016; 6(6): 77-86.
- [26] Zare R, Heshmati F, Fallahzadeh H and Nadjarzadeh A. Effect of cumin powder on body composition and lipid profile in overweight and obese women. *Complement Ther Clin Pract* 2014; 20(4): 297-301.

- [27] Taghizadeh M, Memarzadeh MR, Asemi Z and Esmailzadeh A. Effect of the *Cuminum cyminum* L intake on weight loss, metabolic profiles and biomarkers of oxidative stress in overweight subjects: A randomized double-blind placebo-controlled clinical trial. *Ann Nutr Metab* 2015; 66(2-3):117-124.
- [28] Al-Snafi AE. The contents and pharmacology of *Crotalaria juncea*- A review. *IOSR Journal of Pharmacy* 2016; 6:77-86.
- [29] Lemaure B, Touché A, Zbinden I, Moulin J, Courtois D, Macé K and Darimont C. Administration of *Cyperus rotundus* tubers extract prevents weight gain in obese Zucker rats. *Phytother Res* 2007; 21: 724-730.
- [30] Al-Snafi AE. A review on *Cyperus rotundus* a potential medicinal plant. *IOSR Journal of Pharmacy* 2016; 6:32-48.
- [31] PavaniM, Ramadurg B and Varshitha C. Anti-obesity activities of hydroalcoholic extract of *Echinochloa crus-galli* (L.) P. Beauv grains in albino rats. *Research Journal of Pharmacology and Pharmacodynamics* 2014; 6(1): 13-20.
- [32] Kumar DS, Banji D and Harani A. Antihypercholesterolemic effect of *Echinochloa crus-galli*. National Conference on (New trends in molecular medicine and pharmacogenomics)- India 2013.
- [33] Al-Snafi AE. Pharmacology of *Echinochloa crus-galli* - A review. *Indo Am J P Sci* 2017;4:117-122.
- [34] Astrup A, Breum L, Toubro S, Hein P and Quaade F. The effect and safety of an ephedrine/caffeine compound compared to ephedrine, caffeine and placebo in obese subjects on an energy restricted diet. A double-blind trial. *Int J ObesRelatMetabDisord*1992; 16:269-277.
- [35] Breum L, Pedersen JK, Aglstrom and Frimodt-Møller J. Comparison of an ephedrine/ caffeine combination and dexfenfluramine in the treatment of obesity. A double-blind multi-centre trial in general practice. *Int Obes Relat Metab Disord* 1994;18:99-103.
- [36] Molnar D, Torok K, Erhardt E and Jeges S. Safety and efficacy of treatment with an ephedrine/ caffeine mixture. The first double-blind placebo-controlled pilot study in adolescents. *Int J Obes Relat Metab Disord* 2000; 24:1573-1578.
- [37] Boozer CN, Nasser JA, Heymsfield SB, Wang V, Chen G and Solomon JL. An herbal supplement containing Ma Huang-Guarana for weight loss: a randomized, double-blind trial. *Int J Obes Relat Metab Disord* 2001; 25:316-324.
- [38] Al-Snafi AE. Therapeutic importance of *Ephedra alata* and *Ephedra foliata*- A review. *Indo Am J P Sci* 2017; 4(02): 399-406.
- [39] Joerin L, Kauschka M, Bonnländer B, Pischel I, Benedek B and Butterweck V. *Ficus carica* leaf extract modulates the lipid profile of rats fed with a high-fat diet through an increase of HDL-C. *Phytother Res* 2014; 28(2): 261-267.
- [40] Al-Snafi AE. Nutritional and pharmacological importance of *Ficus carica* - A review. *IOSR Journal of Pharmacy* 2017;7(3):33-48.
- [41] Garg G, Ansari SH, Khan SA and Garg M. Effect of *Foeniculum vulgare* Mill. fruits in obesity and associated cardiovascular disorders demonstrated in high fat diet fed albino rats. *Journal of Pharmaceutical and Biomedical Sciences* 2011;8(8): 1-5.
- [42] Al-Snafi AE. The chemical constituents and pharmacological effects of *Foeniculum vulgare* - A review. *IOSR Journal of Pharmacy* 2018; 8(5):81-96.
- [43] Islam AT. in vivo anti-obesity activity of methanolic extract of *Helianthus annuus* seeds ,<https://ssrn.com/abstract=2862458>, (January 2016).
- [44] Al-Snafi AE. The pharmacological effects of *Helianthus annuus*- A review. *Indo Am J P Sc* 2018;5:1745-1756.
- [45] Alarcon-Aguilar FJ, Zamilpa A, Perez-Garcia MD, Almanza-Perez JC, Romero-NuñezE, Campos-Sepulveda EA, Vazquez-Carrillo LI and Roman-Ramos R. Effect of *Hibiscus sabdariffa* on obesity in MSG mice. *J Ethnopharmacol* 2007; 114(1): 66-71.
- [46] Huang TW, Chang CL, Kao ES and Lin JH. Effect of *Hibiscus sabdariffa* extract on high fat diet-induced obesity and liver damage in hamsters. *Food Nutr Res*2015; 59:29018.doi: 10.3402/fnr.v59.29018.
- [47] Kao ES, Yang MY, Hung CH, Huang CN and Wang CJ. Polyphenolic extract from *Hibiscus sabdariffa* reduces body fat by inhibiting hepatic lipogenesis and preadipocyte adipogenesis. *Food Funct* 2016;7(1):171-182.

- [48] Carvajal-Zarrabal O, Hayward-Jones PM, Orta-Flores Z, Nolasco-Hipolito C, Barradas-Dermitz DM, Aguilar-Uscanga MG and Pedroza-Hernandez MF. Effect of *Hibiscus sabdariffa* L dried calyx ethanol extract on fat absorption-excretion, and body weight implication in rats. Journal of Biomedicine and Biotechnology 2009,doi:10.1155/2009/394592
- [49] Chang HC, Peng CH, Yeh DM, Kao ES and Wang CJ. *Hibiscus sabdariffa* extract inhibits obesity and fat accumulation, and improves liver steatosis in humans. Food Funct 2014; 5: 734-739.
- [50] Al-Snafi Ali Esmail. Pharmacological and therapeutic importance of *Hibiscus sabdariffa*- A review. International Journal of Pharmaceutical Research 2018; 10:451-475.
- [51] Kalaiselvi Mand Kalaivani KPL. Phytochemical analysis and antilipidperoxidative effect of *Jasminum sambac* (L.) Ait. Oleaceae. Pharmacologyonline 2011; 1: 38-43.
- [52] Yuniarto A, Kurnia I and Ramadhan M. Anti-obesity effect of ethanolic extract of Jasmine flowers (*Jasminumsambac* (L.) Ait) in high-fat diet induced mice: potent inhibitor of pancreatic lipase enzyme. IJAPBC 2015;4(1): 18-22.
- [53] Al-Snafi Ali Esmail. Pharmacological and therapeutic effects of *Jasminumsambac*- A review. Indo Am J P Sc 2018;5:1766-1778.
- [54] Han LK, Nose R, Li W, Gong XJ, Zheng YN, Yoshikawa M, Koike K, Nikaido T, Okuda H and Kimura Y. Reduction of fat storage in mice fed a high-fat diet long term by treatment with saponins prepared from *Kochia scoparia* fruit. Phytother Res 2006; 20(10):877-882.
- [55] Al-Snafi AE. A review on pharmacological activities of *Kochia scoparia*. Indo Am J P Sc 2018; 5:2213-2221.
- [56] Suzuki Y, Unno T, Ushitani M, Hayashi K and Kakuda T. Antiobesity activity of extracts from *Lagerstroemia speciosa* L. leaves on female KK-Ay mice. J Nutr Sci Vitaminol (Tokyo) 1999;45(6):791-795.
- [57] Chong P, Beah Z, Grube B and Riede L. IQP-GC-101 reduces body weight and body fat mass: A randomized, double-blind, placebo-controlled study. PhytotherRes 2014;28:1520–1526.
- [58] Tjokroprawiro A, Murtiwi S and Tjandrawinata RR. DLBS3233, a combined bioactive fraction of *Cinnamomum burmanii* and *Lagerstroemia speciosa*, in type-2 diabetes mellitus patients inadequately controlled by metformin and other oral antidiabetic agents. J Complement Integr Med 2016; 13(4):413-420.
- [59] Al-Snafi AE. Medicinal value of *Lagerstroemia speciosa*: An updated review. International Journal of Current Pharmaceutical Research 2019; 11:18-26.
- [60] Muruganandan S, Srinivasan K, Gupta S, Gupta PK and Lal J. Effect of mangiferin on hyperglycemia and atherogenicity in streptozotocin diabetic rats. J Ethnopharmacol 2005;97(3):497-501.
- [61] Ramírez NM, Toledo RCL, Moreira MEC, Martino HSD, Benjamin LDA, de Queiroz JH, Ribeiro AQ and Ribeiro SMR. Anti-obesity effects of tea from *Mangifera indica* L leaves of the Ubá variety in high-fat diet-induced obese rats. Biomed Pharmacother 2017;91:938-945.
- [62] Al-Snafi AE, Ibraheemi ZAM, Talab TA. A review on components and pharmacology of *Mangifera indica*. International Journal of Pharmaceutical Research 2021; 13(2): 3043- 3066.
- [63] Mohammady I, Elattar S, Mohammed S and Ewais M. An evaluation of anti-diabetic and anti-lipidemic properties of *Momordica charantia*(bitter melon) fruit extract in experimentally induced diabetes. Life Sci J 2012; 9(2): 363-374.
- [64] Parmar K, Patel S, Patel J, Patel B and Patel MB. Effects of bittergourd (*Momordica charantia*) fruit juice on glucose tolerance and lipid profile in type-1 diabetic rats. Int J Drug Dev & Res 2011; 3 (2): 139-146.
- [65] Nerurkar PV, Lee YK and Nerurkar VR. *Momordica charantia* (bitter melon) inhibits primary human adipocyte differentiation by modulating adipogenic genes. BMC Complementary and Alternative Medicine 2010; 10: 34-43.
- [66] Huang HL, Hong YW, Wong YH, Chen YN, Chyuan JH, Huang CJ and Chao PM. Bitter melon (*Momordica charantia* L.) inhibits adipocyte hypertrophy and down regulates lipogenic gene expression in adipose tissue of diet-induced obese rats. Br J Nutr 2008; 99:230-239.
- [67] Chan LL, Chen Q, Go AG, Lam EK and Li ET. Reduced adiposity in bitter melon (*Momordica charantia*)- fed rats is associated with increased lipid oxidative enzyme activities and uncoupling protein expression. J Nutr 2005; 135(11): 2517-2523.

- [68] Shobha CR, Prashant V, Akila P, Chandini R, Suma MN and Basavanagowdappa H. Fifty percent ethanolic extract of *Momordica charantia* inhibits adipogenesis and promotes adipolysis in 3T3-L1 pre-adipocyte cells. Reports of Biochemistry & Molecular Biology 2017; 6(1): 22-32.
- [69] Bao B, Chen YG, Zhang L, Xu YLN, Wang X, Liu J and Qu W. *Momordica charantia* (Bitter Melon) reduces obesity-associated macrophage and mast cell infiltration as well as inflammatory cytokine expression in adipose tissues. PLoS One 2013; 8(12): e84075.
- [70] Saad DY, Soliman MM, Baiomy AA, Yassin MH and El-Sawy HB. Effects of Karela (bittermelon; *Momordica charantia*) on genes of lipids and carbohydrates metabolism in experimental hypercholesterolemia: biochemical, molecular and histopathological study. BMC Complement Altern Med 2017; 17(1): 319.
- [71] Zeng Y, Guan M, Li C, Xu L, Zheng Z, Li J and Xue Y. Bitter melon (*Momordica charantia*) attenuates atherosclerosis in apo-E knock-out mice possibly through reducing triglyceride and anti-inflammation. Lipids Health Dis 2018;17(1):251.
- [72] Ramachandra Shobha C, Prashant V, Akila P, Chandini R, Nataraj Suma M and Basavanagowdappa H. Fifty percent ethanolic extract of *Momordica charantia* inhibits adipogenesis and promotes adipolysis in 3T3-L1 pre-adipocyte cells. Rep Biochem Mol Biol 2017; 6(1): 22-32.
- [73] Hussain MS, Jahan N, Or Rashid MM, Hossain MS, Chen U and Rahman N. Antihyperlipidemic screening and plasma uric acid reducing potential of *Momordica charantia* seeds on Swiss albino mice model. Heliyon 2019; 5(5): e01739.
- [74] Raish M. *Momordica charantia* polysaccharides ameliorate oxidative stress, hyperlipidemia, inflammation, and apoptosis during myocardial infarction by inhibiting the NF- κ B signaling pathway. Int J Biol Macromol 2017; 97: 544-551.
- [75] Wang J and Ryu HK. The effects of *Momordica charantia* on obesity and lipid profiles of mice fed a high-fat diet. Nutr Res Pract 2015; 9(5): 489-495.
- [76] Senanayake GV, Maruyama M, Shibuya K, Sakono M, Fukuda N, Morishita T, Yukizaki C, Kawano M and Ohta H. The effects of bitter melon (*Momordica charantia*) on serum and liver triglyceride levels in rats. J Ethnopharmacol 2004; 91(2-3): 257-262.
- [77] Yama OE, Osinubi AA, Noronha CC and Okanlawon AO. Effect of methanolic seed extract of *Momordica charantia* on body weight and serum cholesterol level of male Sprague-Dawley rats. Nig Q J Hosp Med 2010; 20(4): 209-213.
- [78] He Q, Li Y, Li H, Zhang P, Zhang A, You L, Wu H, Xiao P and Liu J. Hypolipidemic and antioxidant potential of bitter melon (*Momordica charantia* L.) leaf in mice fed on a high-fat diet. Pak J Pharm Sci 2018; 31(5): 1837-1843.
- [79] Shih CC, Lin CH and Lin WL. Effects of *Momordica charantia* on insulin resistance and visceral obesity in mice on high-fat diet. Diabetes Res Clin Pract 2008; 81: 134-143.
- [80] Chao CY, Yin MC and Huang CJ. Wild bitter melon extract upregulates mRNA expression of PPARalpha, PPARgamma and their target genes in C57BL/6J mice. J Ethnopharmacol 2011; 135: 156-161.
- [81] Nerurkar PV, Lee YK, Motosue M, Adeli K and Nerurkar VR. *Momordica charantia* (bitter melon) reduces plasma apolipoprotein B-100 and increases hepatic insulin receptor substrate and phosphoinositide-3 kinase interactions. Br J Nutr 2008; 100: 751-759.
- [82] Klomann SD, Mueller AS, Pallauf J and Krawinkel MB. Antidiabetic effects of bitter melon extracts in insulin-resistant db/db mice. Br J Nutr 2010; 104: 1613-1620.
- [83] Wang ZQ, Zhang XH, Yu Y, Poulev A, Ribnicky D. Bioactives from bitter melon enhance insulin signaling and modulate acylcarnitine content in skeletal muscle in high-fat diet-fed mice. J Nutr Biochem 2011; 22: 1064-1073.
- [84] Sridhar MG, Vinayagamoorthi R, Arul Suyambunathan V, Bobby Z and Selvaraj N. Bitter melon (*Momordica charantia*) improves insulin sensitivity by increasing skeletal muscle insulin-stimulated IRS-1 tyrosine phosphorylation in high-fat-fed rats. Br J Nutr 2008; 99: 806-812.
- [85] Al-Snafi AE. Encyclopedia of the constituents and pharmacological effects of Iraqi medicinal plants. Rigi Publication, India, 2015.