Heliyon 9 (2023) e13493

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Review article

A comprehensive review on clinically proven medicinal plants in the treatment of overweight and obesity, with mechanistic insights

Md Abdul Aziz [a], Md Shalahuddin Millat [b], Tahmina Akter [b], Md Shahadat Hossain [c], Md Monirul Islam [a], Shahriar Mohsin [d], Farzana Ansari [e], Asma Kabir [c], Mohammad Nurul Amin [c,f,**], Mohammad Safiqul Islam [b,*]

[a] Department of Pharmacy, State University of Bangladesh, Dhaka, 1205, Bangladesh
[b] Department of Pharmacy, Noakhali Science and Technology University, Sonapur, 3814, Bangladesh
[c] Department of Pharmacy, Atish Dipankar University of Science and Technology, Dhaka, 1230, Bangladesh
[d] Center of Molecular Biotechnology, University of Bonn, 53115 Bonn, Germany
[e] Department of Biochemistry and Molecular Biology, Laboratory of Nutrition and Health Research, University of Dhaka, Dhaka, 1000, Bangladesh
[f] Pratyasha Health Biomedical Research Center, Dhaka, 1230, Bangladesh

ARTICLE INFO

Keywords:
Obesity
Weight loss
Green coffee
Phaseolus vulgaris
Yerba mate
Green tea
Gynostemma pentaphyllum
Cissus quadrangularis
Irvingia gabonensis

ABSTRACT

Background and objectives: Obesity has become a global health issue, more precisely, a pandemic throughout the present world due to its high prevalence in the recent era. Increased risk of morbidity and mortality in obese patients can be attributed to its association with the development of different life-threatening conditions. Plants are considered one of the most important sources of bioactive molecules which are used against a wide range of health disorders. This systematic review explores the efficacy as well as the safety profile of commonly used medicinal plants in the management of obesity that may help people to maintain a healthy weight.

Methods: This review is based on comprehensive literature searches from PubMed, Science Direct, Scopus, and Google Scholar databases using the keywords- "plants in obesity", "plants used in weight reduction" or keywords that are similar to those. Medicinal plants which have been clinically proven for their anti-obesity effect have only been selected for this study and attempts to investigate beneficial effects and adverse effects along with their mechanism of action have also been taken in this review.

Results: A significant reduction of weight in both human and other animals are exhibited by the extracts of Phaseolus vulgaris, green coffee, Yerba Mate, green tea, Gynostemma pentaphyllum, and the combination of Cissus quadrangularis/Irvingia gabonensis. All of those plant extracts seemed to work on different physiological pathways and none of those extracts showed any notable adverse effects in human or animal models.

Conclusion: Our review suggests that the discussed medicinal plants are effective in reducing the weight of obese patients without causing notable adverse reactions. Although further study is necessary to confirm their exact molecular mechanism and safety in human use.

* Corresponding author. Department of Pharmacy, Noakhali Science and Technology University, Sonapur, 3814, Bangladesh.
** Corresponding author. Department of Pharmacy, Atish Dipankar University of Science and Technology, Dhaka, 1230, Bangladesh.
E-mail addresses: amin.pharma07@gmail.com (M.N. Amin), research_safiq@yahoo.com, research_safiq@nstu.edu.bd (M.S. Islam).

https://doi.org/10.1016/j.heliyon.2023.e13493
Received 7 May 2022; Received in revised form 11 August 2022; Accepted 1 February 2023
Available online 4 February 2023

1. Introduction

Bodyweight that is higher than the normally considered healthy weight for a given height is postulated as overweight or obese i.e. a body mass index (BMI) of 30 kg/m^2 or more [1]. Obesity is a serious concern; it is associated with poorer mental outcomes, reduced quality of life, and is also the leading cause of death in the USA and all over the world [2]. Obesity is a rapidly growing public health problem that affects an increasing number of people worldwide because of its prevalence, costs, and health effects [3]. World Health Organization reckons that in 2016, more than 1.9 billion adults aged 18 years and older were overweight and of these over 650 million adults were obese. Moreover, in 2016, about 39% of adults aged 18 years or more (39% of men and 40% of women) were overweight. Overall, nearly 13% of the world's adult population were obese in 2016 (11% of men and 15% of women). The worldwide prevalence of obesity has almost tripled between 1975 and 2016, and most of the world's population lives in countries where the mortality rate of obese people is higher than that people of underweight [4]. It is estimated that 38% of the world's adult population will be overweight and another 20% will be obese by 2030 [5].

Overweight, obesity and associated health problems have engendered a marked economic effect on the worldwide healthcare system. Poor diet and a lack of physical activity have been observed as common causes of obesity [6]. Multiple factors lead to the development of obesity and overweight among which-genetic, cultural, and societal causes are considered most common. Other causes of obesity may include reduced physical activity, insomnia, food habits, medications, food advertisements, and impaired energy metabolism [7]. Obesity and overweight are considered chronic conditions and contribute to many preventable illnesses (e.g., diabetes, coronary artery disease, and high blood pressure) [8]. Overweight is unfortunate for more reasons than just poor physical appearance; it increases the risk of hypertension, type II diabetes, heart disease, stroke, arthritis, elevated circulating cholesterol, cancer, serious hormonal imbalances in women that can lead to infertility, chronic renal disease, worse pregnancy outcome, and even Alzheimer's disease which is commonly observed in adults [9,10].

Obesity may primarily be regarded as a disorder of lipid metabolism and the enzymes involved in this process could be selectively targeted to develop numerous anti-obesity drugs [11]. There are many experiments conducted to date to figure out the appropriate therapeutics for this critical public problem of obesity and a plethora of promising anti-obesity drugs are developed each year with demonstrable efficacy in cell lines and animal models. However, only a few of these reagents enter and sustain in the market because most of them are associated with serious side effects [12]. Strategies adopted to lose body fat typically involve a combination of dietary changes that limit caloric intake, increased physical activity, behavioral therapy, pharmacotherapy, and, in extreme cases, surgery. Although the availability and popularity of natural dietary supplements have risen significantly in recent years intended to help with weight loss, their therapeutic effectiveness remains uncertain in many cases [10]. The potential of natural products for the treatment of

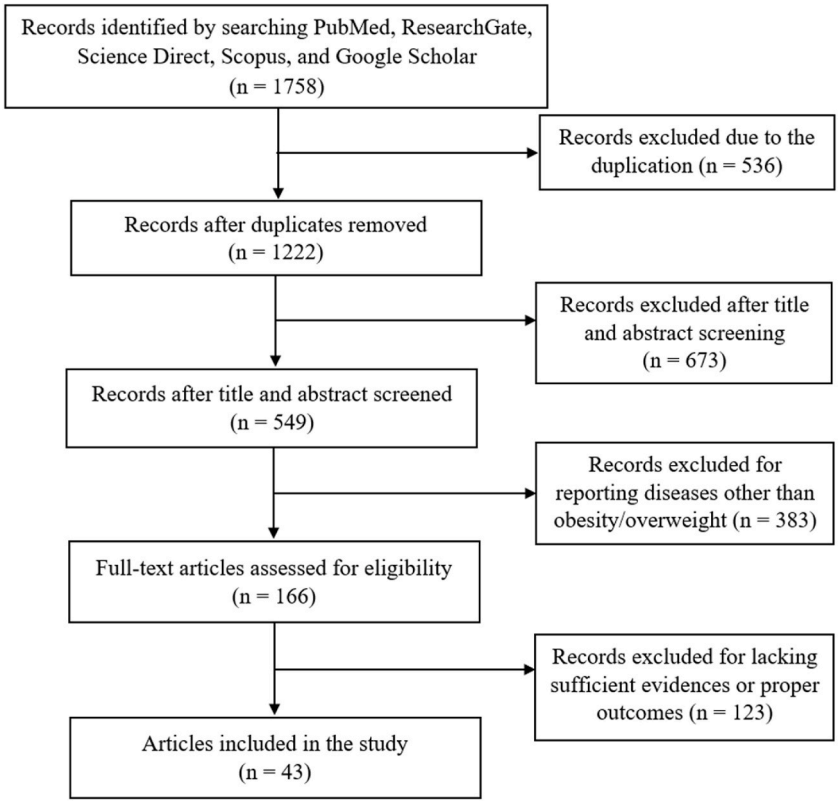

Fig. 1. Flow diagram of literature search and selection.

obesity is still mostly unexplored and it might be an excellent alternative strategy for the development of safe and effective drugs to reduce obesity and overweight [11].

Due to the high global prevalence of obesity and its association with several chronic diseases, the development of safe and effective methods of bodyweight management is crucial. The use of medicinal plants arises from ethnobotanical and ethnopharmacological approaches that test their therapeutic use in treating and preventing numerous diseases. Plant-based medications may contribute to satiety, increased metabolism, and accelerated weight loss [13]. Therefore, through our present article, we will report the pre-clinical and clinical effects of the following medicinal plants i.e. white bean extract of *Phaseolus vulgaris*, green coffee bean extract, Yerba Mate, green tea extract, *Gynostemma pentaphyllum* extract, and the combination of *Cissus quadrangularis/Irvingia gabonensis* in weight loss.

2. Methodology

For this review, we collected our desired pieces of literature by searching comprehensively at various databases, including PubMed, ResearchGate, Science Direct, Scopus, and Google Scholar. We used the following keywords to undertake this review: obesity, body weight, overweight, body fat, BMI (body mass index), anthropometric measures, medicinal plants, white bean extract, *Phaseolus vulgaris*, kidney bean, green coffee bean extract, Yerba Mate, green tea extract, *Gynostemma pentaphyllum* extract, triglycerides, cholesterol, body fat, *Cissus quadrangularis*, *Irvingia gabonensis*, *Cissus quadrangularis/Irvingia gabonensis* combination, α-amylase inhibitor, adipocytes, safety, etc. In addition, during our initial search, we did not take any special considerations regarding the patient's age, gender, status, or geographic area to exclude any kind of bias. The flow diagram of literature search and selection is presented in Fig. 1.

3. Medicinal plants for weight loss

A comprehensive overview of medicinal plants for the treatment of overweight and obesity is described in Table 1.

3.1. White bean extract of Phaseolus vulgaris

The white bean extract is a water extract of a common white bean, *Phaseolus vulgaris* which appears to be a safe and effective aid to consider in weight loss/maintenance programs [10]. A test dietary formula containing 445 mg Phase 2 *Phaseolus vulgaris* extract showed more efficacy in reducing body weight and body fat mass than placebo when taken daily concurrently with a carbohydrate-rich portion of a 2000- to 2200-calorie diet by overweight human subjects [10]. *Phaseolus vulgaris* extract has been shown in vitro to inhibit the activity of α-amylase- a salivary and pancreatic enzyme that converts complex carbohydrates into oligosaccharides- and various other intestinal enzymes that helps in digestion [14] (e.g. maltase, lactase, etc. that convert these oligosaccharides to monosaccharides: the absorbable form of carbohydrates) and therefore may help promote weight loss by interfering with the digestion of complex carbohydrates to simple, absorbable sugars, potentially reducing carbohydrate-derived calories. In addition, through its lowering effect on carbohydrate absorption, it affects the insulin system and possibly leads to a lesser accumulation of fat, glucose, and other monosaccharides produced through this mechanism are then transported to the liver via the hepatic portal vein [10].

Another exploratory analysis revealed that consuming 1000 mg of a proprietary fractioned white bean extract or an identical placebo twice a day before meals in conjunction with a multi-component traditional weight control program, including diet, exercise, and behavioral intervention, can help to reduce a significant amount of weight in a relatively short period by inhibiting the activity of α-amylase [15]. The results also showed that, when the groups were stratified by their total number of carbohydrate intake, the tertile eating the maximum amount of carbohydrate experienced significant differences in both weight loss (8.7 lbs vs. 1.7 lbs, $P = 0.0412$) and waist size (3.3 in vs. 1.3 in, $P = 0.0100$) when using the white bean extract [16].

A further meta-analysis by Udani *et al.* found a significant effect of Phase 2 *Phaseolus vulgaris* supplementation on body weight and body fat [17]. When carbohydrates are taken, they must be converted into monosaccharides for absorption by the body. The transformation of carbohydrates into small monosaccharides is dependent on the enzymatic process. Two major catalytic enzymes, namely amylase and glucosidase, play a key role in this process. Amylase enzymes break down complex carbohydrates (starch) into oligosaccharides that are further converted to monosaccharides by the glucosidase enzymes. Common beans of this plant generally contain inhibitors of amylase enzyme in three common forms, including alpha-AIL, alpha-A1, and alpha-A12. These amylase inhibitors effectively reduce the effect of amylase and help to reduce body weight [17]. Fig. 2 represents the possible mechanism of weight loss by white kidney beans.

3.2. Green coffee bean extract

The raw or unroasted beans (seeds) of Coffee fruits or coffee berries/cherries are the sources of "Green Coffee" [18]. The use of green coffee bean extract (GCBE) combined with an energy-restricted diet is an effective and inexpensive method to control/prevent obesity and related complications in humans. A significantly higher reduction in the body weight, body mass indices (BMI), fat mass indices (FMI), and waist-to-hip circumference ratio have been found in the intervention group receiving 400 mg GCBE for 8 weeks than in the control group (placebo) in a clinical study [19].

Moreover, total cholesterol levels, LDL, leptin, and free fatty acids have also been found in the plasma of the subjects of the intervention group ($p < 0.05$) [20]. These effects of GCBE can be attributed to the presence of chlorogenic acid (CGA) and its related compounds that have an impact on the body composition and lipid profile. An increase in uncoupling protein (UCP) expression in

Table 1
Overview of medicinal plants for the treatment of overweight and obesity.

Ingredients Plants/ Herbs	Study Design	Daily Dosage and Frequency	Treatment Length	Study Population	Female/ Male	Age (y) at Enrollment (Intervention/ Placebo)	BMI (kg/m^{-2}) at Enrollment (Intervention/ Placebo)	Main Outcomes	Adverse Events	References
***Phaseolus vulgaris* extract**	Randomized, double-blind, placebo-controlled clinical trial.	The test product containing *Phaseolus vulgaris* extract and the placebo were taken one tablet (445 mg) per day before a main meal rich in carbohydrates.	30 days	60	42/17	33.7 ± 1.6/34.2 ± 1.6	25.9 ± 2.0/26.0 ± 2.3	*Phaseolus vulgaris* extract produces significant decrements in body weight and suggest decrements in fat mass in the face of maintained lean body mass.	No significant adverse effects were reported.	[10]
Green coffee bean extract (GCBE)	Randomized, double-blind, placebo-controlled clinical trial.	The intervention group received 400 mg green coffee bean extract and control group received placebo.	8 weeks	64	64/0	20–45	31.58 ± 4.37/ 32.07 ± 4.96	Green coffee bean extract combined with an energy-restricted diet affects fat accumulation and lipid metabolism, and is thus an inexpensive method for weight control in obese people.	No significant adverse effects were reported.	[19]
Yerba Mate (the dried leaves of the plant, *Ilex paraguariensis*)	Randomized, double-blind, placebo-controlled clinical trial.	Subjects take three capsules (oral supplements of Yerba Mate capsules) per day, 1000 mg per meal (before breakfast, lunch and dinner).	12 weeks	30	15/15	41.5 ± 11.6/ 44.9 ± 9.6	28.65 ± 2.09/ 27.31 ± 3.10	Yerba Mate supplementation decreased body fat mass, percent body fat and WHR. Yerba Mate was a potent anti-obesity reagent that did not produce significant adverse effects.	Yerba Mate supplementation did not cause any adverse effects.	[28]
Green tea extract (GTE)	Randomized, double-blind, placebo-controlled clinical trial.	500 mg of pure microcrystalline cellulose was capsulized as the placebo, as well as the decaffeinated GTE capsulized 500 mg each. The frequency was three times daily after meals.	12 weeks	102	102/0	44.10 ± 10.9/ 44.9 ± 11.9	31.0 ± 3.8/30.0 ± 3.5	A significant weight loss, reduced waist circumference, and a consistent decrease in total cholesterol and LDL plasma levels without any side effects or adverse effects in women with central obesity.	No major adverse events noted. Only three subjects had mild abdominal discomfort.	[46]
***Gynostemma pentaphyllum* extract (Actiponin)**	Randomized, double-blind, placebo-controlled clinical trial.	All participants were divided into two groups (n = 40 each) given either actiponin (450 mg per day) or a placebo (450 mg per day).	12 weeks	80	48/32	40.10 ± 1.53/ 40.05 ± 1.83	27.80 ± 0.19/ 27.55 ± 0.20	The present study revealed that actiponin is a potent antiobesity reagent that does not produce any significant adverse effects.	Actiponin supplementation did not cause any adverse effects.	[40]
***Cissus quadrangularis*/ *Irvingia gabonensis* combination**	Randomized, double-blind, placebo-controlled clinical trial.	Capsules containing 150 mg *Cissus quadrangularis* and 250 mg *Cissus quadrangularis/Irvingia gabonensis* were administered twice daily before meals.	10 weeks	72	39/33	29.3	>26	Compared to the placebo group, the two active groups showed a statistically significant difference on all six variables by week 10.	Adverse effects included headache, lack of sleep, and gas.	[47]

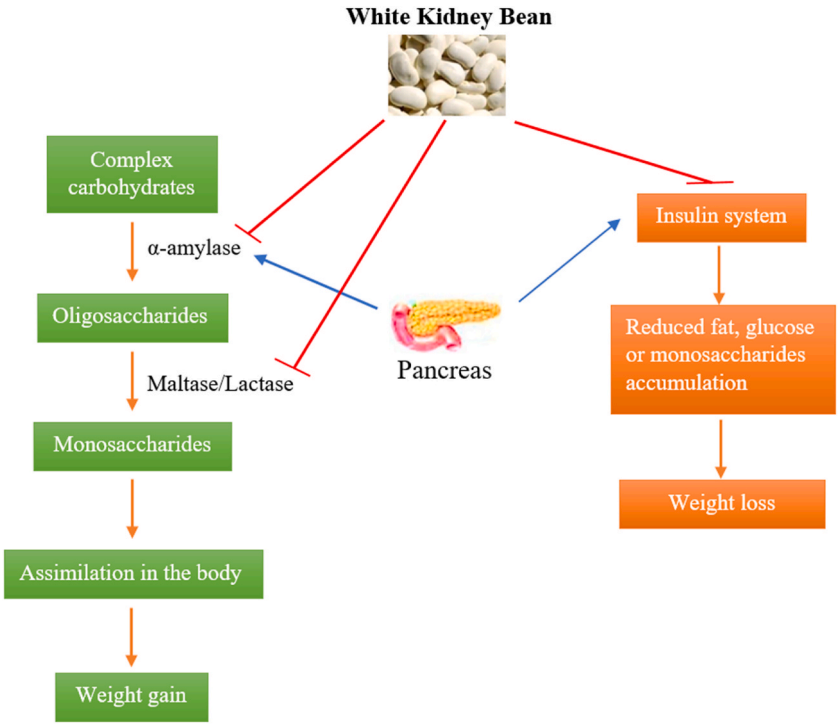

Fig. 2. Mechanism of weight loss by white kidney bean.

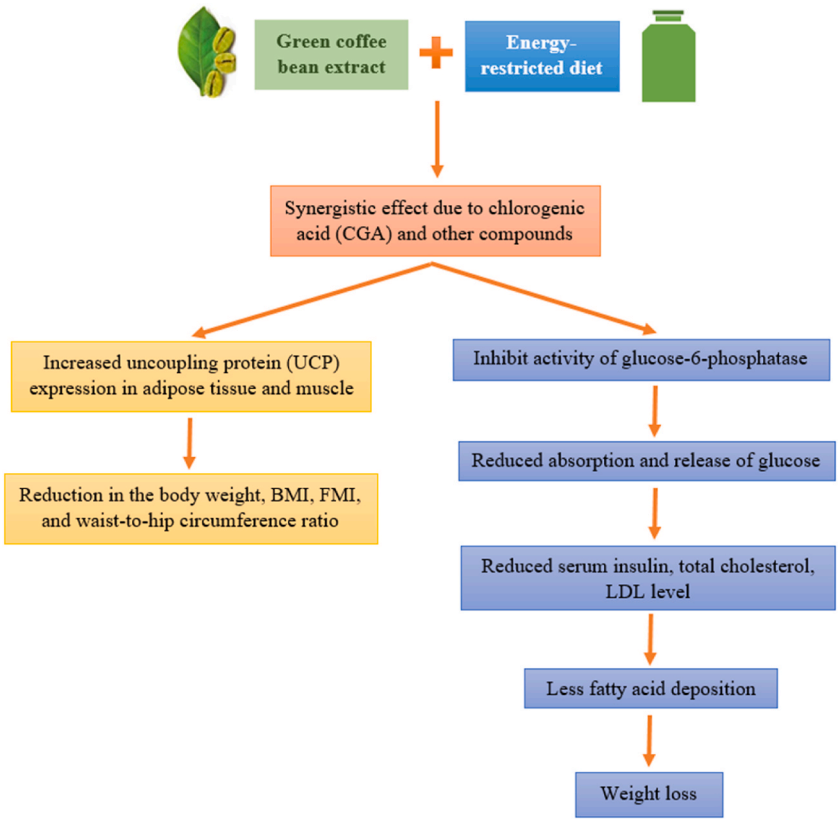

Fig. 3. Mechanism of green coffee bean extract in body weight loss. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

adipose tissue and muscle is also associated with the synergistic effect of GCBE and an energy-restricted diet [19]. A weight loss of more than 8 kg was found after the consumption of 700 mg of GCBE for 6 weeks, which accounted for more than 10% of the body-weight [21]. Another study stated that CGA inhibits the activity of glucose-6-phosphatase by inhibiting the absorption and release of glucose into circulation, which ultimately reduces the serum insulin level. This mechanism leads to less fatty acid deposition resulting in weight loss [22].

A reduced level of leptin (adipocytokine) after CGA intake in obese mice inhibits the activities of fatty acid synthase, 3-hydroxy-3-methylglutaryl CoA reductase, and acyl CoA cholesterol acyltransferase enzymes by inducing body fat loss and increasing adiponectin concentrations [23]. CGA inhibits the principle cholesterol synthesis enzyme (β-hydroxy-β-methyl glutaric acyl-coenzyme A reductase) and strengthens the activity of fatty acid oxidation enzyme (carnitine palmitoyltransferase), causing the anti-hyperlipidemic effect of CGA in rats by reducing total cholesterol and LDL after GCBE intake [24]. CGA also reduces plasma total and LDL cholesterol levels through PPAR-α mRNA regulation in animal models [25,26]. The mechanism of green coffee bean extract in body weight loss is illustrated in Fig. 3.

3.3. Yerba Mate

Yerba Mate is collected from the dried leaves of the plant *Ilex paraguariensis*, which may be useful in reducing body weight and fat. Extracts of Yerba Mate leaf contain components such as chlorogenic acid (mono caffeoylquinic and di caffeoylquinic acids), hydroxyl cinnamic acids (caffeic acid, quinic acid), and several triterpenoid saponins saponins [27]. Yerba Mate may suppress body weight gain and accumulation of visceral fat and reduces serum levels of cholesterol, triglycerides, LDL cholesterol, etc. In a clinical trial for obese Korean people, subjects who completed 12 weeks of clinical treatment with Yerba Mate (3 g/day) showed decreased waist-to-hip ratio (WHR), body fat mass, percent body fat, and trends in declined visceral fat and visceral/subcutaneous fat [28]. Moreover, it can modulate signaling pathways, induce intestinal propulsion, block glycation, inhibit oxidative stress, and has inflammatory action [28]. Another 6-week clinical trial on the Korean population with green mate powder extract (1200 mg/day) exhibited a significant reduction in body fat mass and percent body fat without any adverse effects [29].

In vitro and in vivo studies containing chlorogenic acid 35 mg/g of Yerba Mate have demonstrated its inhibitory effect on adipogenesis by reducing the expression of genes that regulates adipogenesis both in 3T3-L1 cells and in the mouse model of HFD-induced obesity [30]. The differentiation of new fat cells is known as adipogenesis. It is believed that adipose tissue is the largest reservoir of body energy. Adipose tissue consists of adipocytes that are associated with the synthesis, storage, and mobilization of fatty acids according to the needs of the body. Preadipocyte's differentiation into adipocytes is correlated with an enhanced number of oil red O-positive cells as a result of the accumulation of lipids. Yerba Mate reduces preadipocyte differentiation and decreases the accumulation of lipids in adipocytes in a dose-dependent manner ($p < 0.05$) [31]. After feeding Yerba Mate for 4-weeks, a decrease in total cholesterol, leptin levels, and blood glucose levels was found in animals [32]. Based on these pieces of evidence, Yerba Mate may be said to be a potential alternative for controlling the accumulation of body fat and weight, as shown in Fig. 4.

3.4. Green tea extract

Green tea, obtained from the extract of *Camellia sinensis*, is one of the most popular drinks throughout the world and has been

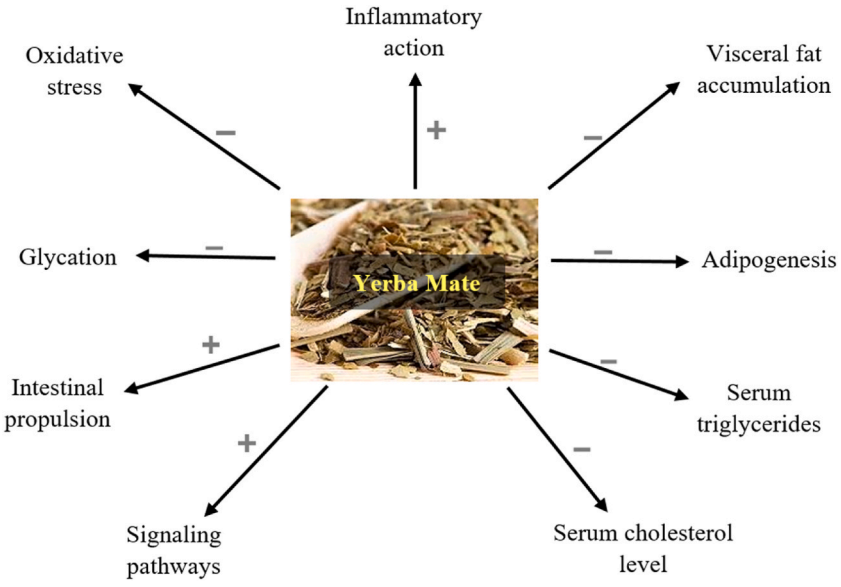

Fig. 4. Different pathways by which Yerba Mate reduces body weight (+ indicates increase/stimulation and – indicates decrease/inhibition).

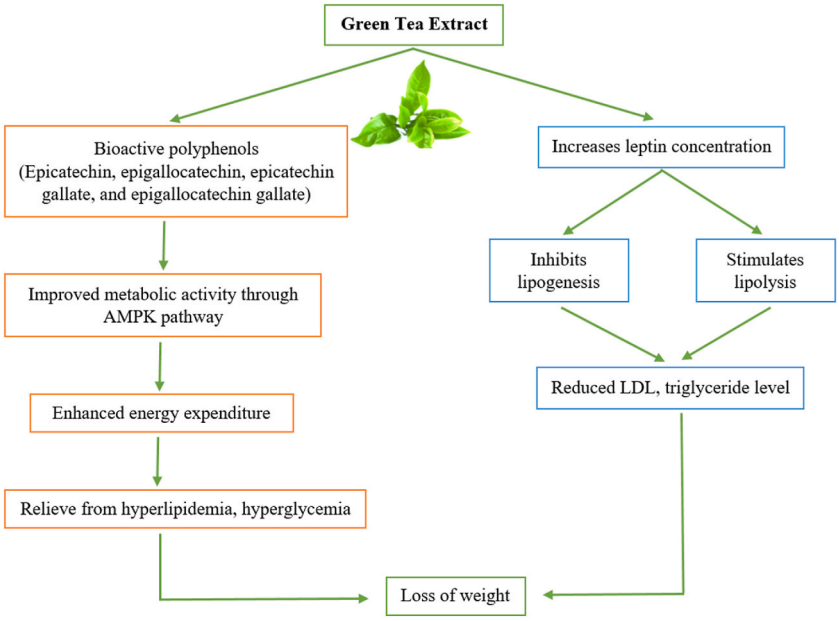

Fig. 5. Pathways by which green tea extract help to loss body weight. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

studied extensively for its beneficial effects on controlling obesity for a long time. Particularly, it has been shown to enhance energy expenditure and rate of metabolism and also has the ability to burn fats and relieve hyperlipidemia and hyperglycemia [33,34]. A significant reduction in LDL-cholesterol and triglyceride levels was found in Taiwanese women after a clinical trial of 12 weeks [34]. Another study stated that green tea extract (GTE) reduces LDL in overweight and obese Taiwanese women after 6-weeks of treatment by increasing leptin concentration, which can inhibit lipogenesis and stimulate lipolysis in the body fat cells [33,35].

Green tea extracts contain polyphenols as the main constitutions that are responsible for anti-lipid effects. Among all the bioactive polyphenols, the four main flavonoids, including epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG), are the catechins. The presence of catechin polyphenols is attributed to the efficacy of GTE, and it is assumed that EGCG might be responsible for the numerous health benefits of green tea [36]. According to Rocha et al., GTE improves the metabolic dysfunction of adipose tissue through the AMP-activated protein kinase (AMPK)-regulated pathway [37]. Another study revealed that EGCG inhibits the catechol-*o*-methyltransferase (COMT) enzyme that is responsible for the degradation of norepinephrine (NE) which ultimately results in increased lipolysis and fat oxidation [38]. The possible pathways by which green tea extract may help to lose body weight are depicted in Fig. 5.

3.5. *Gynostemma pentaphyllum extract (actiponin)*

Gynostemma pentaphyllum (*G. pentaphyllum,* GP), is a herbaceous vine, a member of the Cucurbitaceae family, also known as the cucumber or gourd family. Extracted saponins or total *G. pentaphyllum* extracts (GPE) exert a variety of beneficial effects such as reducing blood glucose and cholesterol levels, strengthening the immune system, and preventing cancer development [39]. A clinical study on Korean people shows-participants who completed a 12-week treatment with actiponin (450 mg/day) showed statistically significant reductions in abdominal fat (total abdominal fat area) and anthropometric parameters such as weight, BMI, body fat mass, % body fat, and waist circumference without the requirement of any major changes in food habit or lifestyle compared to the placebo group [40].

In vitro studies revealed that damulin A and B, two dammarane-type saponins derived from the leaves of GP, can increase AMPK and acetyl-CoA carboxylase (ACC) phosphorylation mediated stimulation of β-oxidation [40,41]. AMPK activation through 5-aminoimidazole-4-carboxamide1-b-D-ribofuranoside (AICAR) inhibits adipogenesis by downregulating the expression of key transcription factors such as peroxisome proliferator-activated receptor c (PPARc) and CCAAT/enhancer-binding protein (CEBP)1a as well as lipogenic factors including fatty acid-binding protein 4 (FABP 4) and lipoprotein lipase [42]. Additionally, AMPK activation directly inactivates ACC through Ser79 phosphorylation, leading to decreased fat synthesis by reducing the production of malonyl-CoA from acetyl-CoA [40].

Wang et al. reported that GPE could effectively alter lipid metabolism and exert its anti-hyperlipidemic effect by increasing the level of phosphatidylcholine and decreasing the level of trimethylamine N-oxide (TMAO) in rats when supplied a dose of 120 mg/kg in a 4-weeks trial [43]. Another preclinical study in the mice model suggested that the supplementation containing a high-dose GPE (0.01%) in the diet reduces the level of blood glucose by changing the activities of metabolic enzymes in the liver [44]. A dietary

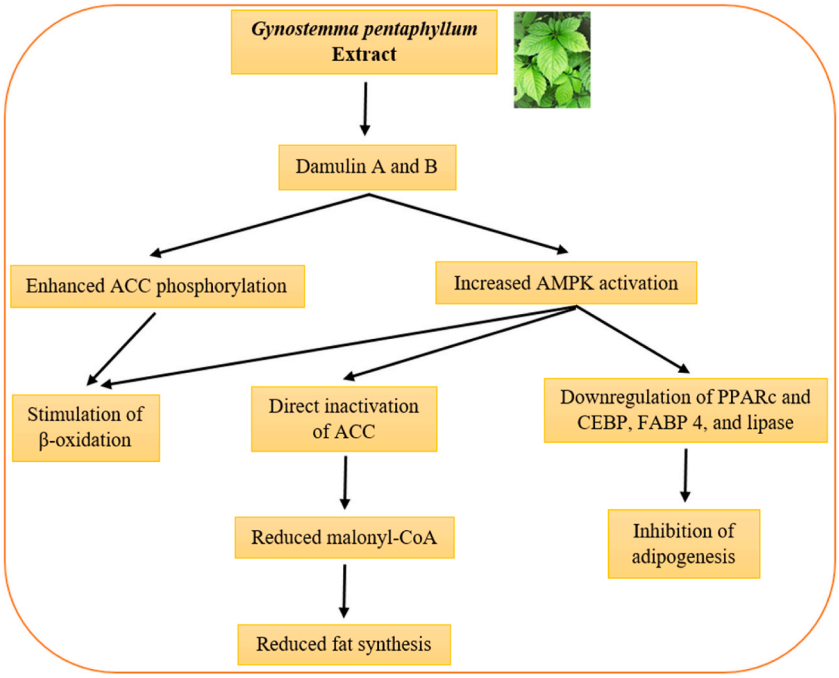

Fig. 6. Mechanism of action of *Gynostemma pentaphyllum* extract in weight loss.

formula containing 250 mg/kg GPE showed reduced triglyceride, total cholesterol, and LDL levels in the Zucker fatty rats by 33%, 13%, and 33%, respectively, after 4-days of a 5-weeks preclinical trial. It was observed that obese Zucker fatty rats experienced hyperlipidemic conditions due to the hypersecretion of very low-density lipoprotein (VLDL). Consequently, triglyceride-rich lipoproteins were removed from the blood circulation. GPE also decreased triglyceride levels by increasing the activity of endothelial lipoprotein lipase (LPL) enzyme by degrading triglycerides as well as decreasing hepatic VLDL production [45]. The mechanism of action of *Gynostemma pentaphyllum* extract in weight loss is graphically represented in Fig. 6.

3.6. Combination of Cissus quadrangularis/Irvingia gabonensis

Cissus quadrangularis (CQ), a succulent vine, has been used for more than a century for its role in fighting obesity and symptoms of metabolic syndrome throughout the world. The efficacy of CQ has been linked to its unique chemical constituents, including novel flavonoids, indanes, phytosterols, and keto-steroids, which appear to be efficient for inhibiting certain enzymes like α-amylase, glucosidase, and lipase leading to weight loss via decreased oxidative stress, dietary fat and carbohydrate [47–50]. The use of a CQ formulation of 1028 mg/day (which also contains green tea, soy, chromium, selenium, and B-vitamins) for 8 weeks has been proven to be effective in lowering body weight, % body fat, BMI, and especially waist circumference of obese and overweight patients [49].

A further study by Oben et al. explained that the use of CORE (standardized extract of CQ antioxidant, 1028 mg/day) and CQR-300 (standardized extract of CQ without antioxidant, 300 mg/day) during the study period of 6 weeks brought about a significant reduction in the weight and BMI of obese patients. This loss in BMI was the result of an increased level of HDL cholesterol in the circulation. It is already established that HDL cholesterol and BMI have an inverse relationship. CQ utilizes this mechanism to impart its anti-obesity activity by reducing overweight [48].

Irvingia gabonensis (IG), on the other hand, belongs to the Irvingiaceae family, containing 50% fat, 26.4% total carbohydrate, 2.3% ash, 7.5% crude protein, and 14% fiber [51]. The high soluble fiber content of IG lowers plasma cholesterol, triglycerides, and glucose concentrations. Moreover, IG seeds possess hypocholesterolemic, hypoglycemic, anti-amylase, anti-lipase, and anti-oxidant properties [47]. IG formulation (350 mg three times a day) taken for one month caused a significant decrease in total cholesterol, LDL-cholesterol, triglycerides, and an increase in HDL cholesterol. IG seeds have higher fiber contents that bind to bile acids in the gut and help to release bile acids out of the body. This process helps to convert more blood cholesterol into bile acids leading to the lowering of cholesterol and circulating lipids [52]. IG supplements exhibited a significant weight loss (up to 4–12 kg) in overweight and obese subjects over 10 weeks, with some reported adverse effects. IG also reduced a significant amount of % body fat ($p < 0.05$) and waist circumference ($p < 0.01$) in obese patients. Moreover, it was reported to bring improvements in fasting blood glucose, total cholesterol, and LDL cholesterol level [53]. The inhibitory effects of IGOB131 on murine 3T3-L1 adipocytes showed a reduction in intracellular triglyceride levels and G3PDH activity, indicating that IGOB131 plays an important role in the control of adipogenesis [54].

Numerous investigations have been carried out by researchers and therapy formulation experts to increase the effectiveness of medicinal plants such as *Cissus quadrangularis* and *Irvingia gabonensis* as natural supplements in reducing body weight. A clinical study

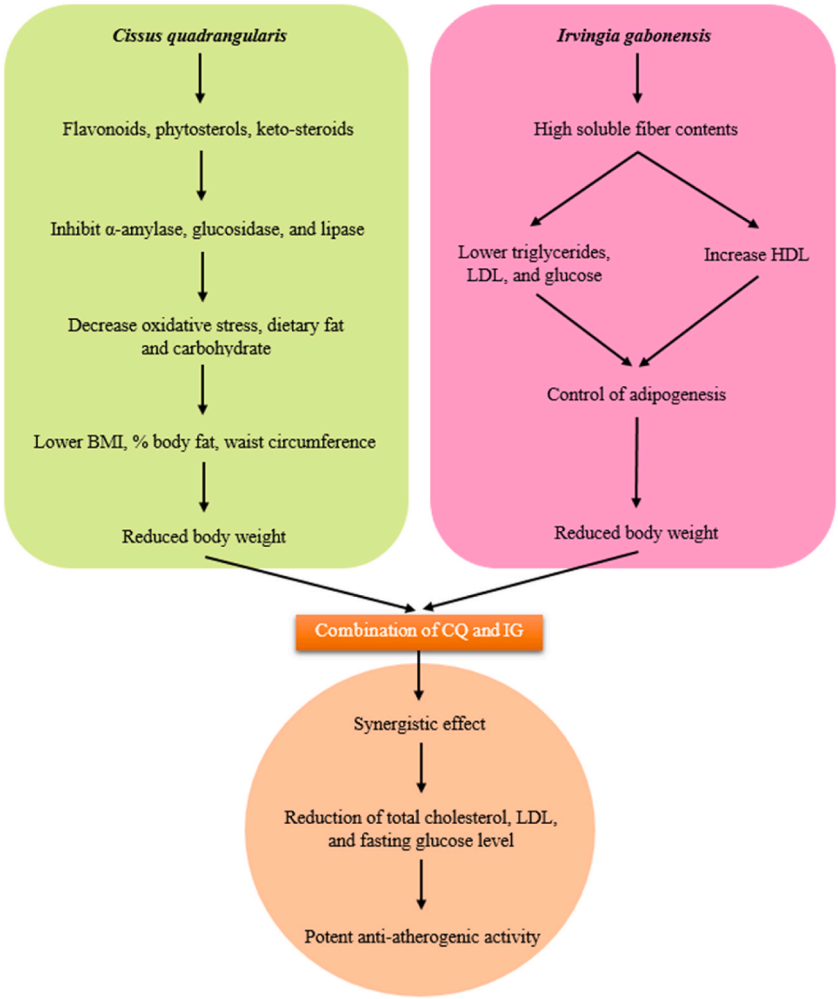

Fig. 7. Combination of *Cissus quadrangularis* and *Irvingia gabonensis* in weight loss.

by Oben et al. revealed that-when an active formulation containing both IG and CQ (150 mg CQ and 250 mg CQ-IG) was administered twice daily for 10 weeks, it showed a synergistic effect on the reduction of total cholesterol, LDL cholesterol, and fasting blood glucose level comparing to CQ alone, thus proving the combination as a better anti-atherogenic agent [47,55]. The combined effect of *Cissus quadrangularis* and *Irvingia gabonensis* in weight loss is schematically represented in Fig. 7.

4. Conclusion and future perspectives

Phytotherapeutic approaches have been used as an important scientific tool over the years for the management of obesity and overweight-related complications. Due to their safety, efficacy, availability, and inexpensiveness, plants have been extensively studied in vitro and in vivo throughout the world to reduce excessive body weight and body fat. Among the studies discussed, most of them narrated phenolic compounds of the plant species to represent the greatest evidence of weight loss and raise the possibility of a new application of these compounds as a health supplement. This literature review has been conducted to assess the clinical pieces of evidence for the advancement of obesity management based on previous studies on medicinal plants. According to these available clinical shreds of evidence, it can be concluded that the discussed medicinal plants have anti-obesity effects and can be safely used for weight reduction without any unwanted effects.

Modern pharmacological science has witnessed rapid development and substantial progress with the time that has enabled researchers easily identify the natural plants with anti-obesity effects and reduce their unwanted effects. However, more clinical trials and standardized procedures are required to confirm their molecular mechanism of anti-obesity effect as well as to ensure the safety and efficacy of these herbal medicines for human consumption. Besides, significant improvement is required to confirm safe, effective, and standardized medicinal agents from natural sources. Moreover, the obesity management procedures should have the prospect of a high cost-benefit ratio for obese patients and also the ability to balance the epidemiological profile of the disease among the populace. Besides, along with the treatments, changing the lifestyle, including food habits, physical exercise, etc., could be the best option for

treating obesity and related complications.

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interest's statement

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

Acknowledgements

The authors express their gratitude to 'Pratyasha Health Biomedical Research Center, Bangladesh' for their cordial cooperation throughout this project work.

References

[1] F. Bianchini, R. Kaaks, H. Vainio, Overweight, obesity, and cancer risk, Lancet Oncol. 3 (2002) 565–574.
[2] M.F. Hossain, M. Rashid, T. Burniston, M. Ahmed, W. Wu, K.A. Kataye, et al., J. Obes. Weight-Loss Medicat. 5 (2019).
[3] J.C. McLaughlin, K. Hamilton, R. Kipping, Epidemiology of adult overweight recording and management by UK GPs: a systematic review, Br. J. Gen. Pract. 67 (2017) e676–e683.
[4] Y. Wu, Overweight and Obesity in China, 2006.
[5] A. Hruby, F.B. Hu, The epidemiology of obesity: a big picture, Pharmacoeconomics 33 (2015) 673–689.
[6] M.R.M. Umstattd, C.K. Perry, J.C. Sumrall, M.S. Patterson, S.M. Walsh, S.C. Clendennen, et al., Physical activity-related policy and environmental strategies to prevent obesity in rural communities: a systematic review of the literature, 2002-2013, Prev. Chronic Dis. 13 (2016) E03.
[7] G.P. August, S. Caprio, I. Fennoy, M. Freemark, F.R. Kaufman, R.H. Lustig, et al., Prevention and treatment of pediatric obesity: an endocrine society clinical practice guideline based on expert opinion, J. Clin. Endocrinol. Metab. 93 (2008) 4576–4599.
[8] M.J. Ormsbee, S.R. Rawal, D.A. Baur, A.W. Kinsey, M.L. Elam, M.T. Spicer, et al., The effects of a multi-ingredient dietary supplement on body composition, adipokines, blood lipids, and metabolic health in overweight and obese men and women: a randomized controlled trial, J. Int. Soc. Sports Nutr. 11 (2014) 37.
[9] M. Agha, R. Agha, The rising prevalence of obesity: part A: impact on public health, Int. J. Surgery Oncol. 2 (2017) e17.
[10] L. Celleno, M.V. Tolaini, A. D'Amore, N.V. Perricone, H.G. Preuss, A dietary supplement containing standardized Phaseolus vulgaris extract influences body composition of overweight men and women, Int. J. Med. Sci. 4 (2007) 45.
[11] D. Iswantini, R.F. Silitonga, E. Martatilofa, L.K. Darusman, Zingiber cassumunar, Guazuma ulmifolia, and Murraya paniculata extracts as antiobesity: in vitro inhibitory effect on pancreatic lipase activity, Hayati J. Biosci. 18 (2011) 6–10.
[12] H.S. Lee, S.-M. Lim, J.I. Jung, S.M. Kim, J.K. Lee, Y.H. Kim, et al., Gynostemma pentaphyllum extract ameliorates high-fat diet-induced obesity in C57BL/6N mice by upregulating SIRT1, Nutrients 11 (2019) 2475.
[13] L.M. de Freitas Junior, E.B. de Almeida Jr., Medicinal plants for the treatment of obesity: ethnopharmacological approach and chemical and biological studies, Am. J. Transl. Res. 9 (2017) 2050.
[14] O.L. Franco, D.J. Rigden, F.R. Melo, M.F. Grossi-de-Sá, Plant α-amylase inhibitors and their interaction with insect α-amylases: structure, function and potential for crop protection, Eur. J. Biochem. 269 (2002) 397–412.
[15] J. Udani, B.B. Singh, Blocking carbohydrate absorption and weight loss: a clinical trial using a proprietary fractionated white bean extract, Alternative Ther. Health Med. 13 (2007) 32–39.
[16] J. Udani, M. Hardy, D.C. Madsen, Blocking carbohydrate absorption and weight loss: a clinical trial using Phase 2^{TM} brand proprietary fractionated white bean extract, Alternative Med. Rev. 9 (2004) 63–69.
[17] M.L. Barrett, J.K. Udani, A proprietary alpha-amylase inhibitor from white bean (Phaseolus vulgaris): a review of clinical studies on weight loss and glycemic control, Nutr. J. 10 (2011) 24.
[18] P. Esquivel, V.M. Jiménez, Functional properties of coffee and coffee by-products, Food Res. Int. 46 (2012) 488–495.
[19] F. Haidari, M. Samadi, M. Mohammadshahi, M.T. Jalali, K.A. Engali, Energy restriction combined with green coffee bean extract affects serum adipocytokines and the body composition in obese women, Asia Pac. J. Clin. Nutr. 26 (2017) 1048.
[20] K. Diepvens, E.M.R. Kovacs, N. Vogels, M.S. Westerterp-Plantenga, Metabolic effects of green tea and of phases of weight loss, Physiol. Behav. 87 (2006) 185–191.
[21] J.A. Vinson, B.R. Burnham, M.V. Nagendran, Randomized, double-blind, placebo-controlled, linear dose, crossover study to evaluate the efficacy and safety of a green coffee bean extract in overweight subjects, Diabetes, Metab. Syndrome Obes. Targets Ther. 5 (2012) 21.
[22] O. Dellalibera, B. Lemaire, S. Lafay, Svetol, green coffee extract, induces weight loss and increases the lean to fat mass ratio in volunteers with overweight problem, Phytothérapie 4 (2006) 194–197.
[23] A.-S. Cho, S.-M. Jeon, M.-J. Kim, J. Yeo, K.-I. Seo, M.-S. Choi, et al., Chlorogenic acid exhibits anti-obesity property and improves lipid metabolism in high-fat diet-induced-obese mice, Food Chem. Toxicol. 48 (2010) 937–943.
[24] H. Shimoda, E. Seki, M. Aitani, Inhibitory effect of green coffee bean extract on fat accumulation and body weight gain in mice, BMC Compl. Alternative Med. 6 (2006) 9.
[25] C. Wan, C.N. Wong, W. Pin, M.H. Wong, C. Kwok, R.Y. Chan, et al., Chlorogenic acid exhibits cholesterol lowering and fatty liver attenuating properties by up-regulating the gene expression of PPAR-α in hypercholesterolemic rats induced with a high-cholesterol diet, Phyther. Res. 27 (2013) 545–551.

[26] L.I. Shu-Yuan, C.-Q. Chang, M.A. Fu-Ying, Y.U. Chang-Long, Modulating effects of chlorogenic acid on lipids and glucose metabolism and expression of hepatic peroxisome proliferator-activated receptor-α in golden hamsters fed on high fat diet, Biomed. Environ. Sci. 22 (2009) 122–129.
[27] N. Bracesco, A.G. Sanchez, V. Contreras, T. Menini, A. Gugliucci, Recent advances on Ilex paraguariensis research: minireview, J. Ethnopharmacol. 136 (2011) 378–384.
[28] S.-Y. Kim, M.-R. Oh, M.-G. Kim, H.-J. Chae, S.-W. Chae, Anti-obesity effects of yerba mate (Ilex Paraguariensis): a randomized, double-blind, placebo-controlled clinical trial, BMC Compl. Alternative Med. 15 (2015) 338.
[29] H.J. Kim, J. Ko, C. Storni, H.J. Song, Y.G. Cho, Effect of green mate in overweight volunteers: a randomized placebo-controlled human study, J. Funct.Foods 4 (2012) 287–293.
[30] D.P. Arçari, J.C. Santos, A. Gambero, M.L. Ribeiro, The in vitro and in vivo effects of yerba mate (Ilex paraguariensis) extract on adipogenesis, Food Chem. 141 (2013) 809–815.
[31] G. Gosmann, A.G. Barlette, T. Dhamer, D.P. Arçari, J.C. Santos, E.R. de Camargo, et al., Phenolic compounds from mate (Ilex paraguariensis) inhibit adipogenesis in 3T3-L1 preadipocytes, Plant Foods Hum. Nutr. 67 (2012) 156–161.
[32] Y.-H. Yang, D. Park, G. Yang, S.H. Lee, D.K. Bae, J. Kyung, et al., Anti-Helicobacter pylori effects of IgY from egg york of immunized hens, Lab. Anim. Res. 28 (2012) 55–60.
[33] L.-H. Huang, C.-Y. Liu, L.-Y. Wang, C.-J. Huang, C.-H. Hsu, Effects of green tea extract on overweight and obese women with high levels of low density-lipoprotein-cholesterol (LDL-C): a randomised, double-blind, and cross-over placebo-controlled clinical trial, BMC Compl. Alternative Med. 18 (2018) 294.
[34] C.-H. Hsu, T.-H. Tsai, Y.-H. Kao, K.-C. Hwang, T.-Y. Tseng, P. Chou, Effect of green tea extract on obese women: a randomized, double-blind, placebo-controlled clinical trial, Clin. Nutr. 27 (2008) 363–370.
[35] Y. Lee, X. Yu, F. Gonzales, D.J. Mangelsdorf, M.-Y. Wang, C. Richardson, et al., PPARα is necessary for the lipopenic action of hyperleptinemia on white adipose and liver tissue, Proc. Natl. Acad. Sci. USA 99 (2002) 11848–11853.
[36] M. Bose, J.D. Lambert, J. Ju, K.R. Reuhl, S.A. Shapses, C.S. Yang, The major green tea polyphenol(-)-epigallocatechin-3-gallate, inhibits obesity, metabolic syndrome, and fatty liver disease in high-fat–fed mice, J. Nutr. 138 (2008) 1677–1683.
[37] A. Rocha, A.P. Bolin, C.A.L. Cardoso, R. Otton, Green tea extract activates AMPK and ameliorates white adipose tissue metabolic dysfunction induced by obesity, Eur. J. Nutr. 55 (2016) 2231–2244.
[38] J. Most, J.G.P. Van Can, J.-W. van Dijk, G.H. Goossens, J. Jocken, J.J. Hospers, et al., A 3-day EGCG-supplementation reduces interstitial lactate concentration in skeletal muscle of overweight subjects, Sci. Rep. 5 (2015), 17896.
[39] R.N. Mishra, D. Joshi, Jiao gu lan (gynostemma pentaphyllum): the Chinese rasayan-current research scenario, Int. J. Res. Pharm. Biomed. Sci. 2 (2011) 1483–1502.
[40] S. Park, T. Huh, S. Kim, M. Oh, P.B. Tirupathi Pichiah, S. Chae, et al., Antiobesity effect of Gynostemma pentaphyllum extract (actiponin): a randomized, double-blind, placebo-controlled trial, Obesity 22 (2014) 63–71.
[41] R. Gauhar, S.-L. Hwang, S.-S. Jeong, J.-E. Kim, H. Song, D.C. Park, et al., Heat-processed Gynostemma pentaphyllum extract improves obesity in ob/ob mice by activating AMP-activated protein kinase, Biotechnol. Lett. 34 (2012) 1607–1616.
[42] H. Lee, R. Kang, S. Bae, Y. Yoon, AICAR, an activator of AMPK, inhibits adipogenesis via the WNT/β-catenin pathway in 3T3-L1 adipocytes, Int. J. Mol. Med. 28 (2011) 65–71.
[43] M. Wang, F. Wang, Y. Wang, X. Ma, M. Zhao, C. Zhao, Metabonomics study of the therapeutic mechanism of Gynostemma pentaphyllum and atorvastatin for hyperlipidemia in rats, PLoS One 8 (2013).
[44] J. Yeo, Y.-J. Kang, S.-M. Jeon, U.J. Jung, M.-K. Lee, H. Song, et al., Potential hypoglycemic effect of an ethanol extract of Gynostemma pentaphyllum in C57BL/KsJ-db/db mice, J. Med. Food 11 (2008) 709–716.
[45] S. Megalli, N.M. Davies, B.D. Roufogalis, Anti-hyperlipidemic and hypoglycemic effects of Gynostemma pentaphyllum in the Zucker fatty rat, J. Pharm. Pharmaceut. Sci. 9 (2006) 281–291.
[46] I.-J. Chen, C.-Y. Liu, J.-P. Chiu, C.-H. Hsu, Therapeutic effect of high-dose green tea extract on weight reduction: a randomized, double-blind, placebo-controlled clinical trial, Clin. Nutr. 35 (2016) 592–599.
[47] J.E. Oben, J.L. Ngondi, C.N. Momo, G.A. Agbor, C.S.M. Sobgui, The use of a Cissus quadrangularis/Irvingia gabonensis combination in the management of weight loss: a double-blind placebo-controlled study, Lipids Health Dis. 7 (2008) 12.
[48] J.E. Oben, D.M. Enyegue, G.I. Fomekong, Y.B. Soukontoua, G.A. Agbor, The effect of Cissus quadrangularis (CQR-300) and a Cissus formulation (CORE) on obesity and obesity-induced oxidative stress, Lipids Health Dis. 6 (2007) 4.
[49] J. Oben, D. Kuate, G. Agbor, C. Momo, X. Talla, The use of a Cissus quadrangularis formulation in the management of weight loss and metabolic syndrome, Lipids Health Dis. 5 (2006) 24.
[50] H. Sharp, J. Hollinshead, B.B. Bartholomew, J. Oben, A. Watson, R.J. Nash, Inhibitory effects of Cissus quadrangularis L. derived components on lipase, amylase and α-glucosidase activity in vitro, Nat. Prod. Commun. 2 (2007), 1934578X0700200806.
[51] J. Okafor, H.C. Okolo, Potentials of Some Indigenous Fruit Trees of Nigeria, 5th Annu. Conf. For. Assoc. Niger. Jos, 1974, pp. 60–71.
[52] J.L. Ngondi, J.E. Oben, S.R. Minka, The effect of Irvingia gabonensis seeds on body weight and blood lipids of obese subjects in Cameroon, Lipids Health Dis. 4 (2005) 12.
[53] A.N. McLendon, J. Spivey, C.B. Woodis, African mango (Irvingia gabonensis) Extract for weight loss: a systematic review, J. Nutr. Therapeut. 2 (2013) 53–58.
[54] J.E. Oben, J.L. Ngondi, K. Blum, Inhibition of Irvingia gabonensis seed extract (OB131) on adipogenesis as mediated via down regulation of the PPARgamma and leptin genes and up-regulation of the adiponectin gene, Lipids Health Dis. 7 (2008) 44.
[55] E. Valizadeh, F. Ghalichi, A. Ostadrahimi, Traditional herbal medicine for weight management: a review, Int. J. Med. Res. Health Sci. 5 (2016) 393–399.