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Cynara scolymus (artichoke) and its efficacy in management of obesity

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ABSTRACT

Obesity, the most prevalent metabolic disorder is associated with elevated body fat mass and body mass index. *Cynara scolymus* L. is famous for its hepatoprotective properties, also it seems to have good potency as anti-obese agent. In this review article, the potency of *C. scolymus* as anti-obese agent has been evaluated. The evidences based information were extracted from accessible international electronic databases (PubMed, Springer, Science Direct, Wiley and Google), and books (Persian or English), by key word of *Cynara scolymus* and artichoke plus obesity or the mechanism of anti-obese drugs. *C. scolymus* inhibits the digestive enzymes such as pancreas lipase, α-amylase, α-glucosidase, increases the bile secretion, inhibits of inflammation and ROS, improves liver function, gut microbiota, enhances lipolysis and lipid metabolism, and reduces blood glucose in preclinical and clinical studies. Designing large multi-center clinical trials on *C. scolymus* and evaluating its effects on weight loss in comparison with famous drug such as orlistate could be the subject of future studies.

1. Introduction

Obesity as the most common chronic multifactorial disorder is associated with multiple diseases with high morbidity and mortality. Obesity with worldwide prevalence is to happen, when the energy intake in the body is higher than energy expenditure, therefore it appears as elevated body fat mass and body mass index (BMI) higher than 30 kg/m^2 [1].

In Unani Traditional Medicine, obesity is known as “Siman-E-Mufrit”, and it is believed to be a cold and damp phlegmatic disease as result of food humor and excess fat accumulation in particular organ or in the whole body. Excessive eating and sedentary lifestyles are believed to be the most important factors in obesity [2]. Mixing the phlegm with blood results in disastrous condition such as cardiovascular, cerebrovascular, respiratory and reproductive diseases [3]. Exercise, medication, surgery, and natural medicine can be effective in management of obesity. Among all therapeutic choices, phytotherapy has gained great space due to its safety and multifunctional properties. Different medicinal plants are currently used as anti-obesity supplements. *Cynara scolymus*, a member of Asteraceae family, is famous for its hepatoprotective properties, also it seems to have good potency as anti-obese agent in herbal supplements. In this review article, the potency of *C. scolymus* as anti-obese agent was evaluated.

2. Methods

The information was extracted from accessible international electronic databases (PubMed, Springer, Science Direct, Wiley and Google), and books (Persian or English), by key word of *Cynara scolymus* or artichoke plus obesity or the mechanism of anti-obese drugs.

3. Results and discussion

3.1. *Cynara scolymus*

C. scolymus or artichoke has been used medically since the 4th century BCE. It is used alone or in combination with other medicinal plants (*Gentiana lutea*, *Curcuma longa*, *Mentha piperita*, *Achillea millefolium*, *Foeniculum vulgare*, *Helichrysum arenarium*) as coated tablet or capsule in different countries. In Australia, 1–2 coated tablets or capsules (300–600 mg), is used three times a day for digestive complaints, dyspepsia, improvement of lipid metabolism, post treatment after hepatitis, sub-acute or chronic diseases of biliary tract or after care of cholecystectomy (surgical removal of the gallbladder) [4]. In Belgium, *C. scolymus* preparations are used for enhancing the bile secretion as cholagogue (promotes bile discharge) [4]. In Bulgaria, coated tablets or oral solution containing *C. scolymus* is used for treatment of dyspepsia, enhancing the fatty acid metabolism [4]. In France, *C. scolymus* is traditionally used as choleretic and cholagogue agents to enhance the functions of urinary and digestive systems [4]. In Germany, 1 coated

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tablet containing 300 mg dry extract (DER 5.8-7.5:1) of *C. scolymus* is used 1–2 times daily to enhance the digestion. In Hungary, *C. scolymus* is used as cholagogue, fat metabolism enhancer, and treatment for feeling of fullness, digestive complaints, nausea, flatulence, and gall-bladder diseases [4]. In Iranian folklore, *C. scolymus* is used as diuretic, stomach tonic, cholagogue, and treatment of fever, liver disorders, bile stones, blood cholesterol, urticaria, asthma, and eczema [5]. *C. scolymus* is traditionally used for obesity in Brazil [6]. According to traditional believes on fat metabolism effects and anti-obesity effects of *C. scolymus*, it can be a good candidate for slimming herbal supplements.

3.2. Chemical composition of C. scolymus

Hydroxycinnamic acids (chlorogenic acid, dicaffeoylquinic acids, caffeic acid, ferulic acid), flavonoids (luteolin and scolymoside and cynaroside), cynarin (1,5-di-caffeoylquinic acid), are the main ingredients of *C. scolymus* leaf extract [7]. Potassium, vitamin C, folate, magnesium and dietary fibers are present in *C. scolymus*. *C. scolymus* is standardized on the base of cynarin as its principal active component, which is responsible for pleasant bitter taste of *C. scolymus* extract. The highest concentration of cynarin is present in *C. scolymus* leaf. *C. scolymus* dried leaves should be containing not less than 0.8% chlorogenic acid [8]. Chlorogenic acid, caffeic acid, isoquercitrin and rutin are present in artichoke leaf tincture [9].

3.3. The relation between C. scolymus biological activity and possible anti-obesity effects

C. scolymus is traditionally used as cholagogue and fat metabolizer. In this article, the potency and different mechanisms are involved in its anti-obesity effects of *Cynara scolymus* will be discussed.

3.3.1. The inhibitory effects of C. scolymus on digestive enzymes

Lipase inhibitors as digestive enzymes are currently known as drugs for obesity treatments. The sugar absorption is suppressed by α-glucosidase inhibitors or other carbohydrate inhibitors [10]. *C. scolymus* leaf extract has weak α-glucosidase, and pancreatic lipase inhibitory activities [11], but its strong inhibitory effects on α-amylase activity was confirmed with IC_{50} of 72.22 μg/μL. Treatment of alloxan induced diabetic rats with *C. scolymus* extract caused a considerable reduction in serum lipase activity, which is associated with significant reduction ($p < 0.001$) in α-amylase levels compared to diabetic rats [12]. Digestive enzymes play a big part in weight control and obesity. Blocking the digestive enzymes by *C. scolymus* provides a valuable approaches to produce beneficial effects on blood glucose levels or satiety signals in patients with obesity.

3.3.2. The bile secretory effects of C. scolymus and obesity

Bile acids are synthesized from cholesterol in liver, with function of fat or fat soluble vitamin absorption in the body. Stimulating the glucagon-like peptide 1 (GLP1) in colon by bile acids, enhances the insulin secretion, carbohydrate and fat metabolisms [13], therefore, increasing in bile secretion in the body can be associated with reduction in cholesterol and elevated metabolism. *C. scolymus* increases the size and number of secreting bile ducts in liver cells, which results in significant increase in bile secretion into duodenum [14]. In randomized placebo-controlled double-blind cross-over pilot study, single dose of standardized *C. scolymus* extract (1.92 g as six capsule 320 mg) in 20 individuals, significantly increased bile secretion, 30 and 60 min after administration, compared to placebo ($p < 0.05$) without any adverse effects [15]. Therefore, *C. scolymus* significantly increases bile secretion, which enhances the carbohydrate and fat metabolism in the body.

3.3.3. Inhibitory effects of C. scolymus on inflammation or oxidative stress in obesity

Obesity is associated with secretion of inflammatory adipokines (leptin, IL-6, TNF-α, resistin and MCP-1) from adipose tissue in subjects with obesity [16]. The inflammation of adipokines is associated with production of reactive oxygen species (ROS) or oxidative stress, which reduce the activity of antioxidant enzymes of superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) [17]. The role of angiotensin converting enzyme (ACE) inhibitors on reducing the body weight, improvement of insulin sensitivity and reduction of inflammatory markers of mice with high fat diet are shown [18]. C. *scolymus* leaf extract (100 μg/ml) proved ACE inhibitory effects (31%) [11]. ACE inhibitors decrease the plasma leptin levels and increases the adiponectin levels in mice [18]. Leptin is increased under oxidative stress and is released from mature adipocytes. Treatment of high fat diet adult female Sprague Dawley rats with *C. scolymus* extract significantly reduced the plasma levels of leptin, resistin and inflammatory cytokines such as NF-kB, TNF-α, CD_{40} and Hepatocyte Growth Factor (HGF) and increased the adiptonectins [19]. C. *scolymus* leaf extract (150, 300, 600 mg/kg orally, for 30 days) decreased IL-1, IL-6, TNF-α, IFN-γ, CRP, oxidized LDL levels in rats. The adipocyte hormone leptin has different metabolic effects related to body weight and energy expenditure. Most individuals with obesity have elevated plasma leptin levels [1]. Resistin as pro-inflammatory cytokine, targets the liver, which is associated with insulin resistant, Type II diabetes mellitus, hepatic fat content and glucose production. Therefore, it is involved in pathogenesis of obesity mediated insulin resistance [20]. Soluble serum CD_{40} level was strongly correlated with BMI. CD_{40} has regulatory role in obesity induced insulin resistance, which activates platelet and lipid peroxidation [21]. C. *scolymus* by its luteolin content inhibits CD_{40} ligand expression [22]. Therefore, reduction of leptin, resistin, and CD_{40} may associate with reduction of body-fat content, BMI and obesity induced insulin resistance [23]. *C. scolymus* leaf ethanol extract had strong antioxidant activity by $ABTS^+$ and antioxidant total capacity *in vitro* condition. Oral administration of *C. scolymus* leaf ethanol extract (200–400 mg/kg) in alloxan induced diabetic rats compared with acarbose (12 mg/kg, b.w) for one month showed a significant increase in anti-oxidative enzymes CAT, SOD and GPx in liver, kidney and pancreas of diabetic rats and significant reduction in advanced oxidative proteins products (AOPP), and malondialdehyde (MDA) levels [12]. *C. scolymus* leaf extract had xanthine oxidase [11]. Xanthine oxidase as oxidative stress related enzymes is linked to BMI score and obesity, which is associated with endothelial dysfunction, cardiovascular risk factors, or inflammatory cytokine levels [24]. *C. scolymus* leaf tincture (0.1 ml/kg body weight for 6 weeks) significantly reduced haemeoxygenase-1 (HO-1), MCP-1 mRNA level, NOx-4 and DNA score of mice aorta compared with the atherogenic group and improve the arterial vessel wall through reduction in oxidative stress [9]. Inhibition of inflammatory cytokines of adipokines has a direct effect on weight control by regulating food intake. Leptin by acting on the limbic system, stimulates dopamine uptake, and creates a feeling of fullness. Inhibition of ROS by adipokines and enhancing the activity of antioxidant enzymes prevent from various abnormalities, especially the endothelial dysfunction in atherosclerotic disease as the result of obesity.

3.3.4. The effects of C. scolymus liver enzymes involved in obesity

The most prevalent liver diseases of metabolic origin are associated with obesity and weight gain [25]. *C. scolymus* is famous as liver medicinal plant. Oral administration of *C. scolymus* leaf ethanol extract (200–400 mg/kg for one month) in alloxan induced diabetic rats increased the hematological parameters (the levels of RBC, Hb, MCV, MCH and MCHC, WBC and platelets) to near normal values ($p < 0.001$). Alanine aminotransferase (ALT), aspartate aminotransferase (AST) improved after treatment with *C. scolymus* extract, which was associated with reduction of vacuolized hepatocytes cells with lymphocytic infiltration [12]. 2700 mg extract *C. scolymus* extract (as 6 tablets per day) for two months improved the serum levels of ALT, AST in patients suffering nonalcoholic steatohepatitis ($n = 30$). The mean weight and systolic blood pressure significantly reduced after *C.*

scolymus administration in patients [26]. Increased in ALT and AST levels are common in obesity and increasing BMI [27], therefore, improving the liver function by *C. scolymus* could be a good strategy for weight management.

3.3.5. *C. scolymus and increased lipolysis and lipid metabolism*

There is a correlation between dyslipidemia and Siman-E-Mufrit in Unani traditional medicine. Traditional scholars believe that dyslipidemia stimulated by Siman-E-Mufrit. Therefore, according to traditional and modern medicines, lipid metabolism has crucial role in management of obesity. The vast amount of studies focused on lipid lowering effects of *C. scolymus*. *C. scolymus* leaf extract (150, 300, 600 m/kg orally for 30 days) in comparison with simvastatin (4 mg/kg) decreased the serum level of total cholesterol, LDL-C of high fat fed rats [23]. *C. scolymus* leaf tincture (0.1 ml/kg body weight for 6 weeks) increased HDL-c in atherogenic rats, while triglyceride, triglyceride/HDL-c ratio was significantly lower in *C. scolymus* group compared to control group [9]. The rats, who orally fed with an atherogenic diet containing 110 mg/kg powdered *C. scolymus* aerial parts, for 120 days had lowered in serum and liver cholesterol high level. Atherosclerotic plaques formation were inhibited by *C. scolymus* [28]. Total cholesterol and triglyceride of hyperlipidemia rats significantly decreased after intraperitoneal administration of 100 mg/kg body weight fresh *C. scolymus* hydro-ethanol extract [29]. Oral administration of *C. scolymus* leaf ethanol extract (200–400 mg/kg for one month) showed a significant reduction in plasma total cholesterol (18.1%), triglyceride (60.5%), LDL-C (37.8%), compared to diabetic rats in alloxan induced diabetic rats [12]. The rats fed on dry *C. scolymus* containing 10% fructooligosaccharides per kg diets for 8 weeks had significant reduction in their glucose and lipid profile (VLDL-C, triglyceride, LDL-cholesterol, LDL/HDL Ratio, total cholesterol, serum total lipids), compared with control group [30].

The lipid lowering effects of artichoke leaf extract were observed in human clinical study [31].

In double-blind placebo-controlled clinical trial, on 80 patients with metabolic disorder, *C. scolymus* leaf extract (1800 mg per day as four tablets) (n = 33) for 12 weeks, decreased serum triglyceride level compared to placebo (n = 35). LDL-C level significantly decreased in men carriers of Taq IBB1B1, in *C. scolymus* leaf group compared to the placebo group [32].

In a randomized double blind clinical trial, *C. scolymus* extract (2700 mg extract) on patients suffering from nonalcoholic steatohepatitis (n = 30) for two months significantly reduced the mean weight, triglycerides, LDL and cholesterol levels, compared to placebo group [26]. In randomized, placebo-controlled, double-blind, multicenter trial on patients (18–70 years old) suffering from hypercholesterolemia (n = 143), who randomly divided in two groups and received either 1800 mg *C. scolymus* leaf extract (900 mg, twice daily) or placebo daily for 6 weeks, *C. scolymus* significantly reduced the total cholesterol (18.5%), low density lipoprotein levels (1.26 mmol/l reduction), compared with placebo group (8.6% and 0.33 mmol/l) ($p < 0.00001$) with no significant effects on high density lipoprotein and triglyceride [33]. In other randomized, placebo-controlled, double-blind pilot study on 44 healthy volunteers (20–49 years old), who randomly divided in two groups of 1920 mg *C. scolymus* extract daily (640 mg artichoke leaf extract, three times daily) or placebo for a 12-week treatment period, a significant reduction in total cholesterol levels were observed in artichoke group, compared with placebo ($p = 0.015$) without major adverse events [31].

In an open clinical study on patients (n = 17), who received 1000 mg daily cynarin over 4 weeks caused significant 15% reduction in serum cholesterol ($p < 0.005$) [34]. In one clinical study on 54 patients, randomly divided in two groups, who received aqueous *C. scolymus* leaf extract (3.8–5.5:1), or placebo (fiber) for 24 days, *C. scolymus* significantly decreased the average of cholesterol and LDL, LDL/HDL-quotient levels compared to placebo group [35]. Daily 1280 mg *C. scolymus* leaf extract (n = 38) for 12 weeks significantly decreased plasma total cholesterol in healthy adults with mild to moderate hypercholesterolemia (n = 132) by an average of 4.2% in comparison with increase in the control group (n = 35) by an average of 1.9% ($p = 0.025$). *C. scolymus* or placebo had no significant differences for LDL-C, HDL-C or triglyceride levels. General well-being improved in treatment (11%) and control groups (9%), but the difference was not significant [36]. Dietary supplementation with 20 ml *C. scolymus* leaf pressed juice positively modulates endothelial function in brachial of moderately hypercholesterolemia on patients under isocaloric hypolipidic diet 6 weeks (n = 18), it reduced VCAM-1 and ICAM-1 and increased brachial flow-mediated vasodilation compared to control group [37]. In double-blind randomized clinical trial, women with metabolic syndrome who received 1800 mg hydro-alcoholic extract of *C. scolymus* as four tablets per day for 12 weeks (n = 25), significantly decreased the serum triglyceride level in carriers of A allele of the FTO-rs9939609, which associated with an increased risk of obesity, type 2 diabetes, and metabolic disorder, compared with placebo (n = 24) [38]. The results of preclinical studies exhibited that the *C. scolymus* reduced the liver lipids and glycogen content. Cholesterol elimination increased by *C. scolymus* due to its choleresis effect, also it prevented the LDL oxidation [39]. HMG-CoA, a key enzyme in cholesterol biosynthesis is inhibited indirectly by *C. scolymus* [40]. Hepatocellular cholesterol biosynthesis was inhibited by luteolin [14]. Reduction of white adipose tissue and inhibition of the liver lipogenesis are very important issue in obesity. The white adipose tissue showed significant increase in high fat fed mice. *C. scolymus* leaf extract significantly decreased the serum triglyceride, total cholesterol, LDL-C levels and significant increase in HDL level of high fat fed mice. *C. scolymus* significantly suppressed the development of inflammation, focal necrosis, and severe macro vascular fatty changes throughout the liver lobules of fat hepatic histopathological samples. It has been confirmed that fatty acid synthase genes, which involved in lipogenesis decreased in presence of *C. scolymus* in high fat fed mice, while hormone sensitive lipase was significantly increased after treatment of high fat fed mice with *C. scolymus*. The expression of acyl-CoA oxidase had no changes among the groups studied [41]. *C. scolymus* enhances lipolysis and suppresses lipogenesis in mice. Stimulation of lipolysis in white adipose tissue, increasing energy utilization in liver and brown adipose tissue are other proposed mechanisms for *C. scolymus* to prevent obesity.

3.3.6. *C. scolymus and its prebiotic effects in obesity*

High inulin content of *C. scolymus* stimulated the *Bifidobacterium* growth in the intestine and exhibited health-promoting prebiotic effects [42]. Physico-chemical properties of *C. scolymus* inulin is similar to chicory inulin, while polymerization degree *C. scolymus* inulin is higher [43]. *C. scolymus* inulin had bifidogenic nature [44] High concentrations of fructo-oligosaccharides in *C. scolymus* with prebiotic effects stimulate the gut probiotic microflora growth. Administration of daily 10 g inulin derived from *C. scolymus* for two 3-week study periods, with 3-weeks washout period, compared with placebo (maltodextrin) significantly increased the numbers of fecal *Bifidobacterium*, *Lactobacilli-Enterococci* and *Atopobium* groups level compared with the placebo, while *Bacteroides-Prevotella* numbers significantly reduced in the human intestinal microbiota of healthy adults (n = 32) [44]. The higher polymerization degree is associated with higher prebiotic effects and higher persistence in colon and manifestation of adverse effects. Significant increase in mild and moderate bloating was observed after *C. scolymus* ingestion, which confirmed by *in vitro* gas production measurements [44]. The slimming action of *C. scolymus* is based on its depurative effect and the presence of fructose polysaccharides, which act as prebiotic compound.

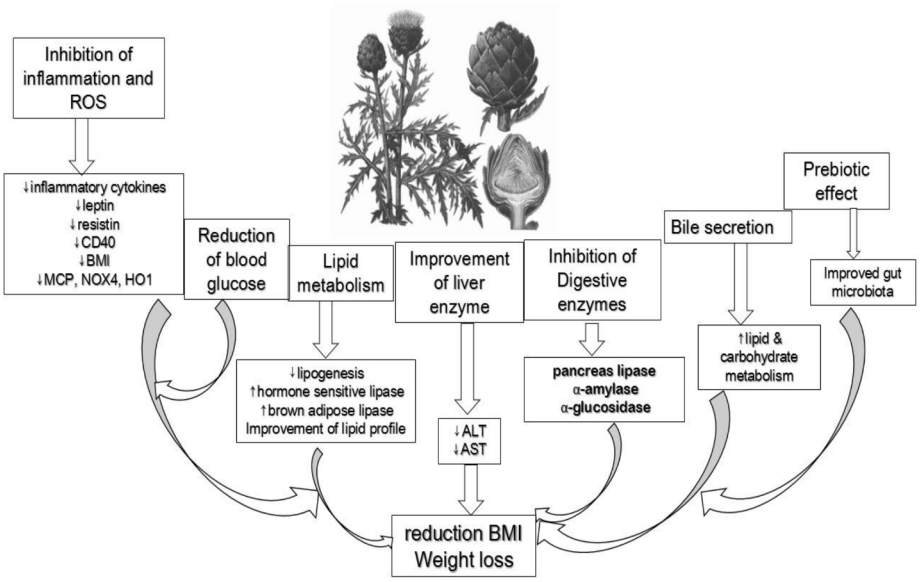

Fig. 1. The proposed mechanism for *Cynara scolymus* in obesity.

3.4. The effects of C. scolymus on insulin resistance

There is strong relationship between BMI and type II diabetes or insulin resistance. Non-esterified fatty acids, cytokines, hormones, ROS and many other compounds are involved in the development of insulin resistance in individuals with obesity. The failure of pancreas β-islet cells causes a lack of control of blood glucose. High BMI and obesity increase the incidence of type 1 and type 2 diabetes. There is positive correlation between obesity with insulin resistance and pancreatic β-cell dysfunction [45]. Alloxan induced diabetes in animals is the model of type 1 diabete, which is associated with reduction in insulin secretion from β-cell of islets of Langerhans. Oral administration of artichoke leaf ethanol extract (200–400 mg/kg, for one month) in alloxan induced diabetic rats, had a partial protective action of β-cells of pancreas, in comparison with acarbose [12]. The reduction in post prandial glucose were observed for fiber-free extract of *C. scolymus* extract (500, 1000, and 1500 mg/kg) in obese and normal rats [46]. The rats feeding with dry *C. scolymus* for 8 weeks was significantly reduced glucose level of rats compared with control group [30].

The beneficial effects of *C. scolymus* extract in diabetic patients were the subject of randomized clinical trial, wheat biscuits containing 5% globe *C. scolymus* powder for 90 days significantly reduced fasting and post prandial blood glucose, in type 2 diabetic patients (n = 15) in comparison with placebo (n = 15) [47]. *C. scolymus* fiber free extract had no effects on fasting glucose, postprandial glucose of hypercholesterolemic type 2 diabetic patients resistant to daily intake of glyburide and metformin [48]. Increasing the blood glucose can lead to obesity [45]. The beneficial effects of *C. scolymus* on blood glucose and pancreas β-cells and its effect on BMI or slimming should be considered in more clinical trials.

3.5. Pharmacokinetics of C. scolymus

C. scolymus compounds cross the gastric and intestinal barriers and reach to human bloodstream. After oral administration of *C. scolymus*, chlorogenic acid rapidly is detected in plasma. Mainly chlorogenic acid and caffeolylquinic acids transformed biologically to caffeic acid and ferulic acid conjugates by esterase throughout the small intestine, which were detected in plasma levels. In large intestine, contact chlorogenic acid is hydrolyzed to aromatic acid metabolites (coumaric acid, benzoic acids) by colon enzymes [7]. Colon microflora play an important role in releasing the caffeic acid and converting it to dihydrocaffeic acid and dihydroferulic acid [7]. Dihydrocaffeic acid and dihydroferulic acid is absorbed and transported to liver and converted to ferulic acid and isoFA. Gut microflora are the predominant location of hydroxycinnamate esters metabolism [7].

3.6. Safety of C. scolymus

The oral LD_{40} and intra-peritoneal LD_{50} of purified extract (46% caffeoylquinic acids) were 2000 and 265 mg/kg, respectively [4]. No cytotoxic effects were observed for primary cultures of rat hepatocytes in presence of up to 1 mg per ml *C. scolymus* leaf aqueous dry extract (4.5:1) [49]. The oral LD_{50} of cynarin in mice was 1900 mg/kg body weight [50]. No apparent side effects or signs or toxicity were observed after intra-peritoneal administration of 800 mg/kg cynarin in rats or intravenous administration of 1000 mg/kg cynarin in rabbits [4]. The global tolerability for *C. scolymus* extract is erased excellent (95.7%) [33]. The potency of anticoagulants decreases in presence of *C. scolymus* [51]. Rare mild laxative effects or hypersensitivity reactions were reported for *C. scolymus* [4]. The liver of animal feeding with dried *C. scolymus* had normal anatomy with normal lobule, parenchymal cells, and sinusoidal pattern in histological samples [30]. No histological changes was observed in kidney samples of rats treated with *C. scolymus* [30]. The daily dose of dry extract (DER 2.5-7.5:1) aqueous extract is 600–1320 mg [4].

4. Conclusion

C. scolymus as hepatoprotective medicinal plant can be the possible ingredient in slimming supplements. There is no big well designed clinical study, which evaluated the efficacy of *C. scolymus* extract on obesity, but in one clinical study, the homeopathic doses of *C. scolymus* (10 drops, three times a day for 3 month) had no significant changes on BMI of obese and overweight patients (BMI $>=$ 27 kg/m^2) with small trend to decrease the BMI [6]. The low participants in this study (n = 14) and nonstandard extract are limitation of study. The significant lowering effects of *C. scolymus* leaf extract (5%) on body weight of high fat fed mice, compared to high fed mice group were confirmed [28]. *C. scolymus* by inhibiting the digestive enzymes (pancreas lipase, α-amylase, α-glucosidase), bile secretory effects, inflammation and ROS, improving of liver enzymes, enhancing lipolysis and lipid metabolism, improving of gut microbiota, and reducing of blood glucose may help the patients with obesity (Fig. 1). It seems that *C. scolymus*

alone may have no significant effects on BMI or weight, but its use as one ingredient of slimming supplement along with strong weight loss plants will be suitable for patients suffering from obesity or other metabolic disorders. Designing large multi-center clinical trials on *C. scolymus* and evaluating its effects on weight loss in comparison with famous compound such as orlistate could be the subject of future studies.

Competing interest

Authors declare no conflict of interest.

Author contributions

Mohaddese Mahboubi gave the idea and designed the study, did the search and drafted the article, reviewed data, and edited the article.

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