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Review

# The role of Tripterygium *wilfordii* extract in weight loss, energy expenditure, glucose and lipid metabolism

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**Summary.** *Introduction:* Obesity is a chronic disease that characterized by the disturbance of the body composition, which is expressed as the relative or absolute increase in the amount of adipose tissue. Tripterygium wilfordii is an herbaceous plant of the Celastraceae family which is widely used in China. The roots of this plant have many therapeutic properties. Recently in animal studies, it has been shown that Celastrol in the root of Tripterygum wilfordii has been associated with weight loss, suppression of food intake, and increased leptin sensitivity. Triptolide is another effective ingredient in this plant, has significantly reduced TG, TC, LDL-C and weight loss in animal models. Also, Celastrol has an anti-obesity effect in ob/ob mice, which reduces the intake of food and the percentage of body fat. *Materials and methods:* Searching for articles based on Electronic databases including Google Scholar (scholar.google.com), Pub Med (www.ncbi.nlm.nih.gov/pubmed), (Science Direct (, and Springer (www.springer.com) until November 2017. *Results:* The use of celastrol significantly reduces dietary intake and body mass in mice. Celastrol increased the energy expenditure (EE) and reduced the amount of respiratory exchange ratio (RER) in the mice. celastrol caused a very marked decrease in plasma cholesterol, triglyceride and LDL levels, as well as a significant increase in plasma HDL levels. also, triptolide reduces serum cholesterol, TG and LDL. *Discussion:* It Can be considered, *Tripterygium wilfordii* roots may be consumed as a therapeutic compound that prevents obesity and complications associated with this disease.

**Key words:** obesity, *Tripterygium wilfordii, Triptolide, Celastrol*

## Introduction

Obesity is a chronic disease that characterized by the disturbance of the body composition, which is expressed as the relative or absolute increase in the amount of adipose tissue. The prevalence of obesity is increasing in all age groups and in developing countries. The main cause of obesity and overweight is the unbalanced intake and caloric intake. When calorie intake is more than needed, a positive calorie balance will add weight. This balance arises from inactivity, high consumption of food, or a set of both(1). Obesity has more than doubled worldwide since 1980. According to the World Health Organization, in 2015, over 2.3 billion people are overweight and over 700 million are obese. At least 8.2 million adults die each year due to overweight and obesity. Obesity plays a key role in chronic diseases and 44%, 23% and 41-7% of the burden of diabetes-ischemic heart disease and overweight and obesity-related cancer are attributed(2, 3). Obesity increases lipolysis process and one of the products of lipolysis is fatty acids. Fatty acids that as a result of obesity, enters the bloodstream and causes insulin resis-

tance in the muscles of the body and gluconeogenesis(4). The United States Heart Association has identified obesity as one of the most important causes of cardiovascular disease, that leading cause of disability and death. The mortality rate from cardiovascular disease among obese women and men is three times higher than the rest of the population, Also, 21% of deaths from cardiovascular disease are in men and 28% in women overweight and obesity(5). Adipose tissue is typically considered as an energy storage and triglyceride, triglyceride acts as a fuel tank for a long time. The secretion of the fatty acids in the adipose tissue into the plasma causes disturbances in serum lipids, which can lead to the development of cardiovascular diseases and multiple chronic diseases(6). More recently and over the past decade, laboratory studies and clinical trials have shown that adipose tissue is an intricate tissue that has important and different functions in regulating metabolism and energy balance in the body. Many factors that control the adipose tissue and control central and peripheral processes include free fatty acids and adipokines. Adipokines with paracrine and autocrine activity cause the homeostasis of the adipose tissue, liver, muscle, and nervous system. Adipokines are associated with chronic conditions such as obesity and overweight, cardiovascular disease, insulin resistance, and diabetes mellitus(7). In people who haven't obesity, the secretion of adipokines such as leptin and adiponectin is normal, these adipokines are mainly responsible for appropriate physiological responses. At the same time as the obesity process begins, various cytokines such as TNF and IL-6 are secreted. These cytokines cause changes in the production and secretion of adipokines.

These changes, which occur with obesity and an increase in cytokines, can flare up type 2 diabetes, metabolic syndrome, insulin resistance, and arteriosclerosis(8).

Several studies have examined various supplements, some of which are encouraging, and with few exceptions and some serious complications, there is no acceptable evidence that certain supplements can definitely use to reduce weight. Consequently, evidence of dietary supplements for weight loss is not convincing(9). Many studies have been conducted to find out about the risk factors for obesity in the hope of preventing it, fighting obesity has been successful only in laboratory models. It cannot be exemplified by the fact that successful and applied interventions that are practically done at the macro level and becoming a serious instruction cannot be exemplified(10).

Since the use of medications has many side effects, the use of supplements and medicinal plants is a good way to reduce chronic diseases such as overweight and obesity(11). The use of supplements and herbal extracts is one of the oldest and most commonly used methods for weight loss(12-14). Natural products have high-quality phytochemicals for the health and prevention of various diseases. The use of supplements has long been used in eastern countries, and is rapidly increasing throughout the world, however, the scientific and precise studies of these products are low and in many cases, its impact and safety are due to advertising and Marketing(15).

Tripterygium wilfordii is an herbaceous plant of the Celastraceae family which is widely used in China. The roots of this plant have many therapeutic properties. It is used to treat a wide range of disorders and diseases, including rheumatoid arthritis, lupus erythematosus (SLE) and psoriasis. It is also used to relieve and heal fever, swelling, chills, wounds, joint pain and inflammation(16, 17).

Biochemical analysis has shown that Tripterygium wilfordii has a range of natural compounds with strong biological activity(7). The roots of this plant have several therapeutic combinations including terpenoids, diterpenes, triterpenes, wilforgine, wilforidine, wilfordine, wilforine, Glycosides, Alkaloids (1.6%) and steroids, and 95% of these compounds terpenoids(16, 18, 19).

In recent animal studies, it has been shown that Celastrol in the root of Tripterygum wilfordii has been associated with weight loss, suppression of food intake, and increased leptin sensitivity. Triptolide, another effective ingredient in this plant that has significantly reduced TG, TC, LDL-C and weight loss in animal models. Also, Celastrol has an anti-obesity effect in ob/ob mice, which reduces the intake of food and the percentage of body fat(20, 21).

## Materials and methods

We reviewed all the articles that examined the effects of Tripterygium wilfordii extract on weight loss,

energy expenditure, glucose and lipid metabolism. There are seven articles in this subject area, a cell study article, and six animal study articles. Searching for articles based on Electronic databases including Google Scholar (scholar.google.com), Pub Med (www.ncbi.nlm.nih.gov/pubmed), (Science Direct), and Springer (www.springer.com) until November 2017. Also, these keywords were used to find articles: obesity, Thunder God Vine, Lee Gong Tang, Tripterygium wilfordii, Triptolide, Celastrol, weight loss, energy expenditure, glucose and lipid metabolism(22). All studies that have done about the effects of Tripterygium wilfordii extract in weight loss, energy expenditure, glucose and lipid metabolism are shown in Table 1.

## Results

*Effect on weight loss*

A significant reduction in weight was observed in a study by Umut Ozcan and his colleagues in 2015 for the effect of *Celastrol* on obesity on mice. The percentage of body fat in these mice was also clearly reduced(24).

The accumulation of proteins in the endoplasmic reticulum (ER) causes an abnormality in the cells called ER stress and subsequently, ER Stress has been associated with various diseases such as obesity and leptin resistance. *Celastrol* reduces stress in the hypothalamus tuberculosis mice, resulting in *Celastrol* being associated with increased leptin sensitivity and obesity prevention(21). The use of celastrol

**Table 1.** Studies were conducted about effect of Tripterygium wilfordii extract in weight loss, energy expenditure, glucose and lipid metabolism.

| Researcher (year)Study design | Intervention / treatment | Findings |
|---|---|---|
| Kug Choi and et al. 2016(23). Cell study/ 3T3-LI adipocytes | Use of *celastrol* and its effect on 3L3-LI adipocytes | *celastrol* causes lipolysis and differentiates in these cells. No damage to the cells. |
| Ozcan and et al. 2015(21). Animal models | Rats were consumed celastrol and saline for 6 weeks. | Leptin sensitivity and glucose hemostasis were significantly increased in rats which consumed *celastrol.* Also, the activation of the hypothalamus receptor and energy homeostasis was observed in rats receiving *celastrol*. |
| Alberobello and et al. 2015(24). Animal models | Rats fed with the high-fat diet with *celastrol* and Rats fed on the high-fat diet was without *celastrol* for 8 weeks | Significant increases in energy expenditure and remarkable reductions in insulin resistance were observed in rats fed with *celastrol*. |
| Chaoyun Wang, et al. 2014(25). Animal models/60 male rats | The rats were divided into six groups. a group of healthy rats, a group of rats received *simvastatin*, a group of rats that received high-fat diet, Three groups of rats received different doses of *celastrol* for 6 weeks. | In rats receiving different doses of *celastrol*, there was a significant decrease in cholesterol, triglyceride and LDL levels. Also, there was a significant increase in cholesterol in these rats. |
| Li-ping Han, et al. 2016(26). Animal models/60 male rats | Rats that received 3 doses of *celastrol* (Lowe dose-Middle dose-High dose) for 8 weeks. | Significant reductions in Insulin resistance, cholesterol and triglyceride in rats treated with *celastrol*. |
| Qing Gao, et al. 2010(20). Animal models/90 mice | Mice treated with *triptolide* for 12 weeks. | In mice receiving different doses of *triptolide*, there was a significant decrease in cholesterol, triglyceride and LDL levels. Also, there was a significant increase in cholesterol in these mice. |
| Jung Eun Kim, et al. 2013(27). Animal models/24 male mice | Mice were divided into three groups. A group of healthy mice, a group of diabetic mice, and a group of diabetic mice taking *celastrol*. | In mice treated with celastrol, energy expenditure was significantly increased. Insulin resistance in this group of mice was also significantly reduced. |

significantly reduces dietary intake and body mass in mice(25).

In laboratory studies (in vitro (, *celastrol* has had a remarkable effect on 3T3-L1 adipocytes. In a study by Seung Kug Choi and his colleague on 3T3-L1 adipocytes, it was observed that *celastrol* therapy prevented the differentiation of adipocytes and increased lipolysis of these cells(23).

*Effect on energy expenditure*

The active heat shock factor (HSF) is applied in certain conditions, such as stress and temperature, and also plays an important role in daily changes in body temperature. HSF1 is regulated by various types of compounds and chemicals. *Celastrol* in the roots of the *Thunder God Vine* plant is a compound that can stimulate the HSF1 genes(24).

Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) is a protein that plays an important role in regulating energy metabolism in cells and in the process of obesity PGC-1alpha protein plays an important role in obesity and type 2 diabetes(24).

*Celastro*l activates the HSF1 by inducing the PGC-1alpha gene and increasing the expression and production of PGC-1alpha leads to increased energy consumption and the treatment of obesity and other metabolic disorders(24). *Celastrol* increased the energy expenditure (EE) and reduced the amount of respiratory exchange ratio (RER) in the mice(21).

*Effect on glucose and lipid metabolism*

In a study by Chaoyun Wang et al. In 2014, celastrol caused a very marked decrease in plasma cholesterol, triglyceride and LDL levels, as well as a significant increase in plasma HDL levels(25). A study that evaluated the effect of triptolide on diabetic mice by Qing Gao et al.in 2010, there was a decrease in cholesterol, TG, LDL and HDL. No significant changes were found in blood glucose levels(20).

Interesting results were observed in a study by Jung Eun Kim and colleagues in July 2013 on the effect of celastrol on insulin resistance in mice. celastrol significantly reduced the amount of saturated fatty acids (SFAs) and also increased the amount of monounsaturated fatty acids(MUFAs) in the mice body(27).

In metabolic situations, such as diabetes, peroxidation of lipids and oxidative stress increase, and will lead to cellular dysfunction. celastrol significantly reduces oxidative stress in various organs of the mice such as the kidneys, liver and fat tissues. The treatment of celastrol significantly reduced urinary cytokines in diabetic mice. celastrol also reduced the levels of 8-Isoprostane urine levels in these rats(27).

Fasting blood glucose levels and blood glucose levels in rats were significantly reduced during treatment with celastrol. Significant effects were also shown on insulin resistance and a decrease in HOMA-IR index. A marked decrease was observed in the level of Glycated hemoglobin (HbA1c), which plays an important role in the sugar content of the last three months. In addition to beneficial effects on serum lipids such as cholesterol and triglyceride lowering, celastrol has a very strong effect on hepatic steatosis. In addition to beneficial effects on serum lipids such as cholesterol and triglyceride lowering, celastrol has a very strong effect on hepatic steatosis. Additionally, the effects of celastrol also significantly increase the expression of adiponectin genes, thereby increasing the level of adiponectin in the blood. adiponectin is associated with recovered insulin resistance and blood glucose modification. The results of the tests of celastrol treatment have shown that it decreases the lipid peroxidation of adipose tissue and inflammation. It also plays an important role in controlling oxidative stress in reducing inflammation and obesity(27).

## Discussion

In this review article, we showed that almost all of the studies examined show that Triptolide and Celastrol in the Tripterygium wilfordii roots cause and modified the harmful fats of blood and insulin and sugar in animal models. According to the lack of human studies and the need for further human intervention, due to the significant effects that the active ingredient in the roots of Tripterygium wilfordii roots in improving the lipid profile and in reducing blood sugar, is necessary. Can be considered, Tripterygium wilfordii roots may be consumed as a therapeutic compound that prevents obesity and complications associated with it. By investigating and intervening in the future on

this plant and its active ingredients, it is hoped to be used to treat many diseases, including type 2 diabetes, metabolic syndrome, and fatty liver.

The side effects of this plant include gastrointestinal disorders, diarrhea, leukopenia, thrombocytopenia, skin pigmentation and rash, as well as disorders in the reproductive system.

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