



Phytotherapy in Obesity: Is It Necessary to Have Surgery?

Obezitede Fitoterapi, Ameliyat Olmak Şart mı?

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ABSTRACT

The prevalence of obesity, which is defined by the World Health Organization as abnormal or excessive fat accumulation in the body that impairs health, is increasing day by day. In addition to behavioral therapy aimed at changing the individual's lifestyle based on the strategies developed against the disease, diet therapy, exercise, medical nutrition therapy, pharmacological and, as a last resort, surgical treatment are recommended. The effect of methods other than surgical treatment on weight loss is slow. For this reason, many obese patients prefer obesity surgery to lose weight quickly, but these methods have many complications such as weight regain, tachycardia, fistula, bleeding, herniation, anastomotic stenosis, gastric erosion, small bowel obstructions, deep vein thrombosis and pulmonary embolism. Post-surgical weight regain and complications have recently led to new searches, and the use of medical nutrition and phytotherapy products has again come to the fore as hope. Phytotherapy products can also be used alone or in combination with other methods. Natural anti-obesity products have functional ingredients such as phytochemicals, polyphenols, flavonoids and phytosterols. There are many natural products used in this field and therefore there are different classifications. Phytotherapeutics are classified according to their effectiveness as those that increase fat burning and stimulate metabolism, suppress appetite, create a feeling of satiety, control blood sugar and insulin, inhibit the absorption of carbohydrates and fats, and inhibit inflammation. However, more clinical research is needed to elucidate the antiobesity effectiveness and mechanism of action of natural products. The risks and side effects of the method to be chosen in obesity treatment should be discussed with the patient. Recommendations to the patient should be given after a multidisciplinary evaluation. Treatment should be started with the most appropriate and least risky method for the patient's current condition. It should be explained to the patient that it is most likely that he/she will lose weight with one of these methods, but that the important thing is to maintain his/her weight through behavioral changes.

Keywords: Obesity, phytotherapy, surgery, lifestyle change, diet

ÖZ

Dünya Sağlık Örgütü tarafından, vücutta sağlığı bozacak ölçüde anormal veya aşırı yağ birikmesi olarak tanımlanan obezitenin prevalansı her geçen gün artmaktadır. Hastalığa karşı geliştirilen stratejiler temelinde bireyin yaşam tarzını değiştirmeye yönelik olan davranış terapisinin yanında, diyet tedavisi, egzersiz, tıbbi beslenme tedavisi, farmakolojik ve son çare olarak ise cerrahi tedaviyi önermektedir. Cerrahi tedavi dışındaki yöntemlerin kilo kaybı üzerindeki etkisi yavaştır. Bu yüzden obez hastaların birçoğu hızlı kilo vermek adına obezite cerrahisi yöntemlerini tercih etmektedir fakat; bu yöntemler başta kilo geri kazanımı olmak üzere taşikardi, fistül, kanama, fıtıklaşma, anastomoz darlığı, gastrik erozyon, ince bağırsak tıkanıklıkları, derin ven trombozu ve pulmoner emboli gibi birçok komplikasyonu da beraberinde getirmektedir. Cerrahi sonrası kilo alımı ve yaşanan komplikasyonlar son zamanlarda yeni arayışlara yol açmış ve tıbbi beslenme ve fitoterapi ürünlerinin kullanımı yeniden bir ümit olarak gündeme gelmiştir. Fitoterapi ürünleri tek başına ya da diğer yöntemlerle birlikte kullanılabilir özelliğine de sahiptir. Doğal obezite karşıtı ürünler; fitokimyasallar, polifenoller, flavonoidler ve fitosteroller gibi fonksiyonel içeriklere sahiptir. Bu alanda kullanılan birçok doğal ürün bulunmaktadır ve bu sebeple farklı sınıflamalar mevcuttur. Fitoterapötikler, etkinliğine göre; yağ yakımını artıran ve metabolizmayı uyarımlar, iştahı baskılayanlar, tokluk hissi yaratanlar, kan şekerini ve insülini kontrol edenler, karbonhidrat ve yağların absorpsiyonunu inhibe edenler, inflamasyonu inhibe edenler şeklindeki sınıflamaya tabii tutulmaktadır. Fakat yine de doğal ürünlerin antiobezite etkinliğini ve etki mekanizmasını aydınlatmak için daha fazla klinik araştırmaya ihtiyaç vardır. Obezite tedavisinde seçilecek yöntemin riskleri ve yan etkileri hasta ile tartışılmalıdır. Hastaya öneriler multidisipliner bir değerlendirmeden sonra verilmelidir. Hastanın mevcut durumuna en uygun ve en az riskli yöntem ile tedaviye başlanmalıdır. Hastanın bu yöntemlerden biri ile zayıflamasının büyük ihtimale sağlanacağını ama önemli olanın davranış değişikliği ile zayıf kalmanın sürdürülmesi olduğu anlatılmalıdır.

Anahtar Sözcükler: Obezite, fitoterapi, ameliyat, yaşam tarzı değişikliği, diyet

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WHAT IS OBESITY?

Many definitions of obesity have been made to date. According to the World Health Organization, obesity is abnormal or excessive fat accumulation in the body that impairs health (1). The question of whether obesity is a disease or a condition resulting from a personal choice and lifestyle has not been answered for many years. It is a complex condition involving social, biological and psychosocial factors, and its prevalence is increasing worldwide. A sedentary lifestyle and high-calorie diet, hereditary and hormonal factors, spiritual-psychological reasons, age and gender-related reasons seem to be the most important factors in the development of obesity.

According to the data announced by the World Obesity Federation in March 2023, the number of overweight and obese adults over the age of 20, which was 813 million, was estimated to be 1 billion in 2025. Overweight and obesity are the fifth leading risk for global deaths. At least 2.8 million adults die each year as a result of being overweight or obese. Additionally, 44% of the burden of diabetes, 23% of the burden of ischemic heart disease, and 7% to 41% of the burden of certain cancers are attributable to overweight and obesity (2).

Global anti-obesity strategies focus on diet and lifestyle changes to slow the development of obesity. In the treatment of obesity, behavioral modification therapy, exercise, medical nutrition therapy, pharmacological and, as a last resort, surgical treatment can be applied.

Bracketing and personal planning have an important place in the fight against obesity. All evaluations regarding the cause of obesity are made multifaceted and the solution is approached gradually after the cause is corrected. At the end of all treatment applications, the expected goal is to create behavioral change and ensure that it is permanent.

1. Lifestyle Change

Lifestyle change is the cornerstone of obesity management. The purpose of treating obesity with behavior modification therapy is to raise awareness and change the lifestyle that the patient has adopted, such as physical activity and nutrition habits, which cause excessive weight gain, and to provide a behavioral model that will keep him/her away from obesity. Behavior changes should include individual efforts such as nutrition education, regulation of the number and quantity of meals, doing what is necessary for a healthy life, switching to an active lifestyle with exercising, avoiding sugary drinks, and eliminating the causes of obesity, as well as government policies such as banning advertisements of foods that encourage obesity, producing healthy products, and changing social habits through regulations in laws (3).

2. Diet Therapy

Weight loss can be achieved through a net kilocalorie (energy unit) deficit. The estimated energy expenditure per kilogram of adult body weight is approximately 22 kcal. Reducing intake to create a net energy deficit can be achieved in various ways.

2.1. Macronutrient Composition

The three basic dietary macronutrients are fat, carbohydrates, and protein. Fat is the least filling, most easily absorbed, and most calorie-dense macronutrient, making it the most attractive target for weight loss intervention. A meta-analysis of low-fat diets shows significant weight loss compared to baseline intake but no weight loss compared to other dieting methods, including high-fat diets (4). Low-carb diets (LCDs) produce rapid results with greater initial weight loss (up to 3.3 kg in 6 months) compared to low-fat diets. However, most of this has been attributed to the loss of glycogen stores and water, reaching 1-2 kg in the first 14 days, after which the rate of weight loss slows down. Protein is very filling and is used in high-protein diets to reduce the consumption of other less filling, energy-dense nutrients. However, recent meta-analyses have concluded that these proteins have either no effect or a minor effect of questionable benefit on body weight (5).

2.2. Calorie Restriction

Another approach to achieving a net energy deficit is to directly limit calorie intake. Low and very low calorie diets (LCD: 800-1,600 kcal/day and VLCD: <800 kcal/day) limit energy intake (6). VLCDs provide superior short-term weight loss compared to LCDs (-16.1 kg vs -9.7 kg, respectively). Weight loss with VLCD is achieved primarily through total body fat loss (7.8% reduction in total body fat in 6 months). However, the long-term benefits of VLCDs are less clear, with higher rebound weight gain (61% versus 41%, respectively). In a systematic review by Franz et al., weight loss with VLCDs was found as 17.9 kg (16%) at six months, after which the weight loss began to decrease (-10.9 kg or -10% at 12 months and -5.6 kg or -5% at 36 months) (7).

2.3. Meal Replacement

Full or partial meal replacement (PMR) includes nutritionally filling but low-calorie meals for daily meals and recommends restricting calorie intake. Meal replacement may lead to greater weight loss than traditional calorie restriction. A meta-analysis of six studies by Heymsfield et al. supported this view. PMR provided greater weight loss in 3 months (-2.54 kg) and 1 year (-2.63 kg) with lower effort (8). Additionally, although subjects who applied PMR gained more weight over the long term compared to conventional diets, overall weight loss remained greater (-7.8% vs. -5.9% at 40 weeks).

However, the effect of behavioral exercise on weight loss is slow and is not suitable for obese patients with cardiovascular diseases. Recently, in nutrition research, great attention has been paid to the use of natural products in the fight against obesity.

3. Pharmacotherapy

Pharmacological treatments are recommended to maintain weight loss in addition to a low-calorie diet and optimal physical exercise. However, the pharmacological options available are very limited. Additionally, if less than 5% weight loss is achieved while using the medication, the treatment should be discontinued in the 3rd month (9). The main drugs used for this purpose are:

3.1. Orlistat

Orlistat irreversibly inhibits pancreatic lipases, which break down dietary fat into absorbable free fatty acids, preventing the absorption of up to 32% of ingested fats and allowing these fats to be excreted in the feces. To reduce side effects, patients are advised to follow a low-fat diet with medications taken during or up to 1 hour after meals. A meta-analysis of 33 randomized controlled studies showed an average reduction in body weight of 2.12 kg, although the average treatment duration varied between 2 months and 3 years (10).

3.2. Liraglutide (Saxenda®)

Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist administered subcutaneously once daily. GLP-1 is an incretin hormone that is released from the gastrointestinal (GI) tract in response to glucose and fat intake and acts both peripherally and centrally. In other words, it both changes glucose homeostasis by slowing down absorption from the GI system and suppresses appetite (11). GLP-1 treatment results in an average weight reduction of 3.2 kg and improvement in glycemic control (1% reduction in HbA1c), cholesterol level and blood pressure.

3.3. Naltrexone/bupropion (Mysimba®)

Naltrexone/bupropion is a fixed-dose combination medication often prescribed in addition to diet and lifestyle changes, but is not currently recommended by healthcare organizations because the long-term effectiveness of the medication is unknown (12). In the multicenter, randomized, double-blind, placebo-controlled phase 3 study, the average change in body weight was determined to be -6.1% in 1,742 patients, while this rate was observed to be -1.3% in the placebo group (13).

Every drug causing weight loss has its own risks, so the doctor needs to fully understand the drug's contraindications and the differences between obese individuals. More importantly, long-term studies are needed to determine whether weight loss with medication will cause side effects.

4. Exercise

Current guidelines recommend at least 150 minutes of moderate-intensity or 75 minutes of high-intensity aerobic exercise per week and training involving all major muscle groups at least twice per week. For patients wishing to maintain weight loss, high levels of exercise (225-420 minutes/week of moderate intensity exercise) provided better weight control compared to lower levels (<150 minutes/week) (14). Although significant weight loss can be

easily achieved, 80% of individuals are unable to maintain weight loss. Potential reasons for the high rate of WR after weight loss include increases in appetite hormones (e.g., ghrelin), decreases in anorexigenic hormones (e.g., leptin, glucagon-like peptide-1), decreased compliance with self-monitoring/weighing habits, and decreased resting metabolism with weight loss (15).

Exercise therapy should be prepared individually. In severely obese people, factors such as cardiovascular problems, joint problems caused by the pressure of excessive weight, and respiratory problems should be taken into consideration, and the type and level of exercise to be chosen should be according to the person's capacity.

5. Intra-gastric Balloon

Intra-gastric balloon (IGB) has been used since 1985 and very good results can be obtained. The balloon, which is usually placed endoscopically, is filled with saline and remains in the stomach for 6 months. IGB is an alternative option for weight loss in patients who refuse or are unsuitable for bariatric surgery. A Cochrane review concluded that there was little data to support its effectiveness for weight loss compared with traditional medical management (16). If the change in eating habits cannot be achieved permanently, weight may be regained after the balloon is removed.

6. Bariatric Surgery

Surgical treatment has become very popular recently. BS is often an effective therapeutic option for weight loss in people with severe obesity as well as for reducing diabetes in patients with low body mass index.

6.1. Laparoscopic Adjustable Gastric Band (LABG)

An inflatable silicone band is placed on the upper part of the stomach to narrow its lumen, restricting the passage of food and creating a small proximal gastric pouch that limits the amount of food that can be swallowed. The patency of the band, and therefore the degree of constriction, can also be adjusted by injecting fluid through a subcutaneous port. Major complications include band slippage (7.9%) and erosion (<1%) (17). Its use has decreased significantly due to recent complications.

6.2. Sleeve Gastrectomy

During sleeve gastrectomy (SG), 80% of the stomach is removed, leaving a narrow middle section. The reduced-sized stomach has lower mobility and restricts the volume of food passing

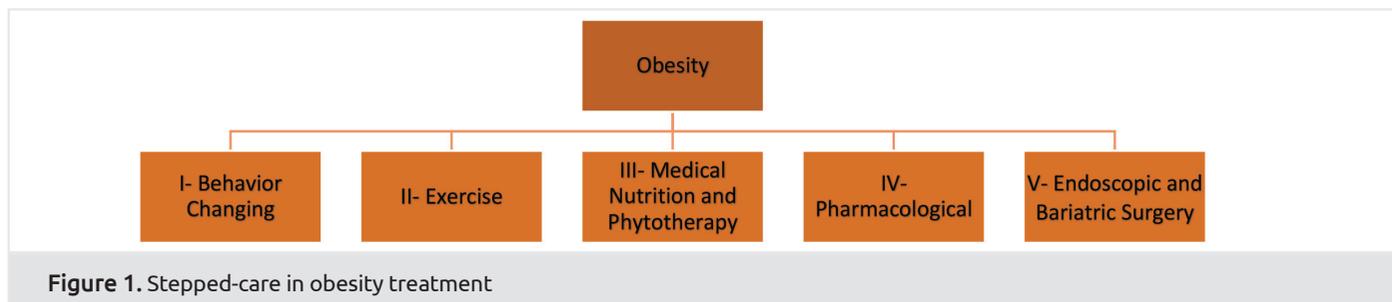


Figure 1. Stepped-care in obesity treatment

Table 1. Five-year follow-up data in laparoscopic sleeve gastrectomy surgery (26)

	Presurgery	Follow-up Year 1	Follow-up Year 2	Follow-up Year 3	Follow-up Year 4	Follow-up Year 5
Number of patients	N=140	N=123	N=99	N=77	N=52	N=44
Body weight (kg)	112.3±20.0	83.1±17.0	84.5±18.6	86.8±18.8	91.0±20.5	89.1±18.3
Rates of patients with successful weight loss (% EWL >50%)		79.2%	71.7%	58.4%	55.8%	54.5%
Rates of patients with unsuccessful weight loss (% EWL <30%)		7.3%	9.1%	13.0%	25.0%	22.7%
Weight regain (% REWL >25%)		--	1.0%	11.6%	19.2%	29.5%

REWL: , EWL: ,

Table 2. Weight gain data after laparoscopic sleeve gastrectomy (27)

	Follow-up duration 33 months
Total number of patients N=110	14 kg (12.7%)
Weight regained	

through it, thus limiting calorie intake. SG is usually performed laparoscopically and can provide up to 70% weight loss within 1 year, which is maintained for at least up to 3 years (18). It is the most commonly used method today.

6.3. Roux-en-Y Gastric Bypass

In Roux-en-Y gastric by-pass (RYGB), the stomach is divided from the upper part to create a small proximal gastric pouch. The small intestine is also separated at the jejunal level, where the distal part of the intestine is connected to the new gastric pouch. As a result, the digested food passes through the lesser sac and directly into the distal part of the small intestine, thus bypassing the proximal part and limiting absorption. The middle part of the cut intestine, the distal part of the stomach, and the proximal part of the small intestine are reconnected to the small intestine further down, allowing digestive enzymes to mix with the more distally digested food. RYGB is most often performed laparoscopically and provides an estimated 73% weight loss within 1 year. Serious complications include anastomotic leaks (3-5%) and internal bowel herniation (3.1%), which has the potential to lead to intestinal obstruction and perforation.

6.4. Biliopancreatic Diversion with Duodenal Switch

Biliopancreatic diversion with duodenal switch (BPD-DS) is a two-stage, open or laparoscopic procedure and is usually irreversible. First, a SG-like gastrectomy is performed by leaving a tube-shaped pouch. Secondly, the small intestine is cut in two places; proximally just after the pylorus and distally approximately 250 cm before the ileocecal valve. The distal small intestine is elevated and anastomosed to the duodenum. The distal end of the middle piece is then anastomosed to the small intestine approximately 100 cm before the ileocecal valve. Although mortality rates remain low (<1%), BPD-DS is a more complex

procedure and is associated with perioperative anastomotic leaks (3-4%) and splenectomy (<1%), and subsequent malnutrition (4%), internal herniation, and small bowel obstruction. It has complications such as (2-7%) (19).

6.5. Complications of bariatric surgery

6.5.1. Weight regain after surgery

Bariatric surgery (BS) is currently the most effective intervention for severe obesity. Unfortunately, patients experience some weight regain (WR) after reaching their lowest weight. Approximately 20-25% of patients struggle with significant WR after BS. Similarly, suboptimal weight loss (SWL) (patients' weight loss <50%) is the most common reason they undergo revisional BS.

Although some researchers have proposed behavioral and biological mechanisms for WR (20), preoperative factors that predispose patients to significant WR remain unclear. Additionally, it is important to note that WR is associated with deterioration of quality of life and recurrence or worsening of obesity-related comorbidities such as hypertension and type 2 diabetes (T2D), which require close monitoring and appropriate management. Additionally, revisional BS performed to manage WR/SWL may result in higher complication and mortality rates compared to primary BS (21). Basic studies focusing on long-term outcomes after BS show that patients generally regain 5% to 10% of their total weight loss within the first decade (22).

WR is defined as progressive weight gain that occurs after initially successful weight loss (defined as extreme weight loss, >50%) has been achieved. Despite the lack of a standardized definition of WR and poor reporting of its clinical significance, according to the results of a study conducted on 1,406 patients, it was reported that the rates of WR ranged between 44% and 87% five years after RYGB. Moreover, the percentage of maximum weight loss, progression of T2D and hypertension, decreased quality of life, and decreased satisfaction with surgery are observed (23).

In a randomized prospective multicenter Swedish study, 10 years after laparoscopic adjustable gastric banding, patients regained 38% of the maximum weight they lost in 1 year (24), and in a long-term follow-up of more than 7 years, patients lost weight after laparoscopic SG. It was stated that the recovery rate was 27.8% (range 14-37) (25). In the light of data obtained from

studies conducted over the years, the tables for WR are presented below.

Publications in BS are largely based on evidences from randomized clinical trials with follow-up of only 1 to 3 years. The evidence includes single-site studies with small sample sizes, inadequate follow-up (>1 year), and lack of non-surgical comparison groups (29). Little is known about long-term (>5 years) maintenance of weight loss after BS. These may be due to factors associated with weight regain, study participant discontinuation, and loss to follow-up, which may lead to an inaccurately optimistic conclusion regarding the effectiveness of BS-induced weight loss when follow-up is not completed (less than 80%).

Despite the lack of quality long-term studies, available evidence suggests that the benefits of BS are not universal. Weight gain and recurrence of diabetes may occur in a significant proportion of patients (30). It is estimated that 10% to 30% of patients undergoing BS experience suboptimal weight loss. Indeed, SWL and WR are key factors associated with diabetes relapse, which may occur in 20-30% of patients who achieve remission 5 years after BS. Additionally, a proportion of patients undergoing BS also experience decreased recovery from other comorbidities (13%, 11%, and 4% of T2DM, hypertension, and LDL-cholesterol patients, respectively, after 6 years). However, the lack of high-quality long-term data makes it difficult to predict effects on many comorbidities.

In addition, all bariatric procedures affect nutritional intake and can also have an impact on the absorption of micro- and macronutrients, especially procedures that affect absorption (RYGB, SG, BPD-DS). Most patients will require lifelong nutritional supplements as well as a balanced diet.

It is also known that surgical treatment has effects on the psychology of patients. An increase in harmful behavior and suicide risk has been reported in patients after BS, and although the biological and behavioral mechanisms behind this are unclear, possible hypotheses include changes in the absorption of drugs, imbalances in peptides, hormones, and glucose. There is also evidence of the development of postoperative eating disorders (such as anorexia nervosa and bulimia nervosa), which may occur as a result of the dramatic changes in eating patterns specific to BS (31). Patients undergoing BS should be counseled regarding potential nutritional disorders.

6.5.2. Other Complications

The increasing prevalence of obesity has also led to an increase in the number of bariatric procedures. As a result, there is an increase in the complications of patients undergoing surgery. Complications encountered in patients can be classified in various ways. These include dumping syndrome, tachycardia, fistula, bleeding, herniation, anastomotic stenosis, gastric erosion, small bowel obstructions, deep vein thrombosis and pulmonary embolism, post-operative pneumonia, complications due to malnutrition, hepatobiliary complications, gastric ulcer, intestinal-related symptoms, mesenteric vein or portal system thrombosis and neurological complications (32).

The high side effects of pharmacological and bariatric surgical treatments and the inability to make regular lifestyle changes and exercise practices have led physicians to search for new approaches in obesity treatment. In this context, the use of medical nutrition treatments and phytotherapy products has recently become the focus of discussions. In addition, phytotherapy products have attracted attention with their ability to be used alone or in combination with other methods.

7. Medical Nutrition and Phytotherapy in Obesity

Phytotherapy is used alone or in support of drug treatment in many diseases. Interest in phytotherapy products is increasing day by day. There are many herbal products on the market in the form of dry extracts, concentrated plant extracts, tablets and capsules containing herbal mixtures, aqueous-alcoholic extracts and tinctures. However, information about the effectiveness, reliability and quality of most of the products used by patients for this purpose is insufficient. However, the mechanism of the active ingredients in the plant used, the bioactive phytochemicals responsible for the anti-obesity activity and the standardized dose should be known. There should be no side effects if possible, and possible side effects should be described.

When looking at the functional ingredients in natural anti-obesity products, it appears that the consumption of phytochemicals can greatly contribute to biological effects. The mechanisms of action of phytochemicals are preventing the proliferation of precursor cells, increasing the effect of apoptosis, inhibition of pancreatic lipase activity and increase in energy expenditure (33).

Polyphenols are functional compounds with anti-carcinogenic, anti-oxidant, anti-bacterial and anti-viral activities. In the last two decades, polyphenols have been reported to have beneficial effects against obesity. For example, dietary polyphenols can regulate adipocyte metabolism to inhibit the growth of adipose tissue (34).

Flavonoids are abundant in nature. It has been proven that it has positive effects against obesity. They can modulate a number of cell signaling pathways to influence carbohydrate digestion, fat accumulation, rate of insulin release, and glucose uptake in insulin-sensitive tissues.

Phytosterols, which include plant-derived sterols and stanols, are compounds structurally similar to cholesterol. They are found in high concentrations in vegetable oils such as corn, soybean and sunflower oil. It has been proven that plant stanols and sterols can block intestinal fatty acid absorption and reduce body weight gain in animal tests (35).

Being natural (safe, harmless), having few side effects, thinking that professional help is not required, being easily purchased (pharmacies, herbalists, internet, etc.), increasing popularity of complementary medicine can be considered as the reasons why people turn to herbal treatments. There are many natural products used in this field and therefore there are different classifications. The classification made by us according to its comprehensiveness and widespread use is given below (Table 4).

Table 3. Weight regain rates for Roux-en-Y gastric bypass (28)

	Weight regain groups			
	<25% N=39	25-30% N=51	30-35% N=73	>35% N=113
Excess weight regain percentage defined as greater than 25% of total weight loss	%38.5	%35.3	%32.9	%38.1
Average weight regain percentage	23.4% N=276			

Table 4. Mechanism of action of phytotherapeutic agents used in the treatment of obesity

A	Those that increase fat burning and stimulate metabolism
B	Appetite suppressants
C	Those that create a feeling of fullness
D	Those who control blood sugar and insulin
E	Those that inhibit the absorption of carbohydrates and fats
F	Those that inhibit inflammation

A. Those that increase fat burning and stimulate metabolism

While they have effects that increase thermogenesis and fat burning, they control energy balance. The most well-known plants that act by stimulating metabolism are sea grape, bitter orange, coffee, green tea and red pepper.

a. Sea grape, Ephedra (*Ephedra sinica*)

Ephedra alkaloids (such as ephedrine) found in the plant are effective on the sympathetic nervous system. Ephedrine reduces appetite by increasing the release of norepinephrine. While its effect on the central nervous system is low, its peripheral effects are much greater than other appetite suppressants. Additionally, ephedrine increases heart rate, blood pressure and thermogenesis (36). The American Food and Drug Administration banned the use of products containing Ephedra in 2004.

b. Fucus, Bladderwrack (*Fucus vesiculosus*)

The most important active ingredient of *Fucus vesiculosus*, a seaweed, is iodine. Due to their high iodine content, seaweeds increase thyroid hormone production and, accordingly, accelerate metabolism and burn fat. Preparations prepared from the thallus of the plant are marketed as helping to lose weight, but there is no scientific study supporting the effectiveness of the plant in weight loss (37).

c. Bitter orange (*Citrus aurantium*)

Bitter orange (*Citrus aurantium L.*) is a plant whose extract is used to treat many ailments and diseases. Bitter orange extract is also used in weight loss supplements. Because it contains weight loss properties such as appetite control and energy conversion. More than 90% of the protoalkaloids contained in it include p-synephrine, a phenylethylamine derivative structurally similar to ephedrine. Pure p-synephrine increases energy expenditure and accelerates resting metabolism, leading to weight loss. Bitter orange extract not only supports weight loss, but also has

antitumor, cytotoxic, sedative, antidiabetic, antioxidant and stomach ulcer protective properties (38).

d. Caffeine and Caffeine-Carrying Plants

Many studies have been conducted on caffeine, thinking that it may cause weight loss due to its thermogenic effect. It is known that caffeine causes thermogenesis by two separate mechanisms (by inhibiting phosphodiesterases responsible for the breakdown of noradrenaline; by stimulating the free fatty acid-triglyceride cycle and the Cori cycle, which converts glycogen and glucose into lactate). Caffeine also suppresses appetite. Although caffeine was found to be a fat burner in studies conducted on experimental animals, no significant change in fat burning was observed with long-term administration to humans, suggesting that the metabolism became insensitive to the effects of caffeine over time (39).

e. Green tea, (*Camellia thea* = *C. Sinensis*)

In addition to caffeine, green tea contains high amounts of phenolic compounds (epicatechin, epicatechin gallate, epigallocatechin, epigallocatechin gallate [EGCG], fractionin, myrcetin). It is known that catechins have a thermogenic effect by inhibiting the catechol-O-methyl-transferase (COMT) enzyme, which breaks down noradrenaline. Thus, tea has a thermogenic effect both by phosphodiesterase inhibition due to caffeine and by COMT inhibition due to catechins and it is thought that it may be effective in the treatment of obesity. It has also been found that EGCG can prevent the development of adipose tissue by inhibiting angiogenesis, thus it can be used to protect against obesity and prevent WR (38).

f. Guarana (*Paullinia sorbilis* = *P. cupana*)

It is declared that Guarana seeds are included in the formulation of many recently released products. While a short-term increase in blood pressure and heart rate was observed, the thermogenic effect was observed to be permanent (40).

g. Mexican Pepper (*Capsicum annuum*)

The fruits of the plant contain high amounts of capsaicinoids. These (capsaicin and dihydrocapsaicin) are the active ingredients that give red pepper its burning taste. Capsaicin has been found to increase thermogenesis by dose-dependently increasing catecholamine release from the adrenal medulla. When administered by injection or orally, capsaicin stimulates the sympathetic nervous system, thereby increasing lipid circulation and causing a decrease in adipose tissue mass (39,40).

B. Those Affecting Appetite

Some of the plants in this group regulate intestinal functions due to the fibers they contain. Soluble fibers swell with water and form mass, delaying the absorption of other nutrients, slowing down the increase in postprandial blood sugar and creating a feeling of fullness.

a. *Amorphophallus konjac*

Three different randomized clinical studies have shown that glucomannan can help lose weight when used 3-4 grams daily. However, the number of subjects used in these studies is very small (n=20-50) and there are some methodologic errors. In another study, glucomannans were found to be ineffective (41).

b. *Plantain, Psyllium, Ispaghula (Plantago ovata)*

The seeds of the plant are widely used in the composition of preparations that help lose weight. Studies have shown that the seeds create a feeling of fullness due to their mucilage content. However, it has been determined that this effect is short-term and although it regulates lipid and glucose metabolism in Type II diabetic patients, it does not have any effect on obesity. The use of seeds in high amounts may cause gastrointestinal side effects such as bloating, nausea, and diarrhea (42). On the other hand, some physicians recommend the use of psyllium to prevent side effects (oily stool, gas, etc.) seen during orlistat treatment (43).

c. *Garcinia (Garcinia cambogia)*

Garcinia fruit and fruit peel extracts are thought to suppress appetite due to the hydroxycitric acid (50%) it carries, increase hepatic glycogen synthesis, and prevent the conversion of carbohydrates to fats and body weight gain through citrate lyase inhibition (37,43). For this reason, this plant is included in most food supplements produced for the treatment of obesity.

d. *Gurmar, (Gymnema sylvestre)*

Gymnemic acid and other triterpenic glycosides found in *Gurmar* leaves are known to reduce blood glucose levels in diabetic patients. Since excessive carbohydrate intake is among the causes of obesity, plant extracts are also used in the treatment of obesity. The only reported side effect of the extract is decreased taste sensation (40).

e. *Hoodia (Hoodia gordonii)*

It has been found that the substance coded P57, which is obtained from *hoodia* and has an oxypregnane type triglycoside structure, has an appetite suppressant effect. This substance is one of the substances found in low amounts in the plant extract, but has been isolated as the substance responsible for the appetite suppressant effect of the plant. Although the exact mechanism of action is unknown, it is thought that this compound creates a feeling of fullness by affecting the nervous system (44).

C. Those that create a feeling of fullness

Fiber-Fibrous or Mucilaginous Plants are not broken down or broken down to a small extent during digestion. They are either poorly absorbed or not absorbed. Fibers soften the stool

by increasing the weight and volume of the stool. They prevent constipation. They reduce the absorption of sugars from the intestine. They improve blood sugar control and the effects of insulin. They lower blood cholesterol levels and reduce the risk of heart disease. They create a feeling of fullness and do not turn into energy. They should be taken with plenty of water. Daily dietary fiber intake should not exceed 30-40 grams. Flaxseed, maltodextrin, beta glucan fibers, fenugreek fibers can be mentioned.

D. Those Which Control Blood Sugar and Insulin

Medicinal plants with hypoglycemic properties have been used all over the world for many years. There is increasing interest in the use of medicinal plants due to their low price, easy availability, and few or no side effects compared to hypoglycemic drugs. In this field, *Moringa oleifera* is used as food and traditional medicine to treat diabetes. Various reviews have reported existing evidence for the hypoglycemic property of moringa leaves (45). In general, the majority of studies have shown that consumption of moringa leaves lowers blood sugar. The mechanisms described in these studies for the hypoglycemic effect of moringa leaves include inhibition of α -amylase and α -glucosidase activities, increased glucose uptake in muscles and liver, inhibition of glucose uptake from the intestine, decreased gluconeogenesis in the liver. Additionally, no adverse effects of consumption of moringa leaves were observed in the studies reviewed. However, more human studies are needed (46).

Spices such as cinnamon, clove, bay leaf, and turmeric exhibit insulin-boosting activity in vitro. Among the various types of cinnamon, *C. zeylanicum* is known as an effective alternative for diabetes. One of the major components in bark oil from *Zeylanicum* is the 'cinna' aldehyde (roughly 65-80%), which appears to reduce plasma blood glucose concentration more effectively compared to metformin. Cinnamon increases the expression of proteins related to glucose transport and insulin signaling and regulates dyslipidemia (47).

E. Those That Inhibit the Absorption of Carbohydrates and Fats

a. Chitosan

Chitosan is a glucosamine polymer obtained from the shells of animals such as lobsters, crabs and shrimps. It is thought to act by binding to fats and preventing absorption, similar to fibers, but its mechanism of action and effectiveness have not been fully proven. Some researchers think that chitosan may aid weight loss when administered with a calorie-restricted diet. However, according to clinical studies, oral use of chitosan without calorie restriction is not effective in weight loss (48).

b. Carnitine

L-carnitine is an amino acid produced from lysine and methionine in the liver and kidneys. It is necessary for the long-chain fatty acids found in dietary fats to be transported to the mitochondria and converted into energy. In carnitine deficiency, many of the fats taken with food cannot be converted into energy and

accumulate in the body, causing obesity. Many studies conducted in animals have shown that carnitine accelerates the conversion of fats into energy. In a study conducted with volunteers who did and who did not do sports, it was determined that carnitine (4g/day) and antioxidant (vitamin C, vitamin E, methionine) supplementation could increase the exercise performance of those who did sports (49).

F. Inhibitors of Inflammation

Metabolic inflammation is a classic symptom of obesity. Chronic systemic inflammation of obesity can lead to adipose tissue and metabolic changes, and such inflammation is one of the fundamental mechanisms of obesity and metabolic syndrome.

a. Curcumin

Curcumin, also called diferuloylmethane, is the polyphenol of turmeric that is responsible for its yellow color. In addition to being used as a culinary spice, turmeric is also traditionally used as an herbal medicine in Asian countries. It has recently been shown that many of the health advantages of turmeric are attributed to curcumin, as it has anti-tumor, antioxidant, anti-inflammatory, antithrombotic, chemopreventive, antimutagenic, anticancer, anti-atherosclerotic (cardioprotective), lipid-modifying properties, anti-diabetic, antimicrobial, analgesic, pulmonoprotective, antidepressant and anti-aging properties. Curcumin may also provide protective effects regarding exercise-induced oxidative stress and inflammation, muscle soreness, and muscle recovery and performance in physically active individuals (50).

In addition, it has been stated that the consumption of **avenanthramide** extracted from oats, pear extract and malaxinic acid, its main antioxidant component, have antiobesity effects by reducing the inflammatory response by regulating the levels of inflammatory factors and inflammatory pathways (51,52).

CONCLUSION

Studies and publications of natural product extracts with antiobesity properties contain much controversy. High-quality research is needed to definitively determine the safety of the natural products. Some active ingredients and mechanisms of action of natural product extracts have not been identified. Research is needed to elucidate the antiobesity effectiveness and mechanism of action of natural products. There are very few natural products that have entered clinical trials and are approved for the treatment and prevention of obesity, because research data on dosages and active ingredients in animal models raise questions about human bioavailability and the availability of effective treatments. Apart from the mechanisms of action and herbs listed above, many other supplements continue to be used and hopeful in this field. Recently, it has been seen that studies on many effective phytotherapy products have been published in this field. Here, it is necessary to approach herbal products with caution, without knowing the product safety and mechanism of action, that is, those that are not recommended by physicians specialized in the field of phytotherapy.

There is no "Slimming Method" that can be applied to everyone regarding obesity. Weight loss treatment should be started after each individual is evaluated in all aspects and all processes are staged.

Changing lifestyle is the main goal of all treatment methods. Successful weight loss can be achieved through staggering therapy, changing the meals and amounts of food, exercises and increasing calorie expenditure, medical nutrition regulation and the use of phytotherapy products. In case of failure, pharmaceutical drugs and endoscopic methods are applied. If no results are obtained and the patient is morbidly obese, surgical methods should be preferred. Which surgical method should be chosen differs from person to person and should be determined according to accompanying comorbidities.

Studies have shown that no matter which method is chosen, there is a risk of SWL and WR. The risks and side effects of the chosen method should be discussed with the patient. Recommendations to the patient should be given after a multidisciplinary evaluation. Treatment should be started with the most appropriate and least risky method for the patient's current condition. A detailed evaluation should be made to ensure the compliance of the individuals, the deficiencies should be determined and the treatment plan should be made accordingly, and the patient should be assured that there is no patient who will not lose weight through staging. There is no patient who will not lose weight, it just takes time. Providing this assurance will increase patient compliance and success.

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