

Review on: Obesity Management

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Abstract

Obesity is a significant global health issue linked to several metabolic disorders, including diabetes, heart diseases, and high blood pressure. Traditional drug treatments often lead to side effects and have limited long-term effectiveness. This creates a need for safer and more effective alternatives. Phytopharmaceutical approaches offer promising methods for managing obesity by using bioactive compounds from medicinal plants. These natural agents help regulate lipid metabolism, boost thermogenesis, suppress appetite, and improve insulin sensitivity. Plant extracts like *Camellia sinensis* (green tea), *Zingiber officinale* (ginger), *Embolica officinalis* (amla), and *Trigonella foenum-graecum* (fenugreek) have shown notable potential in fighting obesity due to their antioxidant, lipid-lowering, and metabolism-boosting properties. This paper focuses on the role of phytopharmaceutical formulations in managing obesity, discussing their mechanisms, therapeutic benefits, and possibilities for creating safer, natural, and sustainable treatments.

Keywords: Obesity, Inflammatory, Adipocytes

Introduction

Obesity is a long-lasting and complex disease that has become a global epidemic, causing significant health and economic issues. Projections suggest that by 2030, about 1 in 2 adults in the United States will be affected by obesity. Additionally, obesity costs the U.S. healthcare system an estimated \$480 billion each year. The World Health Organization defines obesity as having an excess of body fat that raises health risks. Obesity is generally defined by a body mass index (BMI) over 30 kg/m². It impacts nearly every organ system in the body and is a risk factor for many serious conditions, including type 2 diabetes, hypertension, high cholesterol, heart disease, and some cancers. Obesity also directly lowers life expectancy. Furthermore, it is one of the most serious risk factors for hospitalization and death from COVID-19. While smoking is the leading risk factor for global diseases in some countries, high BMI has become the leading concern in areas like Australasia and southern Latin America. The outcomes of obesity and the effectiveness of weight loss treatments—such as lifestyle changes, anti-obesity medication, endoscopic procedures, and bariatric surgery—vary greatly among individuals. Recently developed classifications based on physiology and risk help identify these differences, which include factors like central obesity, metabolic issues, gastric function, and feelings of fullness.

These advances improve the assessment of individual patient risk and assist in identifying various processes related to obesity that could be targeted for treatment.

• Pathophysiology of Obesity

1. Morbidity

The physiological effects of a positive energy balance lead to excess calories being stored mainly in fat tissue. The increase in obesity is linked to diverse metabolic, inflammatory, immune, and mechanical changes that result in tissue damage and obesity-related health issues. The most significant health problems related to obesity include heart disease, type 2 diabetes, and cancer, with the highest costs associated with the first two. Here, we examine major obesity-related physiological changes and the associated health problems.

2. Obesity-related tissue dysfunction

Obesity-related fat accumulation overwhelms the body's ability to metabolize fats. This dysfunction can cause problems with the endoplasmic reticulum and mitochondria, increasing reactive oxygen species and free fatty acids and mediators like ceramide. Free fatty acids trigger various inflammatory kinases, leading to an increase in pro-inflammatory substances and immune cell infiltration. These inflammatory mediators also activate nuclear factor κ B, altering gene expression. These changes directly and indirectly affect insulin signaling, resulting in damaged tissue. All these alterations contribute to local and systemic inflammation.[1]

Causes of Obesity:

The causes of obesity are diverse and not due to a single factor, such as overeating. In most cases, including genetic obesity, the factors leading to obesity can be influenced. A multidisciplinary team is essential in creating a personalized plan and supporting those living with obesity. Healthcare professionals must recognize the complexity of obesity and understand that it is best managed with a multidisciplinary, patient-centered approach. Efforts to prevent and treat obesity must involve individuals and governments to promote a healthier environment.

The causes of obesity result from a mix of interconnected personal and societal factors. While many of these factors can be modified, managing

all contributing elements is challenging. The Foresight report describes these risk factors as 'connected' and categorizes them into clusters on an 'obesity chart' for easier understanding and management. These clusters include the physical activity environment, food consumption and production, individual psychology, and social psychology. Understanding these interconnected factors is vital for grasping the causes of obesity and working toward effective solutions to combat this global epidemic.

The causes of obesity are many and connected. To make it easier, we will describe them as factors that cannot be changed and factors that can be changed.

- Factors that cannot be changed

1. Genetic

2. The leptin-melanocortin pathway - Most research on genetic obesity has shown that the leptin and melanocortin circuit in the hypothalamus plays a key role in regulating appetite. Genes that are only active in this pathway are important for obesity.[2]

3. Hypothalamic obesity - The leptin-melanocortin pathway plays a role in other uncommon causes of non-genetic obesity, which are often called hypothalamic obesity. Lesional hypothalamic obesity happens due to an anatomical change in the hypothalamus, usually affecting the ventromedial and arcuate nuclei. This change can occur with cranial tumors like craniopharyngioma (the most common), glioma, or other tumors that involve the hypothalamus. Treating these tumors typically involves surgery and radiotherapy. Other conditions affecting the hypothalamus, such as neurosarcooidosis, tuberculosis, and Langerhans cell histiocytosis, can also contribute to this issue.[3]

- Factors that can be changed.

1. Epigenetics - Epigenetic changes influence how genes express themselves without altering the DNA sequence. These changes come from interactions with the environment and can be passed down through generations. Some obesity disorders, like Prader-Willi syndrome, occur due to errors in imprinting.[4]

2. Physical inactivity

3. Excessive caloric intake - Historically, the main idea in obesity science has been that it is simply an energy balance disorder, which means calories in, calories out. If this energy-based model of obesity were accurate, then exercising more and eating less should work for everyone. However, this isn't true for many people. Researchers think that the mechanisms behind obesity are more complicated. The carbohydrate-insulin model of obesity was first suggested by Gary Taubes in his book *Good Calories, Bad Calories* in 2007. It was later supported in 2018 by Ludwig and Ebbeling.[5]

4. The intrauterine environment - Obesity in mothers has long been recognized as the biggest risk factor for childhood obesity.[6][7]

5. Postnatal influences - The postnatal environment is very important for influencing weight gain over a person's lifetime. There are factors after birth that can be changed and that impact weight later in life.

6. Insufficient sleep

7. Drugs like Amitriptyline, Phenelzine, Citalopram causes higher levels of serotonin, dopamine, and norepinephrine boost appetite and may disrupt metabolism.[8]

8. Medical conditions like Insulinoma is a rare neuroendocrine tumor of the pancreas. It is mostly benign and causes weight gain along with symptoms of hypoglycemia due to the overproduction of insulin by the tumor cells.[9]

It is critical to understand that obesity is not a single condition but can present in many forms. Recognizing these different types can lead to more targeted and effective treatments. In this section, I describe the various types of obesity in adults, categorized by factors such as fat distribution, metabolic syndrome, genetics, and muscle-fat composition.[10]

Recommendations for obesity prevention and management

Based on the findings of this report, several key recommendations can guide practitioners and policymakers in tackling the obesity epidemic.

- 1) Implement multi-sector prevention programs that adopt comprehensive public health strategies to create healthier environments. Examples include financial measures (like taxes on sugary drinks), regulations on food labeling and marketing, and city planning that encourages physical activity. Such programs help lower population-level risk factors and make healthy choices more accessible.

- 2) Focus on lifestyle intervention programs to ensure that lifestyle changes are central to obesity management. Effective programs should assist individuals in improving their diet quality and increasing physical activity, as these changes can lead to a 5-10% reduction in body weight, significantly enhancing metabolic health and lowering obesity-related risks. Investing in community-based initiatives and support (nutritional education, exercise programs, behavioral therapy) is vital for both prevention and weight management.

- 3) Integrate clinical treatment options for individuals with established obesity, especially if they have related health conditions. Evidence-based medical interventions, such as GLP-1 receptor agonists and other approved anti-obesity drugs, can be offered alongside lifestyle changes for appropriate patients, under medical supervision. In cases of severe obesity, bariatric surgery should be considered, as it can lead to significant and lasting weight loss and improve or resolve comorbidities. Careful patient selection, thorough pre-operative evaluation, and continuous follow-up post-surgery are essential to maximize benefits and manage risks.

- 4) Strengthen early intervention and education. Emphasize obesity prevention early in life and provide ongoing education. This should involve nutrition and physical education in schools, early screening for obesity in primary care, and family-focused initiatives to instill healthy habits from a young age. Public health campaigns should continue raising awareness about the dangers of obesity and promoting lifestyle changes across all

age groups. Healthcare systems must also be ready to treat obesity as a chronic issue, offering long-term support and follow-up for weight maintenance rather than focusing solely on short-term weight loss.[11][12]

Choosing the best treatment for obesity depends on an accurate diagnosis. Many integrative and complementary approaches exist, including dietary programs, exercise, surgery, behavioral therapy, lifestyle changes, medications, and alternative treatments.

Medication strategies are suggested for treating obesity, mainly because they are non-invasive. Recommended drugs include sibutramine, fluoxetine, sertraline, orlistat, and topiramate, among others. However, these should be used cautiously, especially in patients with heart issues, as they might worsen the clinical condition.

When standard medical treatments cannot manage chronic conditions effectively without negative side effects, many individuals look for alternative therapies. Some of these treatments involve plant-based substances that might support weight loss by boosting metabolism or improving nutrition. Currently, obesity treatments based on dietary supplements are popular, indicating that traditional medicine and herbal treatments can be options in obesity management and prevention.

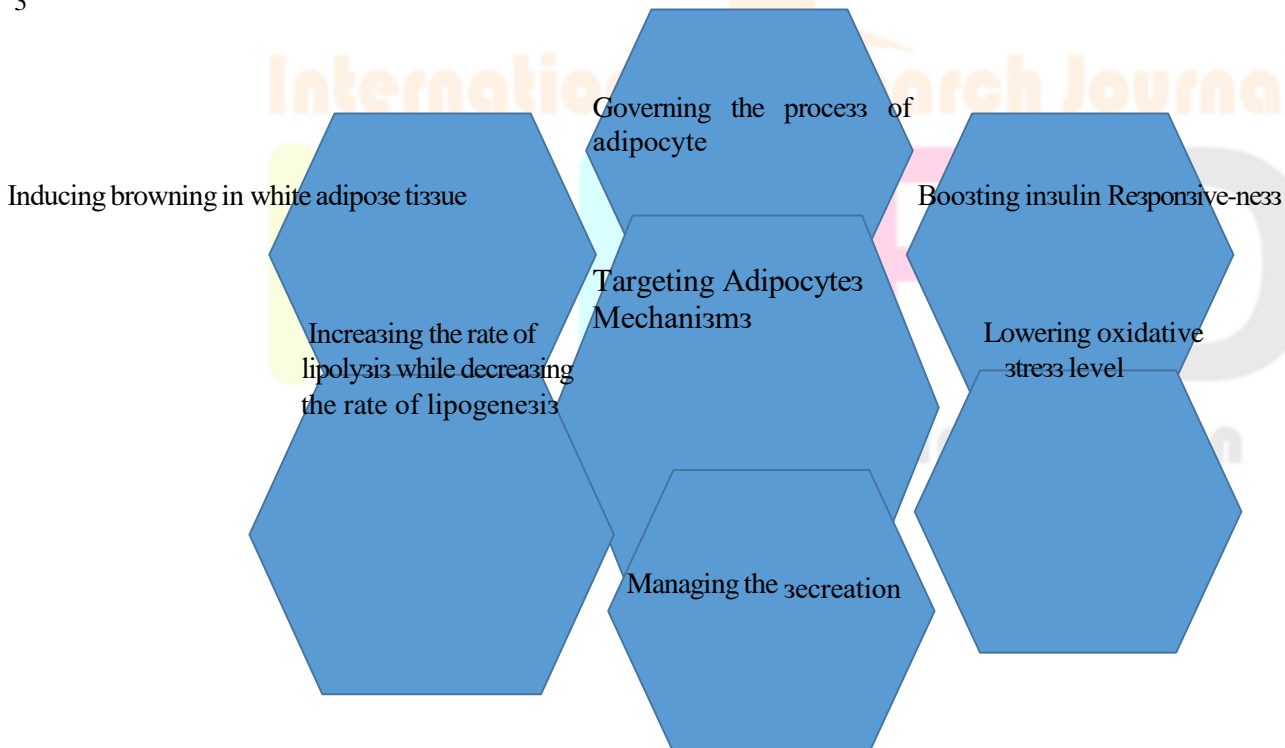
The medicinal use of plants arises from exploring their therapeutic benefits for treating and preventing various conditions. These methods rely on popular knowledge, making traditional practices valuable to scientific research. Such approaches also guide the selection of species for study and the development of herbal medications based on thorough research.

In this context, plant species are essential in providing extracts and chemical compounds that can serve as the basis for developing obesity treatments. However, all factors that qualify a plant as a potential treatment must be rigorously evaluated to ensure robust, safe, and reliable outcomes. Establishing evidence-based public health programs is necessary for creating

treatment strategies that consider cultural, social, environmental, and economic differences among countries. Translational research is key to defining parameters for this purpose, facilitating knowledge sharing among leaders, researchers, inventors, and business.[13]

Obesity is also referred to as chronic low-grade inflammation or "metabolic inflammation," which is often a central focus in understanding conditions like heart disease, atherosclerosis, and insulin resistance. Fat tissue is a complex organ that plays many roles in metabolism, including regulating energy use, appetite, insulin sensitivity, bone metabolism, reproductive and endocrine functions, inflammation, and immunity while storing fat. Visceral obesity is particularly linked to a greater risk of heart disease and diabetes compared to a high body mass index (BMI). However, the biochemical and physiological reasons for this stronger association with visceral fat remain unclear. One possible reason is that visceral fat directly influences the liver through the portal circulation, unlike subcutaneous fat. Adipocytes produce various proteins called adipokines, which are crucial in inflammation. These adipokines include TNF- α , leptin, resistin, visfatin, IL-6, and adiponectin, among more than 50 identified. They are primarily recognized for their roles in inflammation. Differences in adipokine production have been noted based on BMI; obese individuals tend to have fat tissue that produces more pro-inflammatory adipokines, while lean individuals produce more anti-inflammatory ones. Pro-inflammatory adipokines involved in creating inflammation include TNF, interleukin (IL)-6, leptin, angiotensin II, visfatin, and resistin. Anti-inflammatory adipokines include transforming growth factor-beta (TGF), IL-4, IL-10, IL-13, IL-1 receptor antagonist (IL1Ra), and adiponectin.[14]

3



- Approaches of Healthcare professionals

The management of obesity is greatly influenced by how healthcare professionals view and address obesity. Therefore, it is vital to assess our approaches to patients living with obesity.

The public's perception must shift to view obesity through a more compassionate lens for both children and adults. The stigma around being overweight negatively affects mental and physical health, leading to low self-esteem. According to the World Obesity Federation, weight bias contributes to the stigma surrounding obesity. There is a widespread belief where individuals associate laziness, low intelligence, poor hygiene, and lack of willpower with being overweight. While this perception is not a direct cause of obesity, it can be argued that it leads to an increase in obesity rates. Those who are obese often feel discouraged and hesitant to seek medical help. A study involving 10,854 individuals with obesity showed that support from healthcare providers and positive interactions helped encourage people to lose weight.

Clinicians emphasize the importance of a team approach in managing obesity. Obesity stems from various factors and needs input from a diverse team, including specialist nurses and dietitians, to create a personalized plan for each individual.[10]

On the other hand weight loss surgery runs out of the option considering the cost involved. There's a gradual shift towards an increase use of medicines. Medicines are pharmacological agents that reduce or control weight. These medicines alter one

of the abecedarian processes of the mortal body, weight regulation, by altering appetite, metabolism, or immersion of calories. Only one anti-obesity specific orlistat is presently approved by the FDA for long term use. It reduces intestinal fat immersion by inhibiting pancreatic lipase. Rimonabant, A alternate medicine frequently appertained to as "the munchies", had been approved in Europe for the treatment of rotundity but has not entered blessing in the United States and Canada due to safety enterprises. Sibutramine, which acts on the brain to inhibit deactivation of the neurotransmitters, thereby dwindling appetite was withdrawn from the United States and Canadian requests in October 2010 due to cardiovascular side goods. Because of implicit side goods, it's recommended that anti-obesity medicines only be specified for rotundity where it's hoped that the benefits of the treatment outweigh its threat.

The use of allopathic and pharmacological medicines has become a popular means to overcome redundant weight gain. Yet, these medicines generally are effective; severe adverse venom may limit their overall utility. A nutritive grounded intervention is being hailed as an affordable volition to prop weight loss and weight operation. Medicinal herbal supplements are being considerably employed due to their effectiveness in managing numerous habitual diseases. They are cost-effective and ply lower to no poisonous side-goods in comparison with numerous chemically synthesized medicines. Consequently, recent primary reports that sauces with a long history of use and other natural substances, which are less likely to produce severe toxin, might be effective in reducing appetite and promoting significant weight loss, are encouraging.[23]

- Herbs that can help manage obesity are as follows

- Green Tea:

Scientific classification:

Scientific name: *Camellia sinensis* Kingdom: Plantae

Order: Ericales Family: Theaceae Genus: *Camellia* Species: *C. sinensis*



Figure 2. *Camellia sinensis* (Green Tea) [20]

Chinese green tea, derived from *Camellia sinensis*, is originally from mainland China, South, and Southeast Asia, but is now grown worldwide in tropical regions. It is an evergreen shrub or small tree usually trimmed to less than two meters (six feet) for leaf harvesting. It has a strong taproot. The flowers are yellowish-white, 2.5-4 cm wide, and have 7 to 8 petals. The seeds from *Camellia sinensis* and *Camellia oleifera* can be pressed for tea oil, a sweet cooking oil that should not be mistaken for tea tree oil, an essential oil used for medicinal and cosmetic purposes from a different plant. The leaves measure 4-15 cm long and 2-5 cm wide. Young, light green leaves are often harvested for tea production; they have short white hairs on the underside. The older leaves are darker green. Different growing seasons yield various tea qualities, as their chemical compositions vary.

Typically, only the top bud and the first two to three leaves are picked for processing, and this handpicking occurs every one to two weeks.

Obesity and Weight Loss: Green tea extract

Standardized to 8.35% caffeine and 24.7% catechins has been shown to stimulate brown fat tissue in living organisms, producing thermogenesis

that exceeds what the caffeine content alone would cause. Long-term intake of tea catechins prevented body fat accumulation in mice fed a high-fat diet, possibly due to enhanced liver fat metabolism. This effect was also noted in non-obese rats. An open study found that an 80% ethanol extract of green tea, standardized to 25% catechins, led to a 4.6% reduction in weight and a 4.5% decrease in waist circumference over three months. However, a double-blind, placebo-controlled trial with 46 women showed no difference in weight loss or metabolic parameters between the placebo and green tea groups after 87 days. Several studies suggest that drinking green tea might help protect against obesity-related issues like atherosclerosis, diabetes, and hypertension. Interestingly, purified EGCG (50-100 mg/kg), but not other green tea catechins, significantly reduced or prevented weight gain in lean and obese Zucker rats, an effect that seemed reversible and was linked to reduced food intake.[15]

- **Ginger:**

Scientific classification:

Scientific name: *Zingiber officinale* Kingdom: Plantae

Order: Zingiberales Family: Zingiberaceae Genus: *Zingiber*

Species: *Zingiber officinale*



Figure 3. *Zingiber officinale* (Ginger) [21]

Ginger (*Zingiber officinale*) belongs to the ginger family (Zingiberaceae) and is commonly used as a spice and flavoring, particularly in Asia. Ginger contains various biologically active compounds, including phenolic compounds such as gingerols and shogaols, along with active ingredients like flavonoids and terpenoids. Recent research indicates that these compounds have health benefits. For instance, 6-gingerol, responsible for ginger's distinct taste, has been shown to have anti-inflammatory, antiseptic, and antioxidant properties; it also enhances immune function. Studies have revealed that ginger can aid in weight loss, having effects on low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), and triglyceride (TG) levels, while also raising high-density lipoprotein cholesterol (HDL-C) levels. However, the impact of ginger on fat cell metabolism in living organisms remains unclear.

Ginger, derived from the rhizome of *Zingiber officinale* Rosco (Zingiberaceae), is a well-known spice used extensively in cooking. It contains various phytochemicals and biologically active compounds, such as gingerols and shogaols. Beyond traditional medicinal use, ginger and its key active ingredients have been found to reduce obesity both in animal models and cell cultures. For example, ginger extract can prevent obesity induced by a high-fat diet and insulin resistance caused by excessive fructose in rats by regulating certain receptors and inflammatory pathways in fat cells. Additionally, 6-gingerol and 6-shogaol, two major active compounds in ginger, have shown anti-obesity effects by altering lipid metabolism enzyme activities and reducing the expression of various fat-storing proteins in rats and cell cultures. However, the potential of ginger supplementation to affect fat cell browning in obese mice has not been explored yet. [16]

- **Fenugreek:**

Scientific classification:

Scientific name: *Trigonella foenum graecum* Kingdom: Plantae

Order: Fabales or Leguminales Family: Fabaceae

Genus: *Trigonella*

Species: *Trigonella foenum graecum*

Figure 4. *Trigonella foenum graecum* (Fenugreek)



Fenugreek has shown medicinal and nutritional benefits. It has been used to help reduce body weight and manage metabolic issues. This is due to its essential active components, such as flavonoids, fiber, alkaloids, and amino acids, that lower intestinal absorption of carbohydrates and improve glucose regulation in the liver and muscles. Fenugreek also has antidiabetic, antibacterial, anticancer, antioxidant, and anti-anorexic properties. Moreover, it may work as an appetite suppressant by increasing the levels of cholecystokinin and glucagon-like peptide-1 hormones, which play a role in appetite control. When included in meals that contain carbohydrates, its high fiber content boosts the feeling of fullness among both obese and non-obese individuals, leading to reduced food intake and weight loss.

Fenugreek may also enhance insulin sensitivity by improving the insulin signaling pathway through upregulation of insulin receptors. This promotes glucose uptake and lowers blood sugar levels after meals. Its amino acid content, particularly 4-hydroxyisoleucine, encourages insulin release and helps regulate blood sugar, ultimately reducing food cravings and supporting weight loss. Therefore, Fenugreek is beneficial for individuals with diabetes or insulin resistance, as it lessens blood sugar response to carbohydrate meals.[17]

- Amla:

Scientific classification:

Scientific name: *Phyllanthus emblica* Kingdom: Plantae

Order: Malpighiales Family: Phyllanthaceae Genus: *Phyllanthus* Species: *Emblica*



Figure 5. *Phyllanthus emblica* (Amla) [22]

Amla, also known as *Phyllanthus Emblica*, *Emblica Officinalis*, or Indian gooseberry, is a medium-sized tree in the Phyllanthaceae family found throughout Asia and widely distributed in tropical countries. While various pharmacological properties exist within the whole plant, the Amla fruit has been used in traditional medicine. The potential anti-inflammatory, antioxidant, anti-hyperglycemic, and antihyperlipidemic effects of Amla are likely due to its rich content of ascorbic acid, phenols, and tannins, such as gallic acid and flavonoids. These combined compounds may explain its benefits for respiratory issues (like asthma and bronchitis), cancer, and conditions such as obesity, type 2 diabetes, and cardiovascular diseases reported in Chinese and Indian medicine. Additionally, the dietary fiber in Amla helps reduce cholesterol levels by inhibiting the enterohepatic recycling of cholesterol. The hydrophobic properties of Amla enhance its ability to form micelles in the intestine, interfering with cholesterol absorption. Although there is significant potential to explore bioactive compounds in plants for discovering modern medicines, the variability in outcomes from randomized controlled trials (RCTs) examining Amla supplementation on various risk factors for cardiometabolic conditions limits conclusive evidence. Therefore, this systematic review and meta-analysis aimed to assess the current evidence and evaluate the effectiveness of Amla supplementation for improving lipid profiles, blood sugar, and C-reactive protein levels in adults.[18]

The ethanolic extract of *E. officinalis* is reported to have various effects, including antidiabetic, antihyperlipidemic, and antioxidant activity in experimental animals. The goal was to evaluate the anti-obesity effect of dry *E. officinalis* extract in a high-fat diet (HFD)-induced obesity model. Male Wistar rats fed with HFD (20 g/day/rat) for 42 days were used to induce obesity. Dry *E. officinalis* extract (20 mg/kg body weight) was administered orally to the HFD-fed rats from day 8 to day 50 of the 42-day period. Body weight gain, serum lipids, insulin, and leptin levels were measured. The results showed that feeding the dry *E. officinalis* extract (20 mg/kg) to HFD-induced obese rats for 42 days significantly reduced body weight gain, insulin, leptin, and lipid levels compared to the rats fed HFD alone. Additionally, the extract also significantly increased high-density lipoprotein (HDL) levels. These results indicate that dry *E. officinalis* extract holds significant anti-obesity potential.[19]

- Advantages:

1. **Natural Origin and Safety:** Phytopharmaceuticals come from plants and natural sources, which reduces the risk of severe side effects often linked to synthetic anti-obesity drugs. They are generally better tolerated by the body and suitable for long-term use.
2. **Multi-Target Action:** Herbal extracts usually contain various bioactive compounds that work on multiple metabolic pathways at once. They can regulate lipid metabolism, appetite, fat absorption, thermogenesis, and glucose balance, offering a comprehensive approach to managing obesity.
3. **Improvement of Associated Metabolic Disorders:** Many phytopharmaceuticals help manage related conditions like diabetes, hypertension, and high cholesterol. They may lower oxidative stress and inflammation linked to issues arising from obesity.
4. **Reduced Risk of Dependency and Rebound Weight Gain:** Unlike some chemical drugs (such as appetite suppressants), phytopharmaceuticals are less likely to cause dependency or sudden weight regain after stopping use.

5. **Availability and Cost-Effectiveness:** Medicinal plants are often readily available and affordable, making phytopharmaceutical treatments more accessible, especially in developing countries.

6. **Potential for Novel Drug Discovery:** Researching plant-based compounds can lead to discovering new lead molecules that may become effective anti-obesity medications.

7. **Synergistic and Antioxidant Effects:** The interaction between phytoconstituents can enhance effectiveness. Many have antioxidant properties that help combat oxidative stress—a factor in obesity and metabolic problems.

• **Disadvantages:**

1. **Lack of Standardization:** The concentration of active compounds in plant extracts can vary based on the plant source, growing conditions, extraction method, and storage. This leads to inconsistent effectiveness and safety in herbal products.

2. **Limited Scientific and Clinical Evidence:** Many phytopharmaceuticals are mainly backed by traditional knowledge or early studies, with few clinical trials to verify safety, dosage, and long-term effects. This limits their acceptance in modern medicine.

3. **Difficulty in Dose Determination:** Because of multiple active compounds, finding the exact therapeutic dose is challenging. Overdosing or underdosing can decrease effectiveness or lead to side effects.

4. **Possible Drug-Herb Interactions:** Some phytopharmaceuticals may interact with conventional medications, altering how they are processed or their effectiveness. This can result in toxicity or reduced therapeutic effects in patients taking various medications.

5. **Quality Control Challenges:** The lack of consistent quality control standards and manufacturing regulations may lead to adulteration, contamination, or mislabeling of herbal products.

6. **Slower Onset of Action:** Compared to synthetic anti-obesity medications, phytopharmaceuticals often produce results gradually, requiring longer treatment periods for noticeable effects.

7. **Individual Variation in Response:** The effectiveness of phytopharmaceuticals can differ widely from person to person, influenced by genetics, metabolism, and lifestyle factors.

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