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Review Article

A Compherensive Review of the Anti-Obesity Properties of Medicinal Plants

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Abstract

Obesity has emerged as a global health crisis, contributing to numerous comorbidities including diabetes, cardiovascular diseases, and chronic inflammation. Although lifestyle modifications are recommended to prevent obesity, the increase of obesity in last years has revealed the importance of drug research. While bariatric surgery remains an effective approach, the limited number of approved pharmacotherapies for obesity necessitates further investigation into novel therapeutic agents. Currently, there has been growing interest in exploring the potential of plant extracts in the treatment of obesity. Phytoextracts, derived from a variety of botanical sources, have attracted considerable attention due to their therapeutic properties and perceived lower risk profile compared to synthetic pharmaceuticals. These extracts often contain bioactive compounds such as polyphenols, flavonoids, and alkaloids, which have been extensively studied for their anti-obesity effects. Research indicates that certain plant extracts can modulate weight control by influencing metabolic processes, overall health, and lipid metabolism. The integration of herbal extracts into obesity treatment regimens offers a holistic approach to health, presenting a natural alternative to conventional medicine. Moreover, plant extracts often exhibit pleiotropic effects, targeting multiple pathways involved in the pathogenesis and progression of obesity. This multifaceted mechanism holds promise for enhancing clinical outcomes while minimizing the risks associated with monotherapy. However, despite the evident potential, further research is essential to elucidate the precise mechanisms of action, optimize dosage regimens, and evaluate the long-term safety and efficacy of these interventions.

Keywords: Obesity, pharmacological interventions, plant extracts, metabolic processes, weight management

1. Introduction

Obesity is recognized as a global health issue and a condition that can lead to serious health implications. Epidemiological, etiological, and therapeutic research conducted in this field contributes to a deeper understanding of obesity. Various strategies are employed in the treatment of obesity, including pharmacological methods, bariatric surgery, and lifestyle interventions. Pharmacological treatments for obesity include medications such as Orlistat, which reduces fat absorption, and Liraglutide, which suppresses appetite, both of which may support weight loss (1, 2).

Various investigations have demonstrated that obesity is a global health problem associated with serious health consequences and its rapid spread has been well-documented (3, 4). It remains the most prevalent metabolic disease worldwide, driven by lifestyle changes characterized by reduced physical activity and altered dietary patterns. The escalating trend of obesity, affecting both adults and children, is closely correlated with a surge in non-communicable diseases such as type 2 diabetes, dyslipidaemia, cardiovascular ailments, hypertension, and stroke (5). Obesity's pervasive impact extends to various bodily organs, notably central obesity's influence on respiratory disorders like obesity-hypoventilation syndrome and obstructive sleep apnoea syndrome. Efforts to comprehend obesity's roots and devise effective treatments are imperative, alongside the implementation of preventive measures to limit its rising prevalence. Failure to address this issue will exacerbate its global spread, posing significant public health and economic challenges (3, 5).

Obesity, a prevalent and complex condition in the developing world, significantly deteriorates health-related quality of life. Individuals grappling with obesity experience detrimental effects on both physical and psychosocial functioning due to weight-related issues. Besides adversely impacting morbidity and mortality rates, obesity compromises the ability of affected individuals to lead full and active lives. The negative impact of obesity intensifies with higher degrees of obesity, exacerbating public health concerns, particularly with the rising prevalence of associated diseases such as diabetes. Interventions aimed at reducing weight have demonstrated potential to improve health-related quality of life (6).

Obesity, acknowledged as a global epidemic fuelled by the consumption of energy-dense yet nutrient-poor foods and reduced physical activity, remains a significant medical challenge. Despite lifestyle modifications being a primary management approach, demand for more effective treatments like gastrointestinal surgery has increased, albeit their limited use and associated risks. Currently, only orlistat and sibutramine are approved medications for obesity, yet both exhibit limited efficacy and restrictive side effects (1,7). The withdrawal of sibutramine underscores the urgent need for safer and more efficient anti-obesity drugs. While promising, most developed medications have faced approval hurdles or market withdrawal due to adverse effects (8). Notably, orlistat stands as the sole long-term approved drug, highlighting the critical necessity for further effective medication options. Furthermore, studies should carefully evaluate the long-term safety and effectiveness of recently produced medications, taking into account the fact that low-calorie diets are frequently used in clinical trials, which may have an impact on real-world weight reduction results (7,8).

The rising prevalence of obesity worldwide has sparked significant interest from a multitude of disciplines, driving researchers to investigate and synthesize modern approaches to tackle this complex health issue. Obesity, characterized by excessive body fat accumulation, is associated with significant health risks and imposes multiple socioeconomic burdens on both the individual and society. Given these challenges, it is crucial to consolidate the current approaches and methodologies for effectively addressing the obesity epidemic. This discussion aims to synthesize and provide an overview of the varied perspectives and methodologies represented in contemporary obesity research and intervention. By doing so, it will facilitate the ongoing dialogue on effective strategies for obesity management and prevention.

2. Diagnosis of Obesity

A chronic illness brought on by excess body fat is obesity. Ideally, body fat percentage should be considered when defining obesity. However, establishing a population based on body fat measurement is very impossible due to the complex technology needed to assess body fat. Consequently, there isn't always a set amount for body fat (Fig 1). In practical terms, obesity is therefore determined by body mass index (BMI), which takes height and weight into account: Weight (kg) / height (m^2) = BMI. BMI has a beneficial effect on disease and is correlated with total body fat. Different definitions of obesity have been created by the World Health Organization (WHO) based on the link between obesity and mortality and BMI (3). In Fig 1, obesity indexes are given in the BMI chart prepared in the BioRender program (9).

Moreover, changes in the nature of work, with many jobs requiring less physical exertion, along with urbanization, which may limit opportunities for physical activity and exacerbate the problem. Environmental and social shifts associated with development frequently lead to alterations in dietary patterns and levels of physical exercise. Furthermore, the lack of government support in critical areas such as business, education, urban planning, transportation, agriculture, health, and food processing and distribution further compounds these challenges. It is important to recognize that obesity is a multifaceted issue with numerous contributing factors, many of which interact and reinforce one another (11).The factors of obesity are given in Table 1. People must reevaluate their lifestyles, establish healthy eating habits, and get regular exercise in order to prevent and manage obesity.

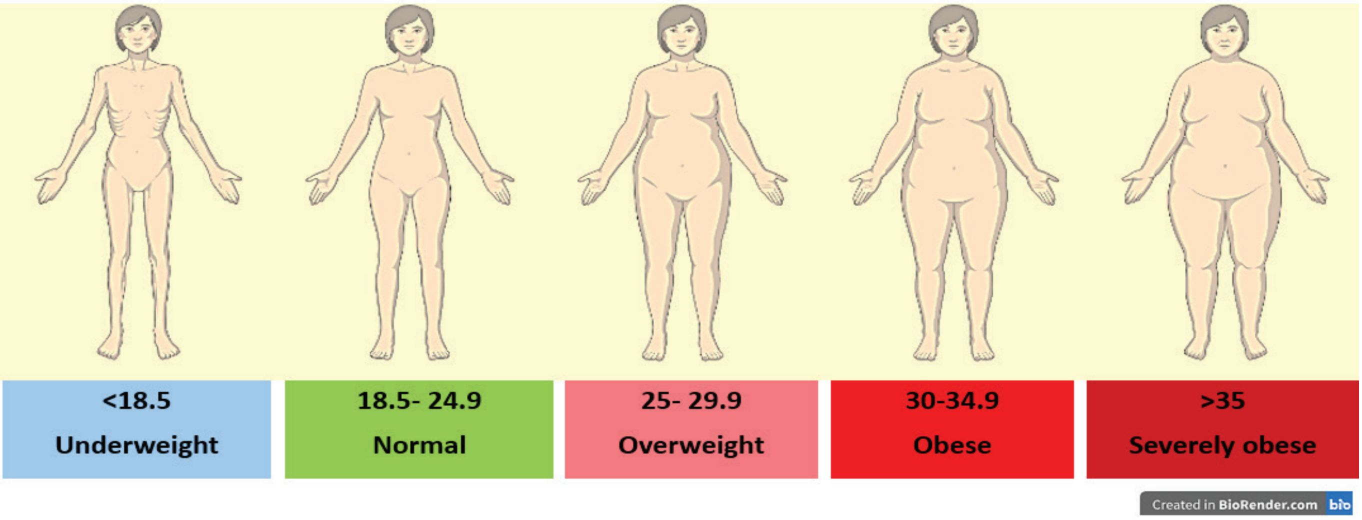


Figure 1. Body Mass Index (BMI) chart

Treatment for obesity should be seen as a way of life rather than as a quick "cure" for obesity. The American College of Physicians (ACP) advises that behavioural and lifestyle interventions, such as regular exercise, fitness, and good nutrition, be a part of fat and obesity control programs (10).

3. Pathophysiology of Obesity

The World Health Organization asserts that the fundamental cause of obesity and overweight is an imbalance between calorie intake and expenditure. This imbalance can be attributed to various factors worldwide, including increased consumption of sugar and energy-rich food, which often lead to reduced physical activity levels (WHO, 2021).

These variables differ from one person to another and frequently the factors above can combine (12). It may appear simple to attribute weight gain and obesity solely to long-term energy imbalance, however the pathophysiology of obesity is considerably more complex (Fig 2). Interactions among genetic, environmental, and psychological factors intricately shape food intake and energy expenditure. Although environmental and economic factors predominantly influence behavior and cannot be directly addressed at the molecular level, identifying genes and molecules associatedwith obesity reveals the underlying voluntary pathophysiological mechanisms at the molecular level (13).

Table 1. Determinants of obesity

Determinant	Description
Sedentary Lifestyle	Insufficient physical activity can disrupt energy balance and lead to weight gain. Prolonged hours of sitting and irregular exercise habits contribute to obesity.
Psychological Factors	Emotional eating, stress, depression, and other psychological conditions may drive some individuals to overeat, triggering weight gain.
Genetic Factors	Obesity may arise as a result of genetic predisposition; individuals with a familial history of obesity are at an increased risk of developing the condition themselves.
Metabolic and Hormonal Disorders	Metabolic and hormonal imbalances such as thyroid issues, insulin resistance, and hormonal fluctuations can affect weight control.
Alcohol Consumption	Alcohol is associated with high-calorie beverages and excessive consumption can lead to weight gain.
Pregnancy	Pregnancy can cause weight gain in women, and losing weight postpartum can be challenging.

4. Mechanism of Obesity and Endochronic Causes

The consumption of various energy-yielding macronutrients, including carbohydrates, proteins, and lipids, elicits undeniable metabolic effects contributing to the initiation of obesity (Fig 3). The relationship between macronutrient intake and the incidence of obesity involves complex physiological mechanisms regulating appetite, thermogenesis, and metabolic pathways, all intricately intertwined with an individual's genetic predisposition and the composition of their microbiota. The intricate interplay between an individual's genetic makeup and microbiota composition, coupled with their dietary behaviours and macronutrient intake, serves to elucidate individualized responses to shifting macronutrient compositions and dietary regimens. These nuanced revelations bear substantial potential in guiding the formulation of tailored precision nutrition interventions and individualized strategies aimed at mitigating the burden of obesity (14).

The convergence of central neurotransmitters and peripheral metabolic cues is widely acknowledged for its pivotal role in regulating energy balance, with profound implications for modulating feeding patterns and, consequently, impacting the development of obesity. Among the principal peripheral hormones implicated in the maintenance of energy equilibrium are leptin, ghrelin, insulin, peptide YY (PYY 3-36), and cholecystokinin (CCK) (15).

Globally, the escalating prevalence of obesity emerges as a pressing and imperative public health dilemma. While unhealthy dietary patterns and sedentary behaviours stand as primary instigators of the obesity epidemic, emerging research underscores the potential contribution of environmental chemicals to the etiologic of this condition. A substantial body of evidence indicates that certain endocrine-disrupting chemicals (EDCs) possess the ability to interfere with hormonally regulated metabolic pathways, particularly during critical developmental periods. Termed as "obesogens," these agents have the capacity to induce weight gain in susceptible individuals, even amidst efforts to restrict calorie consumption and enhance physical activity levels (16).

Figure 2. Obesity Pathomechanism (13)

4.1. Leptin

Leptin, a pivotal hormone in body weight regulation and adipose tissue management, exhibits a robust correlation with body fat composition in human, with serum leptin levels escalating proportionally in individuals with obesity (17). Prolonged activation of the leptin receptor can precipitate leptin resistance, either through hindering leptin signalling pathways or triggering hypothalamic proinflammatory responses due to heightened levels of saturated fatty acids, thereby instigating negative feedback mechanisms. Despite the multifaceted signalling initiated by the long form of the leptin receptor (Ob-Rb), involving over seven distinct pathways, the activity of suppressor of cytokine signaling-3 (SOCS-3) emerges as a plausible mechanism underlying leptin resistance observed in human obesity. Given the intricate integration of leptin-sensitive metabolic pathways with neuronal networks governing energy homeostasis, interventions aimed ameliorating leptin resistance demonstrate limited efficacy (18). Over the past two decades, genetic inquiries into both rare and common forms of obesity have unveiled two fundamental insights: firstly, the leptin-melanocortin pathway constitutes a pivotal circuitry in appetite regulation, and secondly, genes predominantly or exclusively expressed in the brain and central nervous system (CNS) assume a pivotal role in the ethology of obesity (19).

4.2. Adiponectin

In addition to its role in energy metabolism regulation, adipose tissue serves as a significant source of biologically active molecules known as "adipokines," which modulate diverse physiological processes. In the context of obesity, the aberrant production of adipokines stemming from excessive fat accumulation can precipitate the onset of obesity-associated ailments. Despite advancements in therapeutic strategies, extant treatments may encounter limitations, as the expansion of adipose tissue elicits oxidative stress and inflammatory cascades. Disrupted cytokine and adipokine secretion plays a critical role in the pathophysiology of issues such metabolic syndrome, cardiovascular diseases, respiratory disorders, diabetic retinopathy, and cancer. Pharmaceuticals such as pioglitazone and rosiglitazone have shown promise in the treatment of problems associated with obesity since their ability to effectively stimulate the expression of adiponectin (20).

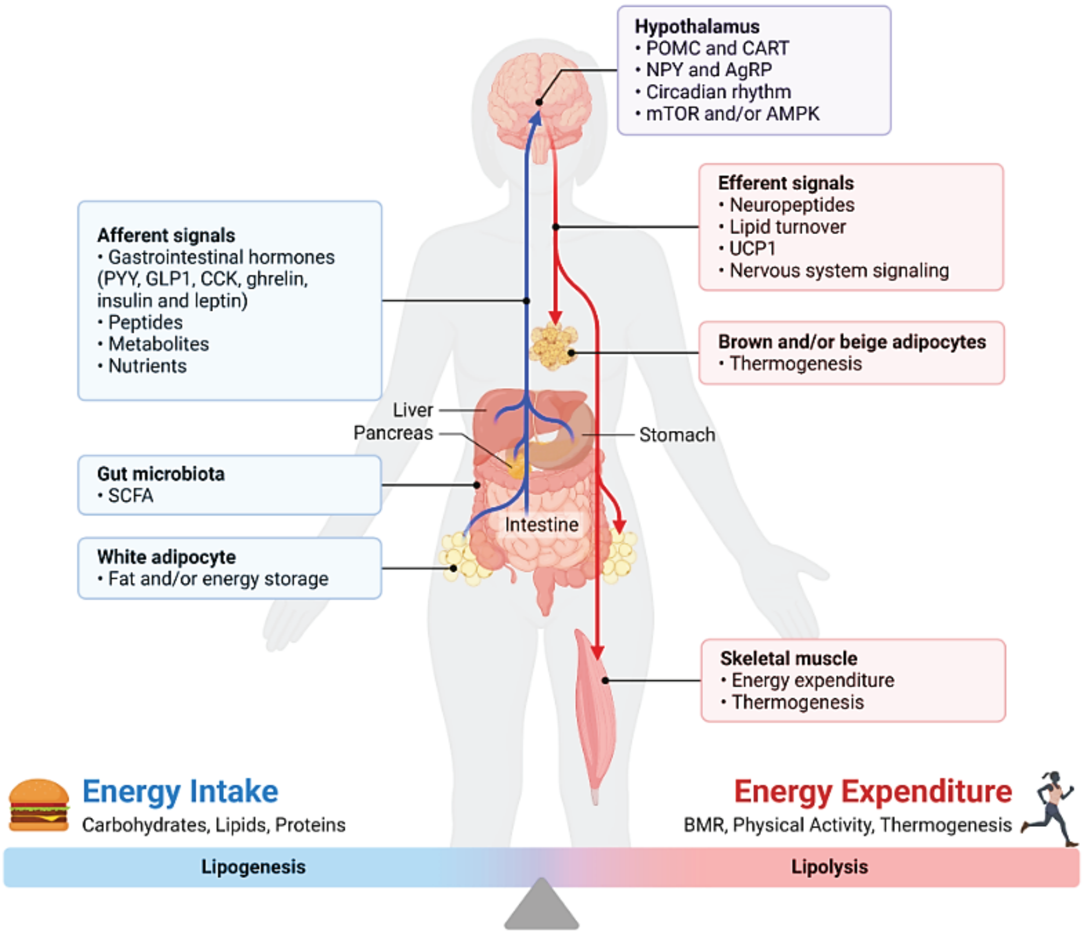


Figure 3. Key metabolic mechanisms of body weight regulation (14).

4.3. Vaspin

Vaspin, classified as a serine protease inhibitor and belonging to the serpin A12 family, was initially identified through research utilizing the Otsuka Long-Evans Tokushima fatty (OLETF) rat model, renowned for exhibiting symptoms of type 2 diabetes and obesity. Initially characterized as an adipokine predominantly secreted from visceral adipose tissue, subsequent investigations involving human subjects have corroborated this finding, highlighting a positive correlation between elevated circulating levels of vaspin and the presence of type 2 diabetes, obesity, and insulin resistance. The expression of vaspin is not limited to adipose tissue but extends to various organs within the human body, including stomach, liver, pancreas, and hypothalamus. Notably, despite being typically undetectable in visceral and subcutaneous adipose tissue among individuals with a lean body mass, vaspin mRNA expression increases with that mass. These findings underscore the potential significance of vaspin, particularly within visceral adipose tissue, elucidating its implications in the metabolic dysregulation observed in obesity (21).

4.4. Visfatin

Visfatin, a 52 kDa protein, is encoded by the PBEF/Visfatin gene situated on chromosome 7q22.2. This gene spans a length of 34.7 kb, encompassing 11 exons and 10 introns, primarily synthesized and secreted by immune cells, particularly macrophages. Visfatin's properties hint at its potential pivotal role in obesity and its related comorbidities. Its production can be attributed to adipocytes within visceral fat deposits or to macrophages dwelling in white adipose tissue, a process accentuated during obesity development. The theory emphasizing the substantial contribution of macrophages to Visfatin synthesis aligns with observed variations in Visfatin production across different adipose tissue types.

While mRNA expression levels in internal organs and subcutaneous fat tissue exhibit near uniformity in non-obese individuals, discrepancies surface among obese subjects. Specifically, visceral fat emerges as a prominent Visfatin source, whereas Visfatin production in subcutaneous tissue either diminishes or remains unaltered in the obese population (22).

5. Obesity and Health-Related Quality of Life

Overweight and obesity represent significant public health challenges due to their association with a wide array of severe medical conditions. These include various cancers such as breast, endometrial, ovarian, colorectal, oesophageal, kidney, pancreatic, and prostate cancers, among others. Additionally, conditions such as Type 2 diabetes, hypertension, stroke, Coronary Artery Disease, Congestive Heart Failure, asthma, chronic back pain, osteoarthritis, pulmonary embolism, gallbladder disease, and an elevated risk of disability are prevalent among individuals with overweight and obesity. The cumulative impact of these conditions results in over three million deaths annually. Moreover, early morbidity and mortality stemming from obesity and overweight during childhood and adolescence consistently correlate with an augmented risk of cardio-metabolic morbidity. The health repercussions of obesity and overweight pose a considerable burden, exerting a profound impact on future healthcare expenditures. A robust correlation exists between chronic medical conditions precipitated by obesity, diminished quality of life, and escalated healthcare and medication costs. Consequently, the healthcare expenses associated with health complications linked to obesity present a formidable challenge for individuals and healthcare systems alike. Thus, the implementation of effective measures to combat obesity and the cultivation of an enlightened society are imperative endeavours to ameliorate overall public health and address the dire consequences associated with this pervasive issue (23). At its very essence, obesity is a systemic condition that impacts much more than just physical appearance; rather, it extends to internal organs and metabolic activity.

Fig 4 represents the complex and multilayered effects of obesity on the human body. This graphic representation clarifies the interactive relation between obesity and some of the physiological systems and thereby provide insight into the profound ramification of excessive adiposity on general health. The figure also shows adverse effects on organ systems such as the respiratory system, with effects like obstructive sleep apnea; musculoskeletal system, with effects such as osteoarthritis; and the reproductive system, as seen with polycystic ovarian disease. Moreover, psychological and social consequences such as depression, stigma, and quality of life impairment are shown to highlight the holistic impact of this condition.

The World Health Organization has linked a number of serious non-communicable diseases to a higher BMI. Heart disease and stroke are indeed the leading causes of mortality among individuals with obesity, and elevated BMI serves as a significant risk factor for the development of these conditions. Similarly, high BMI is associated with diabetes, osteoarthritis, and other musculoskeletal conditions, as well as many types of cancer. The risk of developing these diseases escalates with higher BMI values. Furthermore, childhood obesity not only predisposes individuals to obesity later in life but also amplifies the risk of premature mortality and disability. Obese children may encounter a multitude of health complications, including respiratory difficulties, heightened susceptibility to fractures, hypertension, early indications of cardiovascular diseases, insulin resistance, and psychological ramifications (11).

Obesity is a serious health concern that goes beyond its individual status since it can increase the chance of developing a number of diseases by causing metabolic and cardiovascular problems. In this regard, it has been noted that obesity raises the chance of contracting a number of illnesses, including dyslipidemia, arterial hypertension, hyperuricemia, type 2 diabetes, and cardiovascular disorders (24).

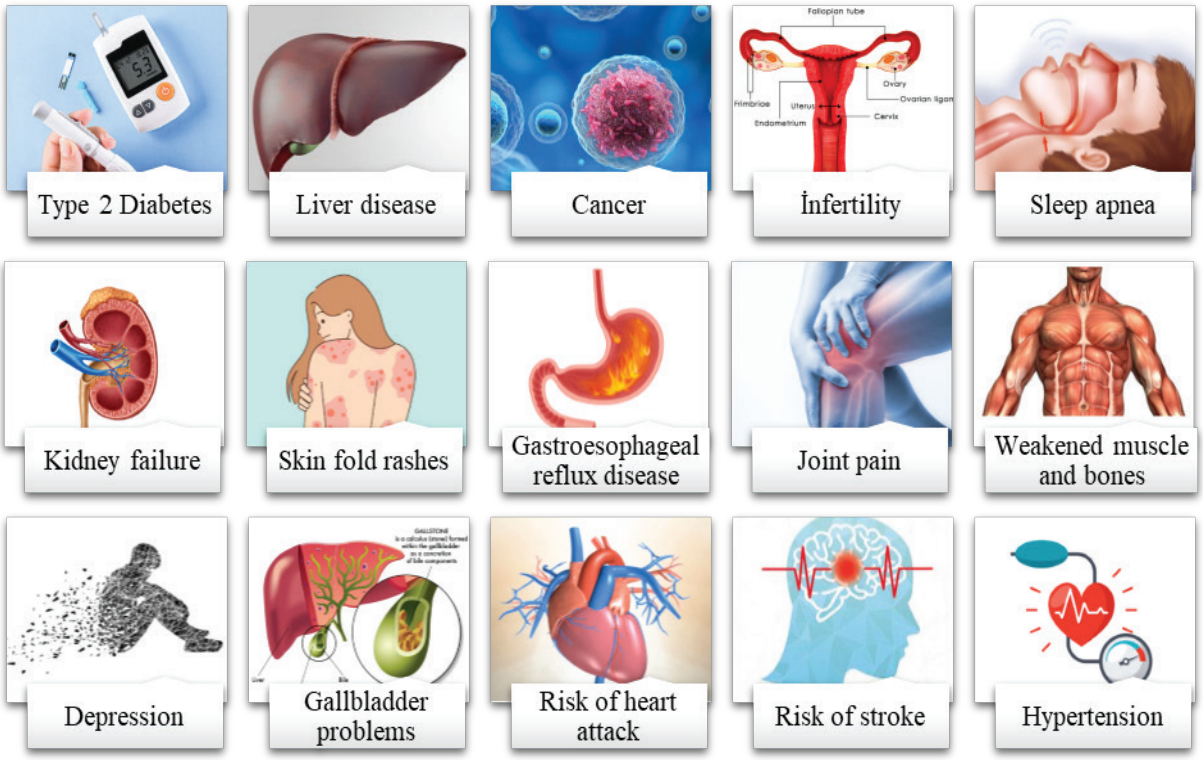


Figure 4. The effects of obesity on the body.

These diseases are among the most commonly triggered health issues associated with obesity. Additionally, obesity can have significant effects on the respiratory system and is strongly linked with respiratory tract diseases. Particularly, it is known to exacerbate respiratory problems such as hypoventilation syndrome and obstructive sleep apnea syndrome. Therefore, it should be emphasized that obesity has serious and diverse effects on overall health beyond being merely an aesthetic concern (3).

6. Treatment of Obesity

Obesity treatment involves many methods designed to address the complexity of this condition. Pharmacological intervention involves the use of medications to help control weight and is part of the treatment of obesity. These medications may work by decreasing appetite, absorption of nutrients, or increasing feelings of satisfaction. Another crucial component of treating obesity is bariatric surgery, which includes operations like sleeve gastrectomy and gastric bypass to change the digestive tract and lower stomach size, leading to weight loss. Lifestyle changes are the cornerstone of obesity management and often include diet, exercise and behavioural changes. These changes are designed to promote healthy eating patterns, increase physical activity levels, and create sustainable habits that encourage weight loss and proper weight maintenance. Additionally, behavioural interventions such as cognitive behavioural therapy or motivational interviewing can also be used to address psychological problems that lead to obesity. In summary, the treatment of obesity is multifaceted and includes medication, surgery, and lifestyle changes depending on the patient's needs and conditions.

6.1. Drug Treatments

A comprehensive multimodal approach to initiate and sustain effective obesity treatment is indispensable and also encompassing appropriate dietary modifications, consistent physical activity, and lifestyle adjustments are needed. Pharmacotherapy represents a viable option for individuals with accompanying comorbidities such as type 2 diabetes or those who are overweight. Anti-obesity drugs, classified based on their mechanisms of action, primarily fall into three categories: agents that enhance energy expenditure and thermogenesis, appetite suppressants, and inhibitors of fat absorption. Despite the numerous treatment

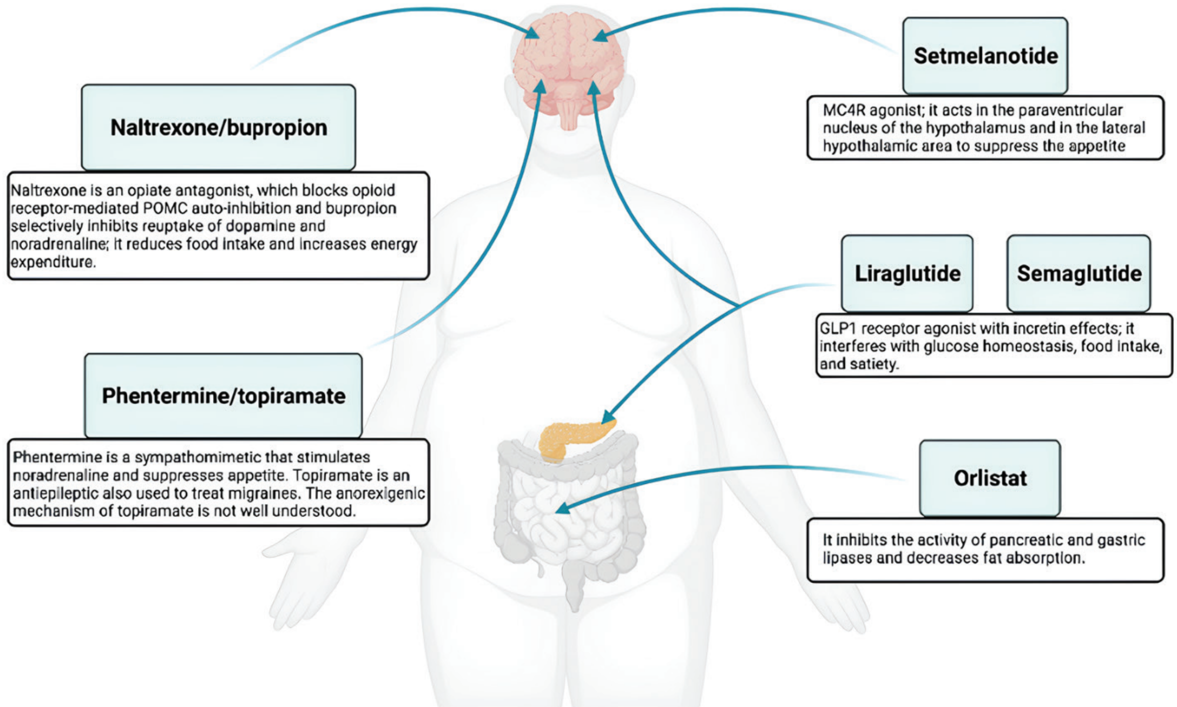


Figure 5. Summary of the mechanism of action for FDA/EMA approved anti-obesity drugs (13).

modalities employed over the years, the majority of anti-obesity therapies endorsed by the US Food and Drug Administration (USFDA) remain largely unavailable due to concerns regarding their safety and efficacy profiles (7). Among the pharmacological interventions recommended for managing obesity, Orlistat emerges as one of the most frequently prescribed medications. Orlistat facilitates weight loss by impeding fat absorption (1). Furthermore, promising outcomes have been observed with medications like liraglutide in combating obesity. It is known that Liraglutide helps weight reduction by suppressing appetite and enhancing feelings of fullness (2).

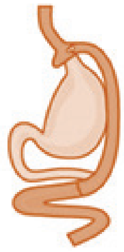
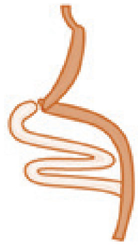
The United States Food and Drug Administration (FDA) has endorsed six major anti-obesity drugs, as depicted in Fig 5. However, the European Medicines Agency (EMA) has sanctioned only four medications for obesity management. This dissimilarity stems from the rejection of the phentermine/topiramate combination therapy by the EMA in 2013 and the ongoing assessment of semaglutide since January 2021 until the date of the current review (13).

6.2. Bariatric Surgery

Another avenue for against obesity is bariatric surgery, which has shown promise in alleviating obesity-related comorbidities (25). This invasive procedure involves altering the structure of the intestines or reducing stomach capacity to facilitate weight loss. However, it is crucial to carefully consider the pros and cons of different surgical techniques, as well as the suitability of each patient. Some bariatric surgery methods applied in the treatment of obesity are given in Table 2.

Bariatric surgery encompasses a range of surgical interventions aimed at promoting weight loss and managing health conditions associated with obesity. Candidates for these procedures typically include individuals with severe obesity, defined as a BMI of 40 or higher, or those with a BMI of 35 or higher who have obesity-related comorbidities, such as type 2 diabetes or hypertension, that may improve with weight reduction. While each bariatric surgery procedure aims to achieve weight loss and mitigate obesity-related health issues, they vary in their benefits, drawbacks, and potential risks. Therefore, selecting the most suitable treatment option requires careful consideration of patients' individual circumstances, medical histories, and lifestyles (26).

Table 2. Obesity bariatric surgery methods

Adjustable Gastric Banding (AGB)	Roux-en-Y Gastric Bypass (RYGB)	Vertical Sleeve Gastrectomy (VSG)	Biliopancreatic Diversion with Duodenal Switch (BPD/DS)
			
- A band is wrapped around the stomach to form a tiny pouch that can contain a tiny quantity of food. -The tightness of the band can be altered by adding or removing saline solution.	-A small gastric pouch is created by cutting the stomach. -Consumed foods are diverted away from the gastric body, duodenum, and proximal jejunum. - On the other hand, malabsorption of micronutrients such as calcium, iron, and vitamin B12 could happen.	-Approximately 80% of the stomach body is resected, creating a tubular-shaped stomach. -There is no need for a gastrointestinal-small intestine anastomosis. -This results in restriction on food intake, while speeding up gastric emptying.	-A sleeve gastrectomy is performed, followed by anastomosis between the bypassed intestine and the proximal duodenum. -This allows for partial malabsorption of nutrients. - Because of the high frequency of both short- and long-term problems, it is rarely practiced. (26)

6.3. Obesity Management Life Style Strategies

Lifestyle interventions are fundamental components of obesity management. Studies by Jensen et al. emphasize the efficacy of interventions such as nutritional counselling, structured physical activity programs, and behaviour modification strategies in tackling obesity. Embracing healthy dietary habits and maintaining regular physical activity are essential for achieving and sustaining weight loss. Additionally, the provision of psychosocial support and motivational guidance is vital for ensuring the success of obesity treatment journeys (27).

Nutritionists emphasize the detrimental impact of certain dietary habits, including reliance on diet culture, consumption of bakery products, processed foods (rich in refined carbohydrates), and excessive alcohol intake, all of which contribute to obesity development. Conversely, evidence suggests that incorporating breakfast and fruit consumption into one's diet can mitigate the risk of obesity, while evening snacking habits may exacerbate it. Attention is also drawn to the influential role of the school food environment and broader food landscapes, particularly in exposing school-age children to obesity risk factors.

Various scholarly investigations underscore the role of factors such as irregular physical activity or sedentary behaviour, excessive screen time, insufficient sleep duration or irregular sleep patterns, stress, obesogenic environments (linked to urbanization and industrialization), smoking, and frequent reliance on motorized transport as determinants of overweight and obesity. Prolonged screen exposure, for instance, may contribute to obesity development due to reduced glucose utilization by the brain during passive viewing. While scientific perspectives on the relationship between stress and obesity development vary, many researchers posit hormonal alterations as a potential contributing factor. Elevated cortisol levels, particularly in response to stress, can stimulate appetite and promote adipose tissue accumulation in the abdominal region, thereby exacerbating obesity risk (28).

Obesity is a complex health problem that is influenced by many lifestyle factors, including dietary habits, sedentary behaviours, psychosocial factors, and environmental influences. Poor dietary choices, such as the consumption of energy-dense, nutrient-poor foods and sugar-sweetened beverages, together with a sedentary lifestyle characterized by low levels of physical activity, explain most of the weight gain and accumulation of adiposity. Psychosocial factors, including stress, emotional eating, and low-quality sleep, disrupt appetite regulation and promote disordered eating, further increasing the risk of obesity. In addition, cultural and environmental factors, such as obesogenic food environments and social disparities, foster the predisposition to gain weight of the individuals' lifestyle choices. Fig 6 shows the closely linked lifestyle factors and overweight and obesity, representing a combined illustration of the multiple interactions between different individual behaviours and weight status.

7. Medicinal Plants in the Treatment of Obesity

Notwithstanding the availability of numerous commercial drugs used in the treatment of obesity and diabetes treatment, many are limited in their suitability for a broad patient population since they may pose adverse effects. Therefore, using various medicinal plants and the phytochemicals they contain to treat diabetes and obesity may lead to the development of safer substitutes. These alternatives not only transiently lower blood sugar levels but also contribute to preventing hypertension and cardiovascular diseases. The significance of these plants lies in their potential to regulate the antioxidant system, insulin effects, and secretion. Identifying dietary components capable of regulating fat accumulation and blood sugar levels is paramount. Flavonoids, or bioflavonoids, derived from the Latin word "flavus," meaning yellow, represent the most prevalent polyphenolic compounds found in plants. These substances, which are found in fungi and plants as secondary metabolites, have a 15-carbon structure with two phenyl rings and one heterocyclic ring. More than five thousand naturally occurring flavonoid types have been found in different plants, and since their unique chemical makeup, each one offers a wide range of advantageous benefits (29).

In order to explore their potential in preventing obesity, numerous edible and medicinal plants have undergone thorough examination in studies employing diverse methodologies, including in vivo animal models and in vitro cellular assays. These investigations aim to uncover the underlying mechanisms related with the observed decrease in body weight (30).

Epidemiological and experimental studies have shown that selected edible and medicinal plants have anti-obesity activity (30-34). These results suggest that plant sources may have contribute effects on weight management and obesity prevention by modulating metabolic processes through their bioactive ingredients (35-37). Furthermore, clinical investigations exploring the potential effects of herbal ingredients on obesity enhance the scientific foundation of treatment and prevention strategies, creating new opportunities for clinical applications (30).

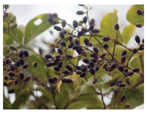
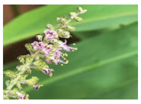
Earlier studies in literature related to the anti-obesogenic effects of such plants and the potential clinical application have been presented in Table 3. This review is based on findings from previous *in vitro* and *in vivo* studies. The table aims to provide a detailed overview of how these plants can contribute to the treatment of obesity by highlighting their mechanisms and evaluating their effectiveness based on scientific evidence.

Figure 6. Lifestyle factors associated with overweight and obesity.

Table 3. Anti-obesity potential of some medicinal plants.

Scientific Name (Plant)	Botanical Plant Images	Active Ingredient	Described Effect	References
Acacia mearnsii *de Wild.* **(Black wattle)**		Flavones (Flavan-3-ol catechins)	Upregulation of genes associated with energy expenditure in skeletal muscle and downregulation of fatty acid synthesis	(33)
Adiantum capilus veneris **(Maidenhair fern)**		Chlorogenic acid, Ellagic acid, Ferulic acid	Reducing weight gain Inhibiting pancreatic lipase activity	(34)
Allium cepa L. **(Onion)**		Quercetin	Significantly reducing lipids in 3T3-L1 cells Decreasing expression of lipogenesis-related genes, Restricting of lipid accumulation	(35)
Aloe barbadensis miller **(Aloe vera)**		Gallic acid, Quercetin	Reducing fat accumulation Activating fat lipolysis Improving oxidative stress	(36)
Brassica oleraea **(Red cabbage)**		Anthocyanidins	Inhibiting the activity of α-glucosidase and α-amylase	(37)
Camellia sinensis L. **(White tea)**		Flavones (Catechins) Alkaloids (Caffeine)	Serum triglyceride and non-esterified fatty acid levels	(38)
Capparis sicula ssp. sicula **(Capers)**		Rutin	Inhibiting pancreatic lipase activity	(39)
Carica papaya L. **(Papaya)**		Alkaloids, Saponins, Tannins, Anthraquinones, Anthocyanidins	Reducing triglycerides levels, LDL-C E VLDL-C	(40)
Centella asiatica **(Spadeleaf)**		Asiatic acid, Madecassic acid	Reducing in pancreatic lipase activity and α-amylase activity	(41)
Cinnamomum zeylanicum **(Cinnamon)**		Cinnamaldehyde	Reducing body weight gain Inhibiting the accumulative food intake Decreasing the secretion of ghrelin Reducing the gastric emptying	(42)

Cirsium setidens **(Gondre)**		Pectolinarin	Reduced intercellular lipid accumulation and lipid droplet sizes and numbers during adipogenesis	(10)
Coccinia grandis L. Voigt **(Scarlet gourd)**		Alkaloids, Cardenolide Glycosides, Phenols, Flavonoids	Reducing intracellular fat accumulation, as well as decreasing expression of PPARγ, C/EBPα, FAS, LPL, and GLUT4	(43)
Crataegus pubescens **(Tejocote)**		Gallic acid	Increasing excretion of faecal triacylglycerol Decreasing the accumulation of adipose tissue	(44)
Curcuma longa **(Turmeric)**		Curcumin	Changing into brown fat-like phenotype in white adipocytes, Cidea, Fgf21, Cited1 Increasing the brown adipocytes marker proteins, such as C/EBP-β, PGC-1α, PRDM16 and UCP1	(45)
Emblica officinalis **(Indian gooseberry)**		Terpenoids	Antidiabetic, hypolipidemic, and antioxidant effect, along with reducing serum AST and ALT levels	(46)
Garcinia cambogia **(Brindleberry)**		Hydroxycitric acid	Potentially inhibiting lipogenesis, including the inhibition of ATP-citrate lyase, and reducing triglyceride levels.	(47)
Garcinia cambogia Desr. **(Mala-bar tamarind)**		Hydroxycitric acid	Inhibiting the enzyme adenosine triphosphatase citrate lyase blocking lipogenesis	(48)
Hibiscus sabdarffa L. **(Roselle)**		Hibiscus acid, Anthocyanins, Flavonoids	Inhibiting activities of pancreatic lipase and α-amylase, cholesterol and triglycerides levels indicated reductions	(49, 50)
Hylocereus polyrhizus **(Red pitaya)**		Betacyanin's	Reducing body weight gain, modulating gut microbiota, downregulating the ratio of firmicutes and Bacteroidetes, increasing Akkermansia	(51)
Lactuca sativa L. **(Purple lettuce)**		Esculin, Chlorogenic acid	Decreasing body weight gain , reducing fat accumulation, Increasing energy consumption Regulating gut microbiota	(52)

Ligustrum robustum **(Kuding tea)**		Pomolic acid 19alpha-Hydroxyursolic acid	Inhibiting α-glucosidase	(35)
Litchi chinensis **(Lychee seed)**		Flavonoids	Inhibiting the differentiation of adipocytes, Downregulating PPAR-γ, C/EBP-α, -β, -δ and KLF9	(53)
Melissa officinalis L. **(Lemon balm)**		Hydroxycinnamic acid, Flavonoids	Blocking visceral obesity observed in female obese mice, Reducing increased fasting blood sugar, impaired glucose tolerance, and pancreatic dysfunction	(54)
Moringa oleifera **(Moringa)**		Isoquercitrin, Chrysin-7-Glucoside, Quercitrin	Decreasing TG accumulation in adipocytes	(51)
Morus bombycis Koidz. **(Mulberry)**		Alkaloids	Increasing lipolytic effects with decreased intracellular triglycerides and release of glycerol	(55)
Ocimum sanctum **(Tulsi plant)**		Ellagic acid, Epigallocatechin Gallate, Rutin	Increasing excretion of faecal triacylglycerol Decreasing the accumulation of adipose tissue	(44)
Orostachys japonicus **(*R*ock pine)**		Epicatechin Gallate, Quercetin, Kaempferol	Anti-adipogenic activity, inhibiting the major (PPARγ and C/EBPα) and minor (SREBP-1c, aP2 and leptin) adipogenic factors	(56)
Perilla frutescens **(Purple perilla)**		Rosmarinic acid	Decreasing body weight gain Upregulating ATGL and HSL in the adipose tissue and liver	(57)
Piper nigrum L. **(Black pepper)**		Alkaloids, Flavonoids, Tannins Saponins	Piperine suppresses the role of body weight, increases insulin and leptin sensitivity and ultimately balances obesity	(58, 59)
Portulaca oleracea L. **(Purslane)**		Crude	Decreasing total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL), increased high-density lipoprotein (HDL)	(60)
Rhizoma polygonati **(Huang jing)**		Kaempferol	Decreasing adipocyte differentiation markers, including PPARγ, SREBP-1c, Rxrβ, Lxrβ, Rorβ, Gpd1, Agpat2, and Dgat2, Increasing TNFα, Lsr, and Cel	(61)
Rubus coreanus **(Rubi Fructus)**		Ellagic acid	Reducing the weight of body and adipose tissue, Decreasing the expression of FAS, SREBP-1c, LXR, ACC, and LPL	(62)

Rumex pulcher L. **(Fiddle dock)**		Rutin, Luteolin, Apigenin	Preventing cardiovascular diseases by reducing oxidation of low-density lipoproteins	(63)
Salacia oblonga **(Ekanayaka)**		Polyphenols	Exhibiting antidiabetic, hypolipidemic, and antioxidant effects, along with reducing serum AST and ALT levels.	(46)
Salvia hispanica L. **(Chia)**		Quercetin, Chlorogenic acid, Caffeic acid	Chia oil increased glucose metabolism and it has revealed potential to protect against the development of obesity-related diseases.	(64, 65)
Solidago virgaurea **(Goldenrod)**		Keampferol-3-O-rutinoside, Chlorogenic acid, Protocatechuic acid	Reducing body weight gain adipose tissue size, WAT and liver fatty acid binding protein-4, PPAR-γ, C/EBP-α, FAS, SCD-1, SREBP-1c and CD36 inhibitory genes related to adipogenesis	(66)
Syzygium aromaticum **(Clove)**		Eugenol, β-caryophyllene	Reducing lipid accumulation Decreasing the weights of body and abdominal adipose tissue, Reducing the lipid deposition, Regulating TG, LDL-C	(67)
Terminalia paniculata **(Kindal)**		Polyphenols, Triterpenoids	Reducing body weight, inhibiting adipogenesis, Decreasing the expression of FAS, leptin, adiponectin, PPAR-γ, and SREBP-1c, Increasing the expression of AMPK-1α	(68)
Urtica dioica L. **(Stinging nettle)**		Caffeic acid, Chlorogenic acid, Malic acid, Rutin	It could potentially result in decreased weight gain induced by diet and improved insulin sensitivity.	(69, 70)
Vitis vinifera L. **(Grapes)**		Resveratrol, Flavonoids, Proanthocyanins, Stilbenoids	Containing tocotrienols, including significant amounts of α- and γ-tocotrienol (T3), which reduce the expression of mRNA protein (e.g., PPARγ and αP2), which are crucial for adipogenesis; reduces proinflammatory gene expression (IL-6 and IL-8)	(71)
Zingiber officinale **(Ginger)**		6-Gingerol	Improving obesity and inflammation downregulating the expression of microRNA-21/132 and activating AMPK in WAT	(72)

Among the plants used in obesity treatment, the primary plant metabolites that demonstrates anti-obesity effects through *in vivo* and/or *in vitro* biological tests explains their impact on delayed fat absorption, suppression of enzymatic activities, mediation of lipid levels, and enhancement of lipolytic effects. The plant species presented to the evaluation protocols for anti-obesity activity can be obtained from leaves, seeds, rhizomes, stems, flowers, fruits, and roots based on extraction solutions obtained through hot maceration, cold maceration, Soxhlet extraction, reflux, and accelerated extraction processes. Solvents used in extractive processes include water, ethanol, methanol, n-ethanol, hexane, n-butanol, dimethyl carbonate, and ethyl acetate. Among the chemical substances responsible for pharmacological effects, phenolic compounds have been presented as primary secondary metabolites related with anti-obesity effects. The anti-obesity effects are attributed to secondary metabolites present and chemically characterized in samples used in biological protocols, including saponins, polyphenols, flavones, flavanols, tannins, and chalcones. Phenolic compounds (especially flavones, flavanols, flavanones, catechins, anthocyanins, isoflavones, and chalcones) and their functional derivatives offer various chemical structures and pharmacological activities, found in fruits, legumes, nuts, beverages, and drugs. These chemical compounds have emerged as significant anti-obesity agents, primarily attributed to their antioxidative properties, which aid in preventing oxidative damage in biological systems. Additionally, they demonstrate inhibitory effects on the proliferation of in vitro predispose cells, induction of apoptosis in adipocytes, mitigation of lipid accumulation, and inhibition of pancreatic lipase activity, consequently impeding the in vivo absorption of fatty acids (31, 32).

8. Conclusion

The findings obtained from the scientific literature concerning the role of medicinal plants in the identification and formulation of anti-obesity medications underscore the significance of this field of inquiry, highlighting the therapeutic promise of bioactive compounds found within these botanical sources. The main objective of these studies is to identify phytogenic compounds that can target the pathophysiological processes of obesity and have a positive effect on metabolic control and insulin sensitivity. For example, polyphenols with antioxidant properties have been shown to regulate adipocyte formation and lipid metabolism. Additionally, some plant responses have been reported to modulate the activity of neurotransmitters involved in appetite control and metabolic responses.

This review was conducted to expand the existing knowledge on medicinal plants used in treating obesity and to highlight the ethnopharmacological approaches implemented in this area. Our review aims to define the effectiveness, safety, and methods of action of traditional medicinal plants used worldwide in weight management. The results of the present study are far-reaching and relevant for the development of alternative or adjuvant therapeutic strategies in the management of obesity based on the use of medicinal plants. The amalgamation of evidence-based traditional knowledge with modern scientific research is expected to close the gap between traditional healing techniques and contemporary health systems and further enhance the scope of integrating plant-derived therapies into standard protocols used for obesity management.

In addition, the ethnopharmacological approach used in this review provides insight into the cultural relevance of medicinal plants and highlights the need for protection of traditional knowledge systems for the next generation. The documentation and scientific validation of traditional utilization of medicinal plants in the treatment of obesity are of great importance to biodiversity conservation and the maintenance of indigenous healing practices.

Overall, the findings of this review highlight the potential of medicinal plants in addressing the global obesity epidemic and support the need for further research. Traditional healers, researchers, and healthcare practitioners working in collaboration would be able to develop evidence-based botanical interventions for a better impact on healthcare and improve the life quality for those suffering from obesity worldwide.

However, more research is needed to evaluate the anti-obesity properties of medicinal plants and to understand their pharmacological properties. Comprehensive studies are needed on the pharmacokinetics, pharmacodynamics and safety of phytoactive compounds. In addition, increasing the number of clinical studies and using standard procedures will help to obtain strong evidence about the effectiveness and safety of herbal compounds in the treatment of obesity. Investigating anti-obesity drugs may represent an important area of research. However, multidisciplinary research and clinical studies are needed to evaluate this potential. A better understanding of the metabolic effects of bioactive compounds found in medicinal plants would help develop new and effective approach in obesity treatments.

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