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A Comprehensive Review on the Causes, Prevention and Plant-Based Therapeutic Strategies of Obesity

Mondal Banani*, Ganguly Shayeri Chatterjee, Dasgupta Ramesh Kumari, Banerjee Sipra Sarkar and Julekha Kazi

Department of Pharmaceutical Technology, Brainware University, Kolkata, West Bengal, India

*Corresponding Author

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Abstract: Currently, obesity affects almost one-third of the world's population together, leading to overweight. It is a complicated, multifaceted, and generally preventable condition. Public health is seriously concerned about the rise in childhood obesity. In addition to being a risk factor for the many difficulties, it causes childhood and teenage obesity, which are major predictors of adult obesity. Accordingly, 20% of obese newborns will become obese children, 40% of overweight children will grow up to obese teenagers, and 80% of obese teenagers will grow up to obese adults. Overweight and obesity are closely associated with conditions like diabetes, hypertension, high cholesterol, cardiovascular illnesses, stroke, and arthritis, according to several studies conducted so far. An estimated 2.8 million deaths worldwide are attributed to obesity each year. Weight control strategies based on pharmacological methods gained precedence. Since plant-based medications contain mixtures of various phytochemicals, these compounds may operate on many molecular targets synergistically, providing benefits over newly developed medicines with lesser side effects and improved efficacy. Pharmacological therapeutics, and strategies like several nutrient absorption blocking, metabolism modulation, regulation of adipose signals, nutritional and lifestyle modifications, such as reduction of calorie consumption, along with regular and sufficient physical activities, are among the current trends in managing obesity. This review intends to give a comprehensive analysis on the root causes of obesity, its preventive measures, and possible treatments, emphasizing on the efficacies and challenges of using phyto-medicines.

Keywords: Metabolism, Obesity, Adipose, Synergistic, Phytochemicals, Molecular targets

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Introduction

A medical disease called obesity could involve an excessive amount of fat to the point that it becomes dangerous for one's health. In addition

to being the product of stored energy, fat also secretes a variety of hormones and cytokines (Lustig *et al.*, 2022). Negative morbidity and

Table 1: Body mass index range chart

Underweight	15 to 19.9 kg/m ²
Normal weight	20 to 24.9 kg/m ²
Pre-obesity	25 to 32.9 kg/m ²
Class I Obesity	30 to 34.9 kg/m ²
Class II Obesity	35 to 39.9 kg/m ²
Class III Obesity	>40 kg/m ²

Table 2: Body Mass Index and Percentage

OBESITY				
	Desirable	Grade I	Grade II	Grade III
BMI	Up to 25	25 to 29.9	30 to 40	>40
PERCENTAGE				
WOMEN	67.6	24	8	0.4
MEN	58.2	34	6	0.2

mortality rates are exacerbated by excessive central fat. Generally speaking, the body mass index (BMI) is calculated by dividing the body height squared by the body mass. This means that a body mass index of more than 25 kg/m² indicates overweight, while a body mass index of more than 30 kg/m² indicates obesity (Middleton *et al.*, 2014). Type 2 diabetes, heart disease, respiratory illnesses, infertility, certain types of cancer, psychological issues, and social problems are among the comorbidities of obesity that pose a risk. These comorbidities become even more likely to be dangerous as BMI rises (Reilly *et al.*, 2006). The health system is bearing a heavy load due to the high cost of treating overweight and its related comorbidities. The failure rate of conservative treatment is substantial (Midgley *et al.*, 2021). Even so, bariatric surgery that is largely performed as a quick fix to lose weight also has the unintended consequence of causing related comorbidities (Karageorgi *et al.*, 2013).

Obesity differs in individuals according to the body mechanism's response to the kind of food and activity they carry out (Albuquerque *et al.*, 2015). There are some reasons of obesity, like

obesity from food, thickness as a result of stomach nerves, diet high in gluten, genetic metabolic leading to being overweight, and obesity from venous circulation, and obesity from inactivity or lack of sufficient exercise (Khosla *et al.*, 2022). WHO (World Health Organization) has established various classifications and terminologies that categorize obesity; however, the BMI-based classifications are the most frequently recognized (Flegal *et al.*, 2010). Because obesity has so many negative effects, there is a growing need for BMI to be routinely calculated (Tables 1, 2) as a critical indication that medical professionals may utilize to evaluate a patient's physical health (Nuttall *et al.*, 2015).

Risk factors

Obesity, at its most basic level, is the outcome of a person consistently consuming more calories than they require. These extra calories are stored by the body as body fat, which results in an accumulation of extra pounds over time (Guyenet *et al.*, 2012). Eat less food that contains calories to help the body break down, which will help the control body weight. However, this formula is

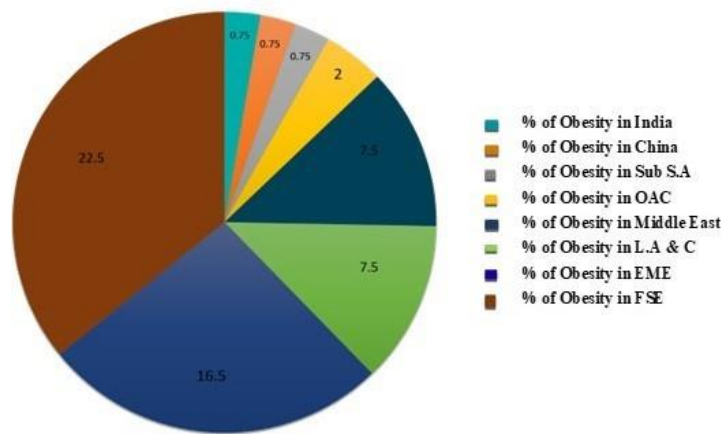


Fig. 1: Global Obesity Prevalence.



Fig. 2: Risk factors of obesity.

frequently misleadingly straightforward because it ignores the plethora of factors that influence our diet, level of exercise, and how the bodies utilize all this energy, which implies that a simple issue is surrounded by a fancy web (Payne *et al.*, 2018). The prevalence of global obesity is shown in Figure 1.

Genetic factor:

Though usually to a much lesser extent than thought, heredity has a role in obesity. Rather than being the only factor contributing to obesity, genes appear to increase the chance of weight gain in conjunction with other environmental risk factors such as poor dietary habits and sedentary lifestyles (Eagle *et al.*, 2018). Figure 2 depicts the risk factors of obesity and Table 3 represents

some genes that are associated with obesity.

Unhealthy Diets:

The most attention has been focused on reducing prevalent obesity and minimizing obesity risk due to bad diets, and for good cause. Even in modern times, the mainstay of both clinical and alternative weight-management and weight-loss strategies is still calorie restriction (Thom *et al.*, 2017).

Psychological factors:

Many people use food as a way to cope with stress, anxiety, depression, or other emotional issues. Emotional eating can lead to consuming excess calories and choosing high-fat or high-sugar foods, which can contribute to weight gain

Table 3: Examples of some genes with variants related to obesity

Gene symbol	Gene name	Gene product's role in energy balance
<i>ADIPOQ</i>	Adipocyte-, C1q-, and collagen domain-containing	Produced by fat cells, adiponectin promotes energy expenditure (Keshvari <i>et al.</i> , 2016)
<i>FTO</i>	Fat mass- and obesity-associated gene	Promotes food intake (Chang <i>et al.</i> , 2018)
<i>LEP</i>	Leptin	Produced by fat cells (Obradovic <i>et al.</i> , 2021)
<i>LEPR</i>	Leptin receptor	When bound by leptin, inhibits appetite (Wada <i>et al.</i> , 2014)
<i>INSIG2</i>	Insulin-induced gene 2	Regulation of cholesterol and fatty acid synthesis (Dong <i>et al.</i> , 2010)
<i>MC4R</i>	Melanocortin 4 receptor	When bound by alpha-melanocyte stimulating hormone, stimulates appetite (Wu <i>et al.</i> , 2023)
<i>PCSK1</i>	Proprotein convertase subtilisin/kexin type 1	Regulates insulin biosynthesis (Demoures <i>et al.</i> , 2018)
<i>PPARG</i>	Peroxisome proliferator-activated receptor gamma	Stimulates lipid uptake and development of fat tissue (Lee <i>et al.</i> , 2018)

(Jacques *et al.*, 2019).

Sleep deprivation:

Numerous studies indicate that routinely getting less than seven hours of sleep every night is a risk factor for overweight due to sleep deprivation. According to a Nurses' Health Study, people with the greatest BMI and largest weight increase were also who also slept the least—five hours or less every night (Flodmark *et al.*, 2006).

Lack of exercise and certain medications:

Due to economic progress, technology advancements, and societal changes, transportation has dropped, and we are more likely to work from home during this pandemic period. These factors have a significant impact on our ability to maintain a healthy work-life balance (Lockwood *et al.*, 2003). People who engage in physical exercise have a favorable boost in their overall consumption of energy, which helps them maintain an energy balance and slow the progression of belly obesity (Palma *et al.*, 2022).

Molecular pathways

Multidisciplinary support teams and general practitioners play a critical role in helping patients lose weight in a long-term, healthy way

(Zolotarjova *et al.*, 2018). A modeling study found that for every two percentage points an individual's average BMI increases, their life expectancy decreases by one year (Pressman *et al.*, 2023). Consequently, in primary care, a clinical route for managing overweight and obesity was established through the development of systematic guidelines. It has been found that many medications, including serotonin receptor agonists, can help in weight loss. Higher brain serotonin levels were linked to greater satiety, which led to the discovery that serotonin, or 5-hydroxytryptamine (5-HT), exhibits anorectic characteristics in the 1970s (Halford *et al.*, 2005). For example, the direct agonists of 5-HT receptors, fenfluramine and d-fenfluramine, demonstrated anti-obesity effects by raising serotonin release in the synaptic cleft. Both substances alter eating habits in a way that is compatible with fullness (Maclean *et al.*, 1997). However, selective receptor reuptake inhibitors (SSRIs) may also be utilized to increase serotonin levels in the management of obesity by blocking serotonin from getting reabsorbed into nerve terminals (Halford *et al.*, 2008). The SSRI fluoxetine decreases appetite and increases sensations of fullness, but it can also have undesirable side effects as tremor, sweating,

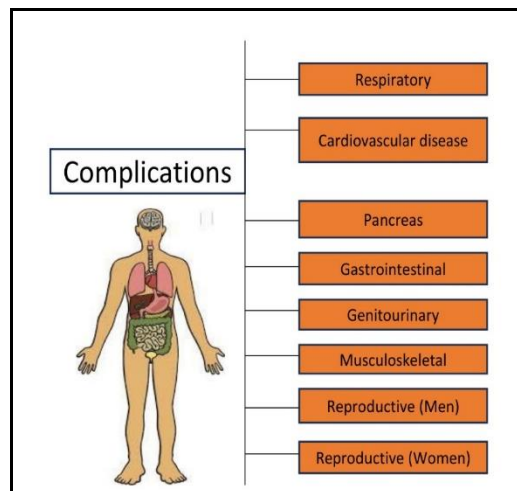


Fig. 4: Complications caused due to obesity.

Preventive approaches and treatment for combatting obesity

Maintain healthy life and losing weight is in hand but for that, one has to focus on himself. Prevention is vital for achieving a proper lifestyle, which is required to stop or reverse obesity. Consume healthy food, enough sleep, physical activity, relaxation also features a positive effect on the body (Wang *et al.*, 2013). The American Academy of Pediatrics advises against requiring toddlers to eat large quantities of food. A person should consume about 40 calories per inch of height between the ages of one and three (Chandrasekaran *et al.*, 2012). Habitually eating nutritious food help grow into a good immune system. Besides eating a healthy diet, nothing is more important to keeping weight in restraint and staying healthy than regular activity. An average adult should engage in 150 min or more of moderate-intensity physical exercise per week, according to the majority of national and international guidelines. implying that for five days a week, at least 30 min a day. Regular physical activity can improve body composition. the planet Health Organization (WHO) recommends that youngsters and teenagers get a minimum of 1 h of physical activity daily (Bouchard *et al.*, 2012). As necessary for our everyday survival as food and drink, is sleep. All through the night, brain is still working. Sleep is

essential for both the brain's and the body's physical processes (Porkka-Heiskanen *et al.*, 2013).

Table 4 includes a detailed list of several herbal plants along with information on their active ingredients and medicinal properties. Figure 5 represents the natural plants used as anti-obesity agents.

Limitation and challenges of natural drugs in treating obesity

Natural drugs, derived from plants, herbs, and other natural sources, present an intriguing option for treating obesity due to their potential for fewer side effects and holistic health benefits. However, their application comes with significant limitations and challenges (Halder *et al.*, 2021). The diversity in natural medicine composition is one of its main drawbacks. Variability in plant species, growth environments, harvesting schedules, and processing techniques are some of the factors that contribute to this variability, which results in inconsistent safety and efficacy profiles (Mench *et al.*, 2009). Natural medications, in contrast to synthetic drugs, frequently have non-standardized formulations and dosage, which makes it challenging to establish the right dosage and guarantee steady therapeutic effects (Wang *et al.*, 2023). There is frequently little scientific proof for the effectiveness and safety of many herbal

Table 4: Effect of plant-based anti-obesity therapeutics on animal models

S. No.	Common Name	Biological Name	Mechanism Of Action for obesity management	Chemical Constituents
1	Chaff flower	<i>Achyranthes aspera</i> (Amaranthaceae)	Effect on reduces LDL cholesterol, total cholesterol, total triglycerides.	Consists primarily of triterpenoids (alkaloids, glycosides, tannins, saponins, and flavonoids) in AEAA (Mahmudur <i>et al.</i> , 2017)
2	Sweet flag	<i>Acorus calamus</i> (Araceae)	A. calamus ethyl acetate extract inhibits α -glucosidase activity.	It contains constituents such as alkaloid, flavonoid, saponin, tannins, etc. (Banerjee <i>et al.</i> , 2024)
3	Niu xi	<i>Achyranthes bidentata</i> Blume (Amaranthaceae)	Effects on adipocyte differentiation and phospho-Akt expression reduction.	Include bioactive substances such as flavonoids, phenols, alkaloids, steroids, and saponins (Bankar <i>et al.</i> , 2021)
4	Golden kiwi fruit	<i>Actinidia polygama</i> Max (Actinidiaceae)	The extract-treated animals showed a decrease in aspartate serum levels but not in alanine transaminase, creatinine serum levels.	Contains vitamins (Vitamin A, C, E, folic acid), minerals, polyphenols, antioxidants etc. (Sung <i>et al.</i> , 2011)
5	Nan Sha Shen	<i>Adenophora triphylla</i> Hara (Campanulaceae)	A. triphylla has an anti-obesity action through lowering adipokines TNF- α , GPDH, and PPAR- α and raising adipocytes adiponectin and activating pathways like AMPK and PPAR- α .	ATREE's antioxidant and anti-inflammatory properties may have an anti-obesity effect (El-Saber <i>et al.</i> , 2020)
6	Onion	<i>Allium cepa</i> (Amaryllidaceae)	A. cepa causes an upregulation of the mRNA levels of fatty acid binding protein 4 (FABP4) and carnitine palmitoyl	Biologically active substances, including flavonoids, thiosulfates, and phenolic acids (Kumar <i>et al.</i> , 2013)

			transferase-1 α (CPT-1 α), while the down-regulation of activating protein (AP2).	
7	Welsh onion	<i>Allium fistulosum</i> (Liliaceae)	Adipocyte size, adiponectin weight, and body weight were significantly decreased. <i>A. fistulosum</i> inhibits genes related to lipogenesis.	substances including polycarboxylic acids, sterols, flavonoids, polyphenols, ajoene, and alliin (Xia <i>et al.</i> , 2010)
8	Garlic	<i>Allium sativum</i> (Amaryllidaceae)	In the hepatic tissue, it inhibits lipid peroxidation and glutathione depletion while raising antioxidant enzyme levels. Acetyl-coA carboxylase, fatty acid synthase, are all downregulated by oil extracted from <i>A. sativum</i> .	Biological activity such as antiviral, antibacterial, antiprotozoal, anti-inflammatory, antioxidant, and anticancer properties have all been assessed (Lee <i>et al.</i> , 2013)
9	Rambutan	<i>Nephelium lappaceum</i> (Sapindaceae)	Reductions in Igf-1 and Igf-1R expression were seen in an obese rat model administered <i>N. lappaceum</i> extract.	Important bioactive components may be found in rambutan (RS) fruit seeds. Studies have revealed that extracts from these seeds have anticancer, antinociceptive, hypoglycemic, and CNS depressive properties (Wang <i>et al.</i> , 2017)
10	Common olive	<i>Olea europaea</i> (Oleaceae)	The extract counteracts the activation of important adipogenic genes (PPAR γ , C/EBP α , CD36, FAS, and leptin) and signaling molecules regulated by WNT10b and galanin that is brought about by a high-fat diet.	According to numerous studies, oleuropein—which makes up as much as 6–9% of the dry matter in leaves—has a variety of pharmacological and health-promoting qualities, such as antiarrhythmic, cardioprotective, hypotensive. (Shaik <i>et al.</i> , 2023)

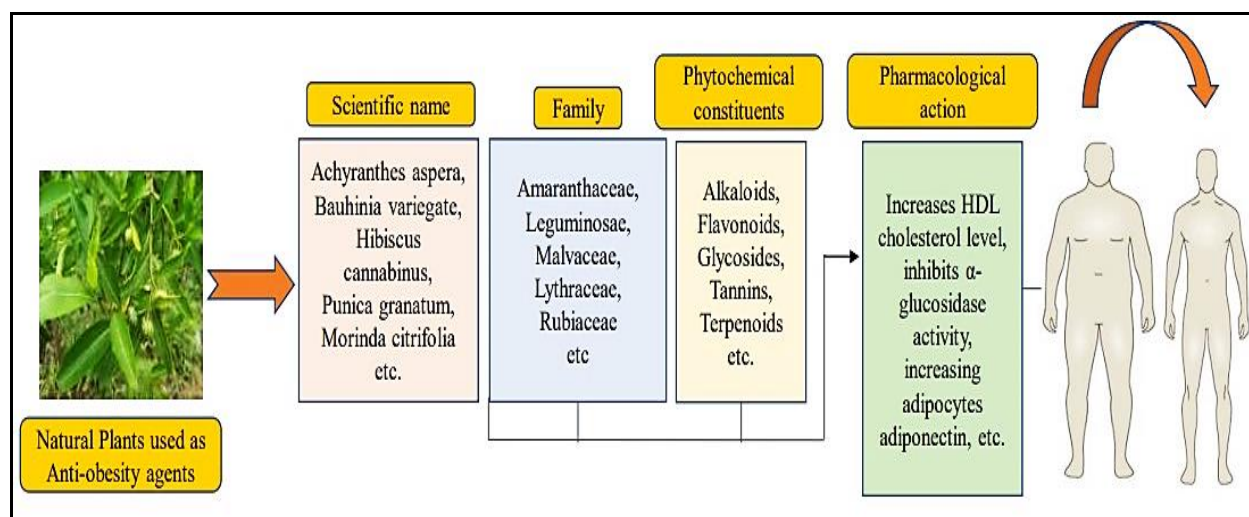


Fig. 5: Natural plants used as anti-obesity agents.

medications. Many are not as widely accepted by patients and the medical community since they have not undergone thorough clinical studies (Kazdin *et al.*, 2008). Moreover, there is a chance that natural medicines will interfere with prescription drugs and cause negative side effects or lessen the efficiency of prescribed treatments. Many times, these exchanges have not received enough attention or understanding (Hassen *et al.*, 2022).

Conclusion

Persistently consuming more calories from food and beverages than what the body requires to power its metabolic and physical processes leads to a chronic energy imbalance, which is what causes obesity. In conclusion, it is anticipated that more straightforward and well-tolerated anti-obesity medications will be created. Drugs that fight obesity are typically favored because of their great efficacy and effectiveness. Regulators, however, will likely demand extensive real-world testing that not only demonstrates efficacy in terms of weight loss but also demonstrates long-term benefits for diabetes prevention and treatment, disorder, and psychiatric safety, even for the substances that meet preliminary requirements for selectivity of action and potential safety profile.

Ethical Statement

This is a review article hence no Ethical Approval needed.

Author Contributions

Mondal Banani: Writing original draft, editing; *Ganguly Shayeri Chatterjee*: Editing, Supervision; *Dasgupta Ramesh Kumari*: Editing; *Banerjee Sipra Sarkar*: Editing; *Julekha Kazi*: Editing, Supervision. All authors have read and agreed to the published version of the manuscript.

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Conflict of Interest

The authors declare no conflicts of interest.

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