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Review Article

Recent Advancements in the Prevention and Treatment of Genetic and Non-Genetic Obesity: A Pharmacological Perspective of Review

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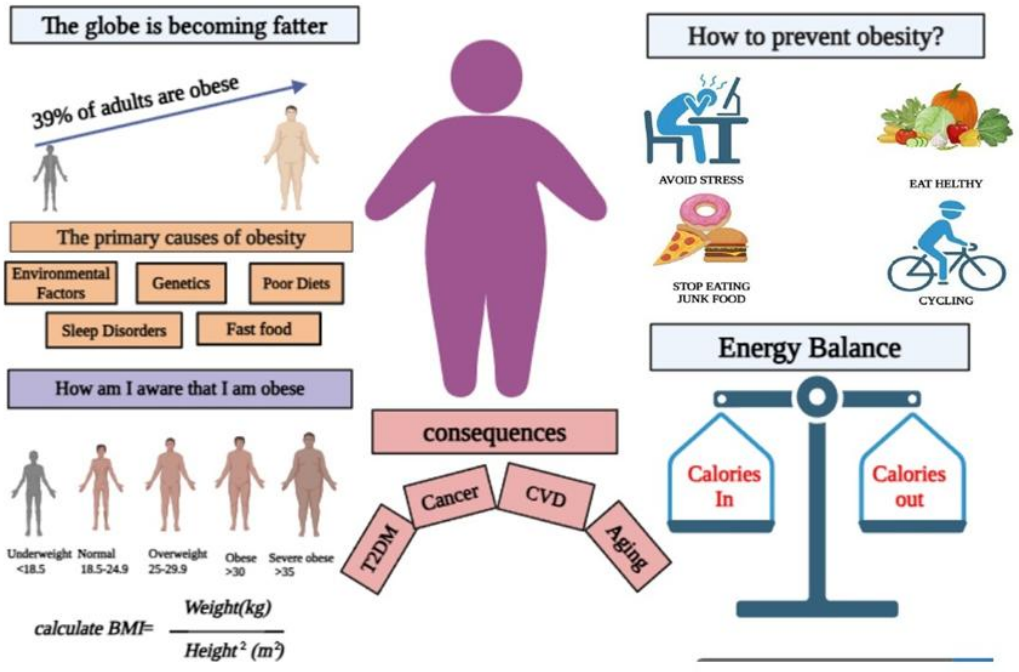
Abstract

Obesity is a complicated, long-term condition caused by a combination of behavioural, environmental, genetic, and epigenetic factors. It is a significant risk factor for a number of metabolic conditions, such as cardiovascular disease, type 2 diabetes, and some types of cancer. New knowledge and treatment options for obesity prevention and treatment, especially in relation to its hereditary and non-genetic variants, have been made possible by recent developments in pharmacological research. Monogenic, syndromic, and polygenic forms of genetic obesity are frequently caused by mutations or polymorphisms that impact energy expenditure, appetite control, or fat storage processes. Novel pharmacotherapies have focused on important targets such proopiomelanocortin (POMC) neurons, the leptin signalling pathway, and the melanocortin-4 receptor (MC4R). Rare hereditary types of obesity may be treated with medications like setmelanotide, a selective MC4R agonist. Excessive calorie intake, physical inactivity, and psychological problems contribute to non-genetic (or lifestyle-related) obesity, which is still more common and is frequently treated with a mix of medication and lifestyle changes. Clinical trials have shown that recently licensed medications like tirzepatide and semaglutide, which work on the glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) pathways, significantly improve metabolism and reduce body weight. The goal of this review is to present a thorough examination of the most recent pharmacological approaches to treating both hereditary and non-genetic obesity. It emphasizes how crucial combination therapy, new drug targets, and precision medicine will be in determining how obesity is treated and prevented in the future.

Keywords: Lipid disorder, genetic obesity, non-genetic obesity, type 2 diabetes, setmelanotide, glucagon-like peptide-1

Graphical Abstract



Highlights:

- A protein that is essential for controlling body weight, food intake, and energy balance is encoded by the MC4R (Melanocortin 4 Receptor) gene.
- MC4R initiates intracellular signaling pathways through the activation of G proteins.
- Leptin's binding to LEPR initiates a signalling cascade that controls hunger, energy expenditure, and fat storage, among other metabolic functions.
- The JAK-STAT (Janus kinase-signal transducer and activator of transcription) signaling pathway activates particular genes that control energy balance and food intake.
- Obesity and metabolic diseases may be exacerbated by leptin resistance or problems in leptin signaling caused by mutations in the LEP or LEPR genes.

1. Introduction:

Excessive bodily fat build up is a hallmark of obesity, a chronic, multifactorial condition that is harmful to one's health.[1] Because it raises the risk of many co-morbidities, such as type-2 diabetes, cardiovascular illnesses, hypertension, some types of cancer, and musculoskeletal disorders, it is a significant global public health concern.[2] Obesity is defined by the World Health Organization (WHO) as having a body mass index (BMI) of 30 kg/m^2 or more. The disorder results from an imbalance between energy intake and expenditure, which can be caused by metabolic, behavioural, environmental, and hereditary variables.[3] Numerous interconnected elements are involved in the complicated causes of obesity. Obesity is significantly influenced by genetic predisposition. According to studies, 40–70% of the risk for obesity is inherited.[4] Increased risk for obesity has been associated with mutations in genes such as MC4R, LEP, LEPR, and FTO. The combination of several genetic variations that affect appetite control, metabolism, and fat storage leads to polygenic obesity.[5] High-calorie meals heavy in processed foods, sweets, and unhealthy fats are among the environmental and lifestyle factors that lead to excessive weight gain.[6] Fat buildup and lower energy expenditure are the results of a sedentary lifestyle with less physical exercise. Dietary and physical activity patterns are influenced by urbanization, social position, and food availability.[7] Increased appetite and fat storage are caused by the dysregulation of hormones such as insulin, ghrelin (the hunger hormone), and leptin (the satiety hormone).[8] Obesity has been connected to endocrinological disorders such as hypothyroidism, Cushing's syndrome, and polycystic ovarian syndrome (PCOS). Emotional eating, stress, and despair can all contribute to overeating.[9] Weight gain is an adverse effect of several drugs, including beta-blockers, antipsychotics, antidepressants, and corticosteroids. Energy balance may be disturbed by underlying illnesses such as hypothalamic abnormalities.[10] Adipose tissue grows as a result of adipocyte hypertrophy, or a rise in size, and hyperplasia, or an increase in quantity. With the help of hormones like ghrelin, which increases hunger, and leptin, which decreases appetite, the hypothalamus controls hunger and energy balance. Leptin resistance, which occurs in obesity, causes people to continue eating even when their energy stores are high. Insulin resistance, which affects glucose metabolism and raises the risk of type-2 diabetes, is brought on by increased fat deposition, particularly visceral fat.[11] Excess insulin, or hyper insulinemia, encourages weight gain and additional fat storage. Pro-inflammatory cytokines, such as TNF-α and IL-6, are secreted by adipose tissue and are linked to insulin resistance, cardiovascular disease, and systemic inflammation. People who are in this inflammatory state are also more likely to develop metabolic syndrome. Atherosclerosis and cardiovascular disease are exacerbated by dyslipidaemia, which is caused by elevated blood levels of free fatty acids (high LDL cholesterol, low HDL cholesterol, and high triglycerides).[12] Liver dysfunction may result from hepatic fat accumulation (non-alcoholic fatty liver disease). Osteoarthritis is caused by increased mechanical stress on joints. Infertility, respiratory conditions including sleep apnea, and several types of cancer are also linked to obesity.[13] India's obesity rate has been rising at an alarming rate. Based on national surveys and reports, we have attempted to compile statistics on the gender distribution of the different Indian states. Below is a graphic representation of the data.

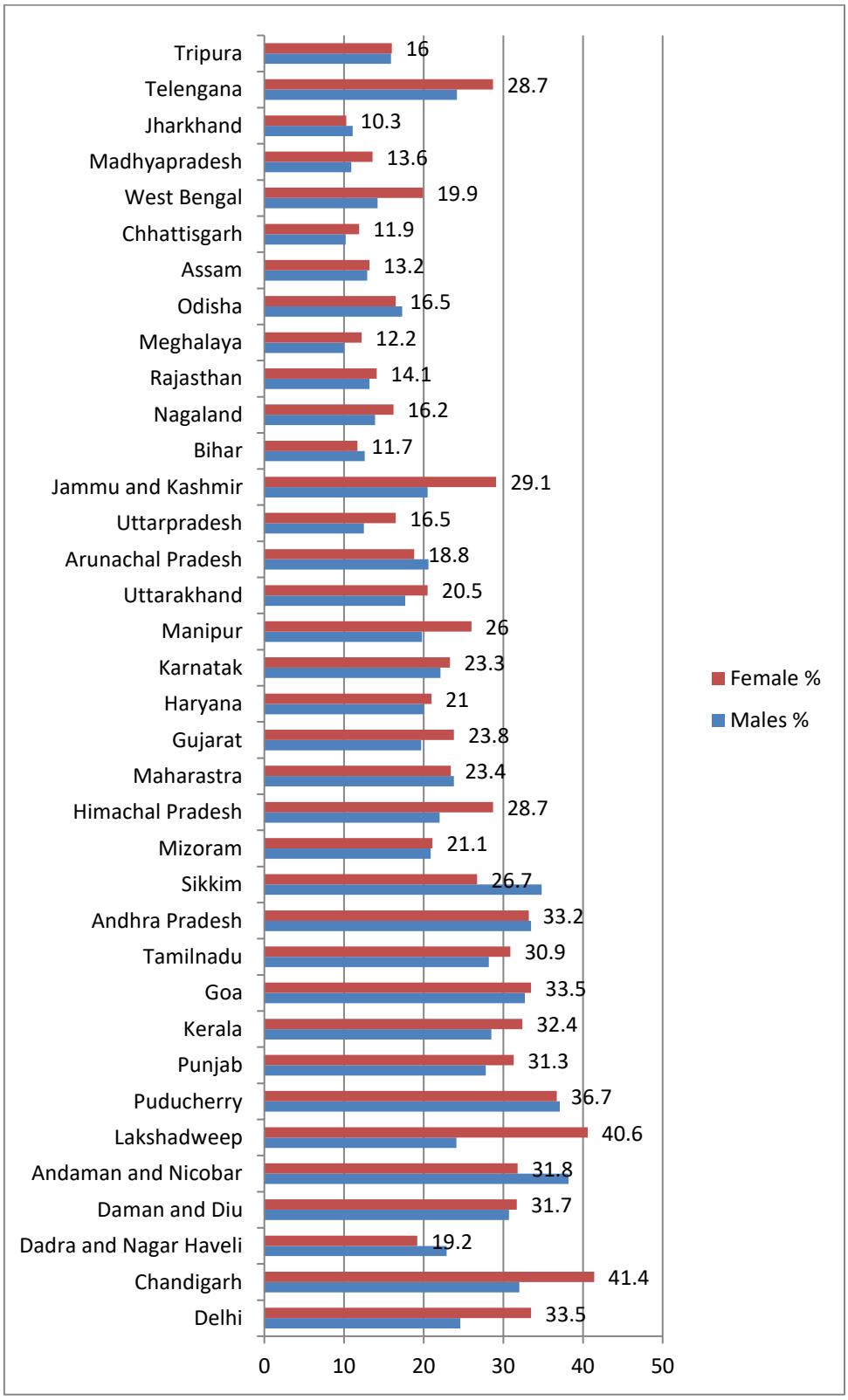


Figure 1: Graphical representation of gender basis obesity in different Indian states (National Family Health Survey Data)

Table 1: Tabular comparison of **Genetic Obesity** and **Non-Genetic Obesity**

Feature	Genetic Obesity	Non-Genetic Obesity	Ref
Cause	Caused by inherited genetic mutations or syndromes.	Result of lifestyle factors such as diet, physical inactivity, and environment.	14
Examples	Prader-Willi Syndrome, Bardet-Biedl Syndrome, MC4R gene mutations.	Poor eating habits, sedentary lifestyle, stress, hormonal imbalance.	15
Onset	Often starts in early childhood.	Can develop at any age, but more common in adulthood.	16
Family History	Strong family history of obesity and related conditions.	May or may not have a family history of obesity.	17
Metabolic Rate	Typically, lower due to genetic predisposition affecting metabolism.	Metabolism may vary but is generally not genetically determined.	18
Response to Diet & Exercise	May not respond well to conventional weight loss methods.	Can be effectively managed with diet, exercise, and lifestyle changes.	19
Medical Treatment	May require specialized treatments, medications, or genetic therapies.	Lifestyle modifications and medical interventions (if necessary).	20
Risk Factors	Inherited from parents, genetic mutations affecting hunger and metabolism.	Environmental factors, processed food consumption, lack of physical activity.	21
Severity	Often more severe and harder to manage.	Varies; mild to severe, depending on lifestyle and health choices.	22

Obesity resulting from inherited genetic characteristics or mutations that impact appetite, metabolism, and weight management is referred to as hereditary obesity. Numerous genes that affect body weight and fat storage have been found, and obesity is closely associated with a few uncommon genetic disorders. The genetic causes of obesity are explained in detail below:

2. Genetic Causes of Obesity:

2.1 MC4R (Melanocortin 4 Receptor) Gene:

A protein that is essential for controlling body weight, food intake, and energy balance is encoded by the MC4R (Melanocortin 4 Receptor) gene. The hypothalamus, a part of the brain involved in hunger and satiety signals, is the primary location for the expression of the G-protein-coupled receptor MC4R. [23] When triggered by melanocortins, such as alpha-MSH (alpha-melanocyte-stimulating hormone), which are produced from pro-opiomelanocortin (POMC), MC4R initiates intracellular signaling pathways through the activation of G proteins. As a result, appetite is suppressed and energy expenditure rises. Furthermore, agouti-related peptide (AgRP), an antagonist that blocks MC4R's function and encourages greater food intake and lower energy expenditure, can also activate MC4R.[24] Thus, preserving homeostasis in energy control depends on the balance of melanocortin signaling via MC4R. Obesity and other metabolic diseases are associated with genetic abnormalities or dysregulation of MC4R, indicating its critical function in appetite regulation and weight control.[25]

2.2 Leptin and Leptin Receptor (LEP, LEPR) Genes:

Adipocytes, or fat cells, are the primary source of the hormone leptin, which is essential for controlling metabolism, body weight, and energy balance. Leptin, which is encoded by the LEP gene, communicates with the brain's hypothalamus to provide details about the body's energy and fat reserves.[26] Leptin levels increase, indicating satiety and decreasing hunger, when fat stores are enough. On the other hand, low fat storage causes leptin levels to drop, which increases hunger and encourages energy conservation and food consumption.[27] The leptin receptor, found in the brain and other organs, is encoded by the leptin receptor gene (LEPR). Leptin's binding to LEPR initiates a signalling cascade that controls hunger, energy expenditure, and fat storage, among other metabolic functions.[28] The JAK-STAT (Janus kinase-signal transducer and activator of transcription) signaling pathway is the main player in this pathway, which activates particular genes that control energy balance and food intake.[29] Obesity and metabolic diseases may be exacerbated by leptin resistance or problems in leptin signaling caused by mutations in the LEP or LEPR genes.[30]

2.3 Prader-Willi Syndrome (PWS):

An uncommon hereditary condition known as Prader-Willi Syndrome (PWS) is brought on by certain genes on the paternal chromosome 15 ceasing to function. People usually receive one copy of chromosome 15 from each parent, one of which is active and the other inert.[31] In PWS, the maternal chromosome 15 copy is silent because of imprinting, whereas the essential region of the paternal chromosome 15 is either deleted or altered.[32] As a result, the affected individual does not have any functioning copies of the affected genes.[33] Due to malfunction in the hypothalamus, which controls hunger and satiety, this genetic abnormality causes a variety of symptoms, including hypotonia (low muscle tone), intellectual difficulties, behavioral issues, and an insatiable appetite.[34] The fundamental mechanism is the disturbance of regular neuroendocrine processes, especially those that regulate hunger and metabolism,

which, if left unchecked, leads to excessive overeating and obesity.[35]

2.4 Bardet-Biedl Syndrome (BBS):

Mutations in one of several genes involved in the development and operation of cilia, which are tiny hair-like structures on the surface of cells, result in Bardet-Biedl Syndrome (BBS), a rare genetic condition.[36] These cilia are essential for signaling pathways that control several cellular functions, such as growth, motility, and sensory perception. Defective cilia in BBS cause problems in several organ systems by interfering with proper cellular signaling.[37] In addition to causing gradual vision loss (retinal degeneration), the disorder is linked to learning impairments, obesity, polydactyly (additional fingers or toes), and kidney failure.[38] It is impeded by BBS genetic mutations, which typically lead to faulty proteins required for ciliary function.[39] As a result, individuals with BBS experience a wide range of clinical symptoms, many of which start in childhood and worsen over time.[40]

2.5 FTO (Fat Mass and Obesity-Associated) Gene:

It is well known that the FTO (Fat Mass and Obesity-Associated) gene is linked to obesity and the control of body weight. It encodes a protein that affects energy expenditure and fat storage mechanisms, which in turn regulates energy balance. In particular, FTO is an RNA demethylase that alters the stability and structure of mRNA molecules. Genes involved in hunger control, fat metabolism, and general energy homeostasis are all impacted by this action.[41] Because they may change the gene's normal functioning and cause disruptions in appetite regulation and energy expenditure, variations of the FTO gene have been associated with an increased risk of obesity.[42] One important factor in the development of obesity has also been identified as the impact of FTO on the hypothalamus, which regulates signals related to appetite and fullness. In conclusion, FTO gene variations influence hunger, energy balance, and fat storage by controlling RNA molecules and the expression of genes related to metabolic processes. This leads to obesity.[43]

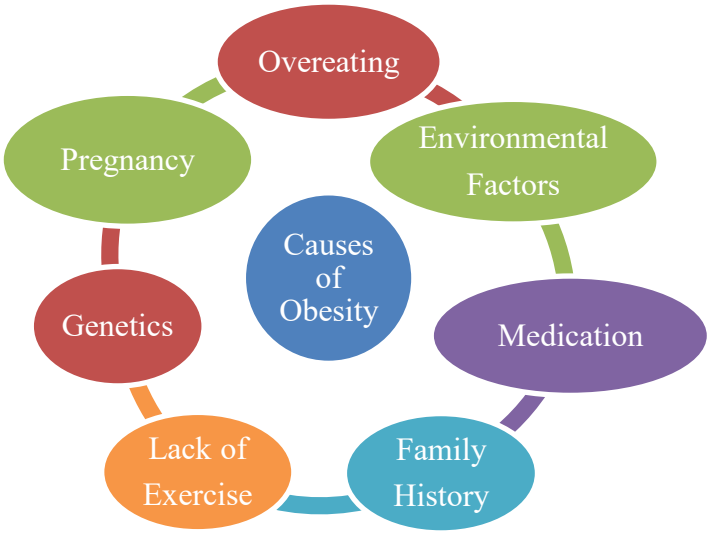


Figure 2: Causes of obesity.

3. Non-genetic causes:

3.1 Environmental Factors: The external variables that can affect how organisms, systems, or processes develop and function are referred to as environmental factors. Physical, chemical, biological, and social effects are some of these elements.[44] Physical elements like light, humidity, and temperature have an impact on plant and animal growth and survival in the natural environment. Ecosystems and human health can be impacted by chemical factors such as the availability of contaminants or nutrients.[45] Predation, competition, symbiosis, and other interactions between species are examples of biological forces that influence populations and ecosystems. Human behavior and decisions are also shaped by social and cultural factors, such as community customs that impact sustainability or environmental regulations.[46] These environmental parameters are essential to comprehending ecological balance and environmental sustainability since they are interrelated and changes to one can have a cascading effect on the larger system.[47]

3.2 Lifestyle Choices:

Lifestyle choices are the everyday routines and choices people make that directly impact their mental, emotional, and physical health.[48] These decisions cover various behaviours, such as social contacts, work-life balance, sleep patterns, food, exercise, and personal growth.[49] For example, eating a well-balanced diet full of fruits, vegetables, and lean meats can help you stay healthier, and getting regular exercise can help you feel better and build your body. Emotional stability can also be improved by practicing mindfulness or spending time with loved ones to manage stress.[50] Conversely, bad lifestyle choices including poor diet, inactivity, and long-term stress can result in several health problems, including obesity, heart disease, and mental health disorders.[51] Ultimately, the combination of these choices defines an individual's overall quality of life and longevity.[52]

3.3 Medications and Medical Treatments:

In order to prevent, manage, and cure a variety of medical diseases, medications and medical treatments

are essential.[53] Prescription pharmaceuticals, over-the-counter medications, and herbal therapies are examples of medications that are used to cure or lessen disease symptoms, manage chronic conditions, and enhance general health.[54] In order to change biological processes like hormone regulation, pain management, or infection prevention, they interact with the body's systems.[55] To cure, manage, or lessen the impact of health conditions, medical treatments, on the other hand, include a wide range of procedures, such as radiation, immunotherapy, physical therapy, and surgery. Treatments might be non-invasive, like physical therapy or psychotherapy, or intrusive, like surgery.[56] Depending on the severity and type of the problem, treatments may involve a combination of different approaches, such as the use of drugs in conjunction with therapies, lifestyle modifications, or surgical procedures.[57] The type of sickness, individual health conditions, and other factors all affect how effective medications and therapies are, necessitating regular monitoring and modifications by medical professionals.[58]

3.4 Inadequate Sleep:

When a person routinely receives less sleep than what is advised typically fewer than 7 to 9 hours per night for adults it is referred to as inadequate sleep. Chronic sleep deprivation can negatively impact one's physical and mental well-being.[59] It can affect cognitive abilities such as focus, memory, and judgment, which can result in a reduction in productivity and a higher chance of mishaps.[60] Additionally, sleep deprivation has been connected to a number of health problems, including a compromised immune system, elevated stress, heightened inflammation, and an increased risk of diseases like diabetes, heart disease, high blood pressure, and obesity. Lack of sleep also affects mood, causing melancholy, anxiety, and irritability. Insufficient sleep over time can negatively impact one's general health and quality of life. making it crucial to prioritize consistent, restful sleep for maintaining good health.[61]

3.5 Hormonal Imbalances:

When a hormone is present in the bloodstream in excess or insufficient amounts, it can cause hormonal imbalances that interfere with regular body processes. Hormones are crucial for controlling several functions, including growth, mood, metabolism, and reproduction.[62] Medical diseases (such as diabetes or thyroid disorders), lifestyle variables (such as stress, bad food, or lack of sleep), or specific drugs can all contribute to imbalances. Depending on which hormone is impacted, symptoms of hormonal imbalances might vary, but they frequently include mood swings, irregular periods, infertility, changes in skin or hair, exhaustion, and weight gain or loss.[63] Depending on the particular imbalance and patient needs, treatment frequently includes addressing the underlying cause, whether with medication, lifestyle modifications, or hormone therapy.[64]

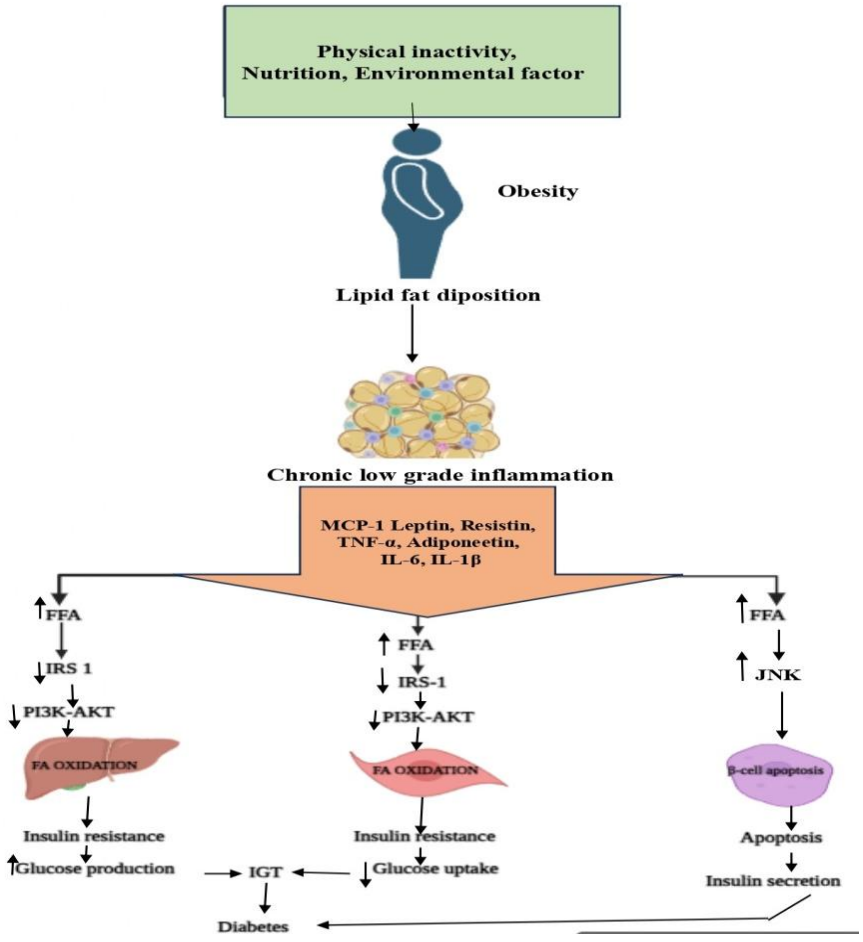


Figure 3: Diagrammatic representation of Hormonal Imbalances.

4. Etiology of genetic and non-genetic obesity:

A combination of hereditary and non-genetic causes causes obesity. Genetic obesity is impacted by inherited characteristics, where a person's susceptibility to obesity is controlled by differences in genes linked to appetite control, fat storage, and metabolism. Increased fat deposition can result from specific gene mutations that interfere with normal weight regulation, such as those in the melanocortin-4 receptor or leptin genes.[65] Conversely, environmental and lifestyle factors such as poor food, lack of physical activity, socioeconomic level, and psychological stress are considered non-genetic factors.[66] The development of obesity is also significantly influenced by factors such as hormone imbalances, stress, and lack of sleep. Obesity is a complicated multifactorial disorder with a variety of causes due to the interaction of both hereditary and non-genetic factors.[67]

5. Complications of obesity:

Numerous severe consequences that affect one's bodily and mental well-being might result from obesity. On a physical level, it raises the chance of getting chronic diseases like type 2 diabetes, heart disease, high blood pressure, stroke, and some types of cancer, especially liver, colon, and breast cancer.[68] Furthermore, obesity can cause joint tension, especially in weight-bearing regions like the knees and hips, which can result in osteoarthritis. Common respiratory issues include sleep apnoea, a condition in which the airway becomes obstructed as you sleep.[69] In addition to impairing liver function and causing fatty liver disease, obesity can also aggravate renal issues. Additionally, those who are obese are more likely to experience mental health problems like anxiety, depression, and low self-esteem, which can be made worse by social stigma. When combined, these issues have the potential to drastically lower quality of life and cause premature death.[70]

Table 2: Summary of conventional therapies for obesity and potential drug-drug interactions

Drug Class	Example(s)	Mechanism of Action	Drug-Drug Interactions	Ref
Lipase Inhibitors	Orlistat	Inhibits pancreatic and gastric lipases, reducing fat absorption.	Reduces absorption of fat-soluble vitamins, may affect warfarin and cyclosporine levels.	71
GLP-1 Receptor Agonists	Liraglutide, Semaglutide	Enhances insulin secretion, slows gastric emptying, reduces appetite.	Increased risk of hypoglycaemia with insulin or sulfonylureas.	72
Sympathomimetic Amines	Phentermine, Diethylpropion	Stimulates norepinephrine release, suppressing appetite.	Contraindicated with MAO inhibitors (hypertensive crisis), may increase heart rate with other stimulants.	73
Combination Therapy	Phentermine-Topiramate	Phentermine: appetite suppression; Topiramate: enhances satiety via GABA modulation.	Avoid with MAO inhibitors, risk of metabolic acidosis with carbonic anhydrase inhibitors.	74
Serotonin Receptor Agonists	Lorcaserin (withdrawn)	Selective 5-HT2C receptor agonist, reducing appetite.	Risk of serotonin syndrome with SSRIs, SNRIs, MAO inhibitors.	75
Dopamine/Norepinephrine Reuptake Inhibitor & Opioid Antagonist	Bupropion-Naltrexone	Bupropion: appetite suppression via dopamine/norepinephrine modulation; Naltrexone: reduces cravings via opioid antagonism.	Lowers seizure threshold (avoid with other seizure-risk drugs), CYP2B6 interactions.	76
Metformin (Off-label Use)	Metformin	Decreases hepatic glucose production, increases insulin sensitivity, may reduce appetite.	Risk of lactic acidosis with alcohol, renal clearance interactions.	77

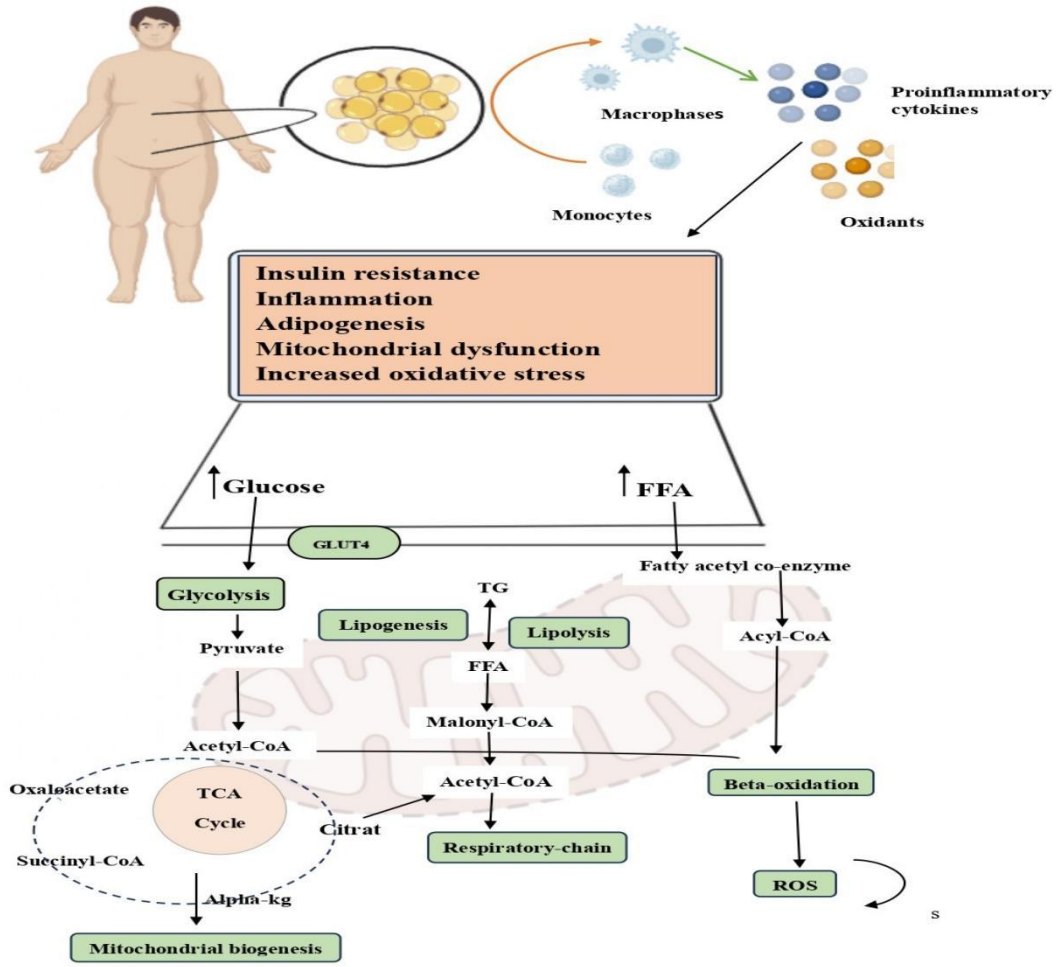


Figure 4: Role of Pro-inflammatory cytokines in Obesity

Table 3: Advantages and disadvantages of individual conventional therapies with drug-drug interaction.

Therapy Type	Advantages	Disadvantages	Ref
Monotherapy (Single Drug Therapy)	1. Simple to manage with fewer chances of complex drug interactions. 2. Easier to monitor and assess effectiveness. 3.Lower risk of polypharmacy-related issues.	1. May not be effective for all patients or conditions (limited therapeutic effect). 2. Risk of resistance (in case of infections or chronic conditions like HIV). 3. Could lead to suboptimal treatment outcomes if only one drug is used.	78
Polypharmacy (Multiple Drug Therapy)	1. Effective in treating complex or multi-faceted conditions. 2. Combines synergistic effects of different drugs for better outcomes. 3. Helps manage comorbidities in elderly patients.	1. High risk of drug-drug interactions (DDIs) leading to adverse effects. 2. Increased complexity in managing dosages and timing. 3. Increased monitoring requirements for therapeutic drug levels and side effects.	79
Combination Therapy (Two or more Drugs in one Therapy)	1. Better therapeutic outcomes due to synergistic effects. 2. Often reduces resistance in chronic conditions (e.g., HIV, TB). 3. Simplifies adherence when combined into one pill (fixed-dose combinations).	1. Risk of additive or synergistic drug interactions. 2. Difficulty in identifying the exact cause of adverse effects. 3. May increase pill burden or lead to treatment fatigue.	80
Adjunctive Therapy (Adding another Drug to Primary Treatment)	1. Helps enhance or complement the effect of the primary drug. 2. Reduces the need for escalation of primary therapy. 3. Can offer better symptom control in	1. Potential for harmful drug-drug interactions, especially if drugs act on similar metabolic pathways. 2. Increased complexity in treatment plans and monitoring.	81

	chronic conditions.	3. Risk of over-medication and polypharmacy.	
Targeted Therapy (Drugs tailored to specific disease markers, e.g., cancer)	1. Higher specificity to disease, reducing off-target effects. 2. Can be more effective for conditions with clear molecular targets. 3. May result in fewer side effects compared to conventional chemotherapy.	1. Expensive and may not be accessible to all patients. 2. Limited effectiveness in the absence of specific molecular targets. 3. Potential for interaction with other treatments (e.g., chemotherapy, immunotherapy).	82
Herbal and Natural Therapies (Alternative Medicine)	1. May provide additional treatment options for patients who prefer non-pharmacologic approaches. 2. Fewer documented major adverse drug interactions in many cases. 3. Perceived as safer by some patients, especially in chronic disease management.	1. Potential for unrecognized drug-drug interactions (especially with prescription medications). 2. Lack of standardized formulations, leading to inconsistent dosing and efficacy. 3. Limited scientific evidence for efficacy and safety in many cases.	83

6. Considerations for Drug-Drug Interactions:

6.1 Metabolism Pathways:

Drugs that compete with one another for the liver's cytochrome P450 enzyme system may result in elevated drug levels or toxicity. Within cells, metabolism pathways are complex sequences of metabolic reactions that create the chemicals required for life and transform foods into energy.[84] The two primary groups of these pathways are anabolic and catabolic. Large molecules like proteins, lipids, and carbohydrates are broken down by catabolic processes, which releases the energy contained in their chemical bonds.[85] The main energy currency of the cell, ATP (adenosine triphosphate), is frequently formed from this energy. Glycolysis is a well-known catabolic mechanism that produces ATP by breaking down glucose into pyruvate.[86] On the other hand, anabolic processes employ energy to create complex molecules from simpler building pieces, including lipids, proteins, and nucleic acids.Protein synthesis, in which amino acids are joined to form proteins, is an example of an anabolic mechanism. To preserve homeostasis, these metabolic processes are strictly controlled, guaranteeing that cells have the ideal ratio of chemicals and energy for optimal operation. Furthermore, because the metabolic network is interdependent, alterations to one pathway frequently have an impact on other pathways, which in turn impacts the general health of the cell.[87]

6.2 Additive Effects:

Combining some medications can increase their harmful or therapeutic effects and increase the likelihood of adverse effects. When two or more drugs, agents, or factors interact in a way where their combined influence is greater than the sum of their separate impacts, this is referred to as an additive effect.[88] This idea is frequently seen in disciplines including environmental science, toxicology, pharmacology, and even the social sciences. Each element alone contributes to the final result in an additive effect; their combination does not affect the total impact.[89] For instance, rather than creating a stronger or weaker effect, the combined effect of two medications with identical modes of action may be equivalent to the sum of their individual effects.[90] This is not the same as antagonistic effects, where one element reduces or neutralizes the effect of the other, or synergistic effects, where the whole result surpasses the sum of the separate effects. In many situations, knowing additive effects is essential since it aids in forecasting the overall results of exposure to several elements or compounds, guaranteeing appropriate handling and safety in a range of applications.[91]

6.3 Pharmacokinetics and Pharmacodynamics:

Interactions can change a drug's intended effect by affecting its distribution, metabolism, excretion, or absorption. Two fundamental areas of pharmacology that explain how medications move through the body and their effects are pharmacokinetics and pharmacodynamics. The absorption, distribution, metabolism, and excretion (ADME) of medications are the main topics of pharmacokinetics. It describes how a drug enters the body, travels to different parts of the body, gets broken down (mostly by the liver), and is finally removed (primarily by the kidneys).These procedures are essential for figuring out a drug's proper dosage and frequency of delivery. Pharmacodynamics, on the other hand, studies how the medication affects the body. This entails being aware of the drug's mode of action, the connection between effect and concentration, and both its dangerous and therapeutic effects.[92] Pharmacodynamics essentially examines how a drug affects the body, including how it interacts with enzymes, receptors, and other cellular constituents to produce the intended biological response. Pharmacokinetics and pharmacodynamics work together to offer a thorough grasp of a medication's effectiveness, safety, and best use.[93]

6.4 Co-morbidities and Patient-Specific Factors:

The probability of drug interactions can be raised by the coexistence of several illnesses or by aging-related changes. In the treatment and prognosis of a number of medical illnesses, co-morbidities and patient-specific factors are crucial.[94] When a primary ailment coexists

with one or more other diseases or conditions, this is referred to as co-morbidities. These can impact the progression of the illness, make treatment approaches more difficult, and have an impact on general health outcomes.[95] For example, a patient with diabetes may also have hypertension, making both disorders more difficult to control. Furthermore, the way a patient reacts to treatment can be greatly influenced by patient-specific characteristics like age, gender, genetics, lifestyle choices (such as smoking or exercise habits), and socioeconomic position.[96] Elderly people may have greater adverse drug reactions or a decreased capacity to metabolize drugs. Similarly, genetic variables can influence both the likelihood of disease and the efficacy of particular therapies by predisposing individuals to particular disorders. Customizing care plans, maximizing treatment approaches, and enhancing patient outcomes all depend on an understanding of these components.[97]

Table 4 Advanced therapies to treat obesity, an individual drug with adrug-drug interaction

Drug name	Mechanism of action	Potential drug-drug interactions	Common interactions	Ref
Orlistat	Inhibits pancreatic lipase, reducing fat absorption in the gastrointestinal tract.	Warfarin (increased bleeding risk)	Reduced absorption of fat-soluble vitamins (A, D, E, K)	98
Liraglutide (Saxenda)	GLP-1 receptor agonist that increases insulin secretion and suppresses appetite.	Insulin (risk of hypoglycemia)	May increase the risk of hypoglycemia when combined with other antidiabetic agents.	99
Semaglutide (Wegovy)	GLP-1 receptor agonist, similar to liraglutide, but with longer half-life and stronger effects on weight loss.	Insulin (risk of hypoglycemia)	May increase the risk of hypoglycemia when combined with other antidiabetic agents (especially with sulfonylureas).	100
Phentermineu	Sympathomimetic that suppresses appetite by increasing norepinephrine release in the brain.	MAO inhibitors (hypertensive crisis risk)	Caution when combined with other stimulants or drugs that affect serotonin levels (e.g., SSRIs).	101
Bupropion/Naltrexone (Contrave)	Bupropion (antidepressant) and Naltrexone (opioid antagonist) work synergistically to reduce hunger and increase energy expenditure.	Antidepressants (risk of seizures)	Caution with alcohol use, may increase seizure risk.	102
Topiramate (Qsymia)	Anticonvulsant that may reduce appetite and promote weight loss by enhancing GABA activity and inhibiting glutamate receptors.	Carbamazepine (reduced efficacy of topiramate)	Use with caution in combination with other CNS depressants (e.g., alcohol, benzodiazepines).	103
Bariatric Surgery	Surgical procedure to restrict stomach size or bypass portions of the small intestine, leading to reduced food intake and nutrient absorption.	Drug absorption may be altered due to anatomical changes, requiring dose adjustments for many medications.	Requires lifelong monitoring of vitamins and minerals, especially vitamin B12, calcium, and iron.	104

Table 5 Gene therapy and anti- obesity therapy to treat obesity

Therapy Type	Therapy/Technology	Mechanism of Action	Stage of Development	Potential Advantages	Ref
Gene Therapy	Leptin gene therapy	Aims to restore normal leptin signaling in obese individuals with leptin resistance.	Preclinical/Clinical Trials	Potential for long-term regulation of appetite and energy balance.	105
Gene Therapy	FTO gene silencing	Targets the fat mass and obesity-associated (FTO) gene to reduce appetite and enhance fat metabolism.	Preclinical/Clinical Trials	Could reduce genetic predisposition to obesity.	106
Gene Therapy	Adiponectin gene therapy	Involves increasing adiponectin levels, a hormone that enhances insulin sensitivity and fat metabolism.	Preclinical/Clinical Trials	Helps improve fat metabolism and reduce fat accumulation.	107
Gene Therapy	Ghrelin gene therapy	Targets the ghrelin hormone pathway to regulate hunger and satiety signals.	Preclinical	May help reduce excessive hunger in obese individuals.	108
Anti-Obesity Therapy	GLP-1 Receptor Agonists	Mimics glucagon-like peptide-1 (GLP-1), improving insulin secretion and promoting satiety.	Approved/Clinical Trials	Proven efficacy in weight loss and improving metabolic health.	109
Anti-Obesity Therapy	Anti-NPY/AgRP (Neuropeptide Y)	Inhibits NPY/AgRP signaling, which is involved in appetite stimulation.	Preclinical	Could decrease appetite and food intake.	110
Anti-Obesity Therapy	Brown Adipose Tissue (BAT) Activation	Stimulates the browning of white adipose tissue to increase energy expenditure and fat burning.	Clinical Trials	Potential to increase energy expenditure and improve fat loss.	111
Anti-Obesity Therapy	Endocannabinoid System Antagonists	Blocks cannabinoid receptors to reduce appetite and food intake.	Preclinical/Clinical Trials	Reduces overeating without affecting mood.	112
Anti-Obesity Therapy	Semaglutide (GLP-1 Agonist)	A GLP-1 receptor agonist that slows gastric emptying, enhances insulin secretion, and reduces appetite.	Approved/Clinical Trials	Significant weight loss and improved blood sugar control.	113
Anti-Obesity Therapy	Bariatric Surgery (Endoscopic)	Involves non-surgical, endoscopic procedures to shrink the stomach or bypass sections of the intestine.	Approved/Clinical Trials	Non-invasive, with significant weight loss effects.	114

Table 6: List of herbal therapies with their moa for the treatment of obesity (genetic and non-genetic)

Herb	Mechanism of Action (MOA)	Usage & Dosage	Past work done	Ref
Green Tea (Camellia sinensis)	Contains catechins (EGCG) and caffeine that enhance fat oxidation, increase thermogenesis, and promote fat burning.	2-3 cups of green tea daily or 250-500 mg of green tea extract (50-60% EGCG).	Meta-analysis shows significant fat loss and fat oxidation boost	115
Garcinia Cambogia	HCA (Hydroxycitric Acid) inhibits citrate lyase, blocking fat storage, and increases serotonin levels to reduce appetite.	500-1000 mg before meals.	Small but positive effects on weight loss	116
Glucomannan	A water-soluble fiber that expands in the stomach, promoting fullness and reducing calorie intake.	500-1000 mg, 3 times daily before meals, with lots of water.	Significant weight loss observed in clinical trials	117
Cayenne Pepper (Capsaicin)	Capsaicin increases thermogenesis and fat oxidation, helping to burn more calories.	1/4 tsp of cayenne pepper in food or 1-2 mg capsaicin supplement before meals.	Enhances calorie burning and fat loss	118
Coleus Forskohlii (Forskolin)	Increases cAMP levels, which stimulate fat breakdown and prevent fat accumulation.	250 mg standardized to 10-20% forskolin, taken twice daily.	Studies show fat loss and muscle preservation	119
Berberine	Activates AMPK, improving metabolism, increasing fat oxidation, and lowering fat storage.	500 mg, 2-3 times a day with meals.	Significant reduction in fat and improved insulin sensitivity	120
Turmeric (Curcuma longa)	Curcumin increases adiponectin (fat-burning hormone), improves insulin sensitivity, and reduces inflammation.	500 mg of curcumin, standardized to 95% curcuminoids, or 1 tsp of turmeric powder, taken with black pepper for absorption.	Positive effects on fat reduction and insulin sensitivity	121
Cinnamon (Cinnamomum verum)	Improves insulin sensitivity, stabilizes blood sugar, and reduces cravings.	1-2 teaspoons of ground cinnamon per day, in food or capsules.	Improves glucose metabolism and reduces hunger	122
Hoodia Gordonii	Suppresses appetite by affecting the hypothalamus, which controls hunger.	400-800 mg daily.	Appetite reduction effects are noted, but more research is needed.	123
Ashwagandha (Withaniasomnifera)	Reduces cortisol (stress hormone) levels, which helps control stress-related eating and improve sleep.	500–600 mg of ashwagandha extract per day, preferably in the evening.	Reduces stress and promotes weight loss via cortisol regulation	124
Fennel (Foeniculum vulgare)	Fennel seeds act as a mild diuretic and appetite suppressant, reducing bloating and cravings.	1 teaspoon of fennel seeds (in tea or capsule) 1-2 times daily.	May help reduce appetite and bloating	125
Chitosan	A fiber that binds to fats in the digestive tract, preventing fat absorption.	500 mg before meals.	Moderately reduces fat absorption	126
Moringa (Moringa oleifera)	Contains antioxidants and anti-inflammatory compounds that may reduce fat accumulation and support metabolic health.	1-2 teaspoons of moringa powder or 500 mg of moringa extract per day.	Potential effects on fat reduction and metabolism	126
Dandelion (Taraxacum officinale)	Acts as a diuretic and digestive stimulant, promoting detoxification and reducing bloating.	1-2 teaspoons of dandelion root in tea or capsules.	May help with water retention and metabolism	127

Flaxseed (Linum usitatissimum)	High in omega-3 fatty acids and fiber, flaxseeds promote fat burning and reduce hunger.	1-2 tablespoons of ground flaxseeds daily, added to smoothies, yogurt, or baked goods.	Improves fat metabolism and reduces fat storage	128
Alfalfa (Medicago sativa)	Rich in vitamins, minerals, and fiber, alfalfa helps regulate blood sugar and improve fat metabolism.	500 mg of alfalfa supplement or 1-2 teaspoons of dried leaves in tea, daily.	Supports blood sugar regulation and fat loss	129
Ginger (Zingiber officinale)	Improves digestion and reduces bloating, also has thermogenic properties that increase calorie burning.	1–2 grams of fresh ginger root or 500 mg of ginger extract per day.	Boosts metabolism and fat oxidation	130

Green Tea (Camellia sinensis)

Green tea (Camellia sinensis) is a type of tea made from the leaves of the Camellia sinensis plant, known for its rich antioxidant content and health benefits. Unlike black tea, green tea undergoes minimal oxidation during processing, which helps preserve its natural compounds, particularly catechins, a group of antioxidants.[131] These antioxidants, especially epigallocatechin gallate (EGCG), are credited with various health benefits, including improved heart health, weight management, and cancer prevention. Green tea is often praised for its calming effects due to the presence of the amino acid L-theanine, which promotes relaxation without causing drowsiness.[132] It is traditionally enjoyed in East Asian cultures but has gained global popularity for its purported health benefits and refreshing taste. The leaves can be brewed into a light, grassy, and slightly astringent beverage, and green tea is available in various forms, such as loose-leaf, bags, or powdered matcha.[133] The plant thrives in subtropical and tropical climates, particularly in China, Japan, and Taiwan.The main way that green tea (Camellia sinensis) works is through its bioactive ingredients, especially polyphenols like catechins. These substances work as potent antioxidants by scavenging the body's free radicals, particularly epigallocatechin gallate (EGCG).[134] It lessen inflammation and oxidative stress, helping to protect cells. Additionally, catechins help to boost mood and mental clarity by blocking the breakdown of key neurotransmitters, such as serotonin and dopamine, by enzymes.[135] Green tea has also been demonstrated to boost metabolic function and increase fat oxidation, which may help with weight management. Green tea's caffeine boosts the central nervous system, which makes you more focused and awake. Green tea promotes general health and well-being through a complex mechanism of action that includes antioxidant, anti-inflammatory, metabolic, and neuroprotective benefits.[136]

Garcinia Cambogia

Garcinia Cambogia is a tropical fruit, also known as Malabar tamarind, native to Southeast Asia and India. It has gained popularity in the wellness and weight loss industry due to its potential health benefits.[137] The fruit contains a key active ingredient called hydroxycitric acid (HCA), which is believed to help suppress appetite and inhibit the fat-producing enzyme called citrate lyase. Some studies suggest that Garcinia Cambogia may aid in weight loss by reducing fat accumulation and curbing hunger, although results can vary from person to person. Additionally, it is thought to improve exercise endurance and lower cholesterol levels. However, while many people use Garcinia Cambogia as a supplement for weight management, scientific evidence supporting its effectiveness remains mixed, and there are concerns about potential side effects, particularly when taken in high doses or for extended periods. As with any supplement, it's advisable to consult a healthcare provider before starting a Garcinia Cambogia regimen.[138] The tropical fruit garcinia cambogia is well known for its possible weight-loss benefits. HCA, its main active component, is thought to work by blocking the activity of an enzyme known as citrate lyase, which is essential for the conversion of carbs into fat. HCA lessens the body's fat buildup by inhibiting this enzyme. Furthermore, it is believed that Garcinia Cambogia raises serotonin levels in the brain. This can lessen emotional eating and hunger.[139] Although the effectiveness of Garcinia Cambogia for weight reduction varies from person to person and more research is required to understand its impact completely, these mechanisms are thought to work together to help weight loss by reducing appetite and fat accumulation.[140]

Glucomannan

Glucomannan is a natural, water-soluble polysaccharide derived from the root of the *Amorphophallus konjac* plant, commonly known as the konjac plant. It is primarily used as a dietary supplement due to its ability to absorb water and expand in the stomach, leading to a feeling of fullness or satiety. This makes it popular as a weight-loss aid.[141] Glucomannan is rich in dietary fiber and is often included in low-calorie foods and meal replacements. It has also been studied for its potential benefits in managing cholesterol levels, blood sugar, and constipation. In addition to weight loss, it may support heart health by helping to lower cholesterol and regulate blood sugar levels.[142] However, it is important to consume glucomannan with plenty of water, as it can cause choking or blockage in the throat if not taken with enough liquid. The supplement is generally considered safe when used appropriately, but users should consult

healthcare providers before starting any new supplement regimen, especially those with existing medical conditions.[143] The body uses glucomannan mainly as a soluble fiber. When ingested, glucomannan expands in the stomach and absorbs water, creating a gel-like material. This can aid in lowering total food consumption by increasing satiety, or the sensation of fullness. Additionally, glucomannan promotes a steady release of nutrients into the bloodstream and aids in blood sugar regulation by slowing down gastric emptying.[144] Additionally, it binds to carbohydrates and fats in the digestive system, which may lessen their absorption and decrease cholesterol. Glucomannan is often used as a weight loss supplement and to control blood sugar levels in people with type 2 diabetes because of its capacity to promote satiety and decrease nutrient absorption.[145]

Cayenne Pepper (Capsaicin)

Capsicum annuum, the scientific name for cayenne pepper, is a hot red spice made from powdered and dried chili peppers. Capsaicin, the main active ingredient in cayenne pepper, is what gives it its potent heat.[146] Capsaicin produces a burning or heated sensation by interacting with pain receptors in the skin and mucous membranes. This substance improves digestion, speeds up metabolism, and increases calorie burn to help people lose weight, among other health benefits.[147] In addition to its anti-inflammatory qualities, capsaicin has the ability to reduce pain when applied topically as creams or ointments. Furthermore, cayenne pepper has been used for millennia in traditional medicine to cure a variety of conditions, including digestive problems, sore throats, and even poor circulation.[148] Cayenne pepper, which is high in vitamins A and C, also possesses antioxidant qualities that help prevent oxidative stress and shield cells from harm. Despite having a hot flavour, cayenne pepper is a flexible ingredient that may be used in a broad variety of international cuisines, including soups, marinades, and spicy sauces.[149] Primarily recognized for its main ingredient, capsaicin, cayenne pepper works by primarily targeting the body's pain receptors. TRPV1 (Transient Receptor Potential Vanilloid 1) is a receptor found on sensory nerve cells that capsaicin binds to. When capsaicin attaches to this receptor, which is normally activated by heat and physical abrasion, it produces a burning or heated sensation.[150] Ion channels open as a result of this interaction, letting calcium and sodium ions enter the cells. This causes nerve signals, which the brain interprets as heat or pain. Repeated exposure to capsaicin gradually reduces the body's reserves of substance P.A neurotransmitter that efficiently desensitizes the area and lessens pain by transmitting pain signals.[151] It has also been proposed that capsaicin's capacity to enhance blood flow and encourage thermogenesis and the generation of heat contributes to its effects on metabolism. Because of these processes, cayenne pepper is good for reducing pain and may be used therapeutically to treat conditions like neuropathic pain or arthritis.[152]

Coleus Forskohlii (Forskolin)

Coleus Forskohlii, also known as Forskolin, is a tropical plant belonging to the mint family, Lamiaceae, native to Southeast Asia, particularly India and Nepal. It has been used in traditional medicine for centuries due to its various health benefits. The active compound, forskolin, is found in the root of the plant and has gained popularity in modern supplements for its potential therapeutic properties.[153] Forskolin is believed to support weight loss, improve cardiovascular health, and promote fat loss by stimulating the production of cyclic AMP (cAMP), which plays a key role in fat metabolism. Additionally, it has been explored for its potential benefits in managing asthma, glaucoma, and high blood pressure due to its ability to relax smooth muscles and improve blood flow. Despite its promising effects, more research is needed to fully understand the extent of its benefits and possible side effects.[154] Forskolin is often marketed as a natural supplement, but like all herbs and supplements, it should be used cautiously and ideally under the guidance of a healthcare professional. The active ingredient in Coleus forskohlii, forskolin, functions by activating the adenylate cyclase enzyme, which raises cyclic AMP (cAMP) levels in cells. Protein kinase A (PKA) is activated by elevated cAMP, which subsequently sets off a series of cellular reactions. This method can increase the breakdown of fat (lipolysis), promote vasodilation by relaxing blood vessel smooth muscle cells, and boost thyroid hormone synthesis, among other benefits.[155] Furthermore, forskolin's effect on cAMP has been connected to enhancements in respiratory and cardiac performance. Forskolin is therefore frequently researched for its possible advantages in treating asthma, cardiovascular disease, and weight management. Commonly recognized for its active ingredient forskolin, Coleus forskohlii functions by activating the adenylate cyclase enzyme, which raises cyclic AMP (cAMP) levels in cells.[156] Protein kinase A (PKA) is activated by elevated cAMP, and this in turn sets off a variety of cellular reactions. This method has multiple impacts, including increasing the synthesis of thyroid hormones, promoting vasodilation by relaxing smooth muscle cells in blood arteries and increasing fat breakdown (lipolysis). Furthermore, forskolin's effect on cAMP has been connected to enhancements in respiratory and cardiac performance. Forskolin is therefore frequently researched for its possible advantages in the treatment of asthma, cardiovascular health, and weight management.[157]

Berberine

Berberine is a natural compound found in several plants, including *Berberis* species, such as *Berberis aristata* and *Berberis vulgaris*. It has been used for centuries in traditional medicine systems like Ayurveda and Traditional Chinese Medicine for its potential health benefits. Berberine is most commonly known for its effects on blood sugar regulation. It can help lower blood glucose levels and improve insulin sensitivity, making it a popular supplement for managing type 2 diabetes.[158] In addition to its role in glucose metabolism, berberine has antimicrobial, anti-inflammatory, and

antioxidant properties. Research also suggests that berberine may support heart health by lowering cholesterol levels and improving lipid profiles. Furthermore, it is thought to have a positive effect on gut health by influencing the gut microbiome. However, despite its potential, berberine can interact with certain medications, so it is important to consult with a healthcare provider before starting supplementation. The main way that berberine functions is by triggering the AMP-activated protein kinase (AMPK), which controls the equilibrium of energy within cells.[159] Berberine is especially helpful in controlling type 2 diabetes because AMPK activation improves insulin sensitivity, decreases hepatic glucose synthesis, and increases glucose absorption. Berberine also affects lipid metabolism, boosting the expression of LDL receptors and blocking enzymes such as HMG-CoA reductase, which lowers LDL cholesterol, triglycerides, and total cholesterol. Additionally, it has antioxidant and anti-inflammatory qualities that aid in lowering the body's levels of inflammation and oxidative stress. Additionally, it has been demonstrated that berberine alters the gut microbiota, encouraging a more balanced population of intestinal bacteria, which may further support metabolic health. It is a promising treatment drug for several metabolic illnesses due to its diverse activities.[160] Berberine is a bioactive substance that supports health through a variety of methods. It mainly functions by triggering the activation of AMP-activated protein kinase (AMPK), an enzyme that controls the energy balance within cells. AMPK activation improves the absorption of glucose, enhances insulin sensitivity, and lowers the synthesis of glucose in the liver, making berberine very helpful in the treatment of type 2 diabetes. Berberine also affects lipid metabolism by blocking enzymes such as HMG-CoA reductase and upregulating the expression of LDL receptors, which lowers total cholesterol, triglycerides, and LDL cholesterol. Additionally, it has antioxidant and anti-inflammatory qualities that aid in lowering the body's levels of inflammation and oxidative stress. Additionally, it has been demonstrated that berberine alters the gut microbiota, encouraging a more balanced population of intestinal bacteria, which may further support metabolic health.[161]

Turmeric (Curcuma longa)

Turmeric (Curcuma longa) is a perennial plant belonging to the ginger family (Zingiberaceae) and is native to Southeast Asia. Known for its vibrant yellow-orange color, it is most commonly used as a spice, particularly in Indian cuisine, where it is a key ingredient in curry powders and other dishes. The active compound in turmeric, curcumin, is responsible for its characteristic color and is widely studied for its potential health benefits, including anti-inflammatory, antioxidant, and anti-cancer properties. The plant's rhizomes (underground stems) are harvested, dried, and ground into powder for culinary and medicinal uses.[162] Beyond cooking, turmeric has a rich history in traditional medicine, especially in Ayurvedic and Chinese practices, where it is believed to treat a variety of ailments, including digestive issues, skin conditions, and joint pain. The versatility of turmeric extends to cosmetics, where it is used in skin treatments, and in the dye industry, where it has been used as a natural dye for centuries. While it is generally safe for consumption, high doses or long-term use of curcumin supplements should be approached with caution, as it may interact with certain medications.[163] Curcumin primarily modulates signaling pathways involved in inflammation and cell survival to produce its potent anti-inflammatory, antioxidant, and anti-cancer effects. It prevents nuclear factor-kappa B (NF-κB), a crucial transcription factor implicated in the production of pro-inflammatory cytokines, from becoming activated. Furthermore, curcumin eliminates oxidative stress, which is linked to several chronic illnesses, by neutralizing free radicals. Curcumin is a possible anticancer drug since it also affects detoxification-related enzymes like cytochrome P450 and controls cell cycle progression and apoptosis. Curcumin's efficacy in metabolic and cardiovascular diseases is further supported by evidence that it lowers cholesterol, enhances endothelial function, and alters immunological responses.[164] Curcumin, the active chemical, works in multiple ways to produce its therapeutic effects. Curcumin primarily modulates signaling pathways involved in inflammation and cell survival to produce its potent anti-inflammatory, antioxidant, and anti-cancer effects. It prevents nuclear factor-kappa B (NF-κB), a crucial transcription factor involved in the production of pro-inflammatory cytokines, from becoming activated. Furthermore, curcumin eliminates oxidative stress, which is linked to several chronic illnesses, by neutralizing free radicals. Curcumin is a possible anticancer treatment since it also affects detoxification-related enzymes like cytochrome P450 and controls apoptosis and cell cycle progression. Curcumin's efficacy in metabolic and cardiovascular diseases is further supported by evidence that it lowers cholesterol, enhances endothelial function, and alters immunological responses.[165]

Cinnamon (Cinnamomum verum)

Cinnamon (Cinnamomum verum), often referred to as "true cinnamon," is a spice derived from the inner bark of the Cinnamomum verum tree, native to Sri Lanka, southern India, and some other parts of Southeast Asia. This tree thrives in tropical climates and grows up to 15 meters tall. The bark is harvested, dried, and then rolled into tight, thin quills, which are the cinnamon sticks commonly seen in stores. True cinnamon has a delicate, sweet, and slightly citrusy flavour, making it prized in both culinary and medicinal applications. The distinct aroma and taste come from compounds like cinnamaldehyde.[166] In contrast to its more common counterpart, Cassia cinnamon (Cinnamomum cassia), true cinnamon has a lighter colour and more complex flavour profile, and is also lower in coumarin, a naturally occurring substance that can be harmful in large amounts. True cinnamon has been used for centuries, not only for flavouring food and beverages but also for its potential health benefits, such as aiding digestion, reducing inflammation, and acting as an antioxidant. Although cinnamon (Cinnamomum verum)

has several bioactive chemicals, its main active ingredient is cinnamon aldehyde. It has been demonstrated that cinnamon aldehyde has antibacterial, anti-inflammatory, and antioxidant qualities. By improving insulin sensitivity, encouraging glucose uptake in cells, and blocking enzymes that break down carbs such as α-glucosidase, it helps control blood sugar levels.[167] Cinnamon has also been shown to affect lipid metabolism, possibly reducing triglyceride and cholesterol levels, which promotes heart health. Compounds like polyphenols, which shield cells from oxidative stress and lower the risk of chronic diseases, give it its antioxidant qualities. Cinnamon also possesses antibacterial effects, which can help in preventing infections and supporting digestive health. Among the many bioactive substances that cinnamon (Cinnamomum verum) has, cinnamon aldehyde is the main active ingredient. It has been demonstrated that cinnamon aldehyde has antibacterial, anti-inflammatory, and antioxidant qualities. It aids in regulating blood sugar levels by improving insulin sensitivity, encouraging cell uptake of glucose, and blocking the breakdown of carbs by enzymes like α-glucosidase.[168] Cinnamon has also been shown to influence lipid metabolism, possibly reducing triglyceride and cholesterol levels, which promotes heart health. Its antioxidant qualities stem from substances like polyphenols, which lower the risk of chronic diseases by shielding cells from oxidative stress. Additionally, cinnamon has antibacterial properties that can support digestive health and help stave off infections.[169]

Hoodia Gordonii

Hoodia gordonii is a succulent plant native to the deserts of Southern Africa, primarily found in Namibia and South Africa. It has a long history of use among indigenous groups, particularly the San people, who traditionally used it as an appetite suppressant during long hunting trips to help prevent hunger and thirst. The plant's active ingredient, a steroidal glycoside called P57, is believed to work by affecting the brain's hunger-regulating mechanisms, particularly in the hypothalamus, leading to a reduced desire to eat. In recent years, Hoodia gordonii has gained attention in the weight loss industry as a potential natural appetite suppressant, though research on its efficacy and safety remains limited. Commercial products often claim that Hoodia can help with weight loss, but concerns about the sustainability of wild harvesting, potential side effects, and lack of regulatory oversight in supplements have raised doubts about its true effectiveness.[170] While Hoodia's use is still popular in some circles, it is important to approach products containing it with caution, as some may be adulterated or contain little to no actual Hoodia. Because of its main ingredient, P57, Hoodia gordonii has become well-known as a natural hunger suppressor. P57 is assumed to interact with the hypothalamus, the area of the brain in charge of controlling appetite and fullness, as part of Hoodia gordonii's central nervous system mode of action. It is believed that P57 reduces sensations of hunger by imitating glucose molecules and fooling the brain into believing the body is full. By suppressing appetite, this activity reduces the desire to consume food. Although there is some evidence that it suppresses hunger, more research and clinical trials are still necessary to fully determine its efficacy and safety, as well as to validate any potential negative effects and long-term advantages.[171] Because of its main ingredient, P57, Hoodia gordonii has become well-known as a natural hunger suppressor. P57 is thought to interact with the hypothalamus in the central nervous system, which is where Hoodia gordonii is thought to work. area of the brain in charge of controlling hunger and fullness. It is believed that P57 reduces sensations of hunger by imitating glucose molecules and fooling the brain into believing the body is full. By suppressing appetite, this activity reduces the desire to consume food. Although there is some evidence that it suppresses hunger, more research and clinical trials are still necessary to fully determine its efficacy and safety, as well as to validate any potential negative effects and long-term advantages.[172]

Ashwagandha (*Withania somnifera*)

Ashwagandha (*Withania somnifera*), commonly known as Indian ginseng or winter cherry, is a powerful herb widely used in traditional Ayurvedic medicine for its adaptogenic properties, which help the body cope with stress and maintain balance. Native to India and parts of Africa, it is a small shrub with yellow flowers and red fruits. The root and sometimes the leaves of the plant are used for medicinal purposes. Ashwagandha is known for its ability to reduce cortisol levels, boost energy, enhance stamina, and improve mental clarity. It has also been studied for its potential to support immune function, lower anxiety, and improve sleep quality. Additionally, it is thought to have anti-inflammatory, antioxidant, and neuroprotective effects, making it a popular choice for those seeking to improve overall health and wellness.[173] Despite its numerous benefits, it's important to use Ashwagandha under the guidance of a healthcare provider, especially for individuals with specific health conditions or who are pregnant or breastfeeding. *Withania somnifera*, or ashwagandha, works through a variety of pathways, chiefly through regulating the body's immune system, inflammation, and stress response. It is categorized as an adaptogen, which means that it balances the body's natural defenses against stress. The hypothalamic-pituitary-adrenal (HPA) axis controls the release of cortisol and other stress hormones.[174] Bioactive substances found in ashwagandha, like withanolides, interact with bodily and brain receptors to lower inflammation and oxidative stress. By promoting brain health and cognitive function, these substances also increase the activity of antioxidants and encourage neuroprotection. Furthermore, ashwagandha has been demonstrated to affect neurotransmitters such as serotonin and GABA, which adds to its soothing and mood-regulating properties.[175]

Fennel (*Foeniculum vulgare*)

Fennel (*Foeniculum vulgare*) is a highly aromatic herb belonging to the parsley family, Apiaceae. Native to the

Mediterranean region, fennel is widely cultivated for its edible leaves, seeds, and bulbs, all of which have culinary and medicinal uses. The plant can grow up to 6 feet tall, with feathery, fern-like leaves and yellow flowering umbels that bloom in late summer. Fennel seeds are particularly prized for their sweet, anise-like flavor, which makes them a popular spice in many cuisines, especially in Mediterranean, Indian, and Middle Eastern dishes. The bulbs are crisp and have a mild licorice flavor, often used in salads, roasted, or braised. Fennel is also known for its health benefits, including aiding digestion, reducing inflammation, and acting as an antioxidant. In traditional medicine, fennel has been used to treat a variety of ailments, from digestive issues to respiratory conditions. Its essential oil contains compounds like anethole, which contributes to its characteristic scent and therapeutic properties.[176]

Chitosan

Chitosan is a biopolymer derived from chitin, a substance found in the exoskeletons of crustaceans like shrimp and crabs. It is a natural polysaccharide, composed of glucosamine and N-acetylglucosamine, and is known for its wide range of applications in the fields of medicine, agriculture, and food industries. Chitosan is commonly used as a dietary supplement due to its purported benefits, including weight loss support, cholesterol reduction, and its ability to promote healthy digestion. It is also used as a fat blocker, as it is believed to bind to fats and prevent their absorption in the body. In the food industry, chitosan functions as a natural preservative and can be found in certain food packaging materials, extending shelf life by inhibiting microbial growth. In agriculture, it is used as a bio-pesticide and a natural plant growth enhancer. Additionally, chitosan has potential applications in wound healing and drug delivery due to its biocompatibility, biodegradability, and antimicrobial properties. Despite its many benefits, its effectiveness in some areas, such as weight loss, remains a subject of ongoing research and debate.[177]

Moringa (*Moringa oleifera)*

Moringa (*Moringa oleifera*) is a fast-growing, drought-resistant tree native to parts of Africa and Asia, often referred to as the "drumstick tree" or "miracle tree" due to its impressive nutritional and medicinal properties. The tree is known for its nutrient-rich leaves, pods, flowers, and seeds, which are utilized for a variety of health benefits. Moringa leaves are particularly high in vitamins (such as vitamin A, C, and E), minerals (like calcium, potassium, and iron), and antioxidants, making them a powerful natural supplement to support immune health, reduce inflammation, and boost energy levels. Additionally, Moringa has been traditionally used in herbal medicine for its anti-inflammatory, anti-bacterial, and blood sugar-regulating properties. The tree's leaves, pods, and seeds have become popular in both culinary and wellness practices worldwide, often consumed in powder form, teas, or as oil. Moringa's ability to thrive in arid environments and its versatility in supporting human health make it a valuable resource in combating malnutrition, particularly in developing regions.[178]

Dandelion (*Taraxacum officinale*)

Dandelion (*Taraxacum officinale*) is a common perennial plant found in temperate regions around the world. Characterized by its bright yellow, composite flowers, dandelions are often seen in lawns, meadows, and roadsides. The plant features deeply lobed, jagged leaves that grow in a rosette pattern at the base. Its stem is hollow and usually leafless, culminating in the familiar puffball seed head after the flowers have matured. The seeds, attached to fine, silky hairs, are dispersed by the wind, allowing the plant to spread quickly. Dandelions have long been recognized for their medicinal properties their roots, leaves, and flowers are used in traditional herbal remedies for various ailments, including digestive issues and inflammation. Additionally, dandelions are highly nutritious, containing vitamins A, C, K, and several B vitamins, as well as minerals like iron and calcium. Despite their reputation as a weed, dandelions are beneficial to ecosystems, providing food for pollinators such as bees and butterflies.[179]

Flaxseed (*Linum usitatissimum*)

Flaxseed, scientifically known as *Linum usitatissimum*, is a highly nutritious seed derived from the flax plant, native to the Mediterranean region but now widely cultivated around the world. It is one of the oldest cultivated crops, known for its use both in the textile industry (as flax fibers) and as a food source. The small, flat, oval-shaped seeds are available in two primary varieties: brown and golden, with minimal nutritional differences between them. Flaxseed is rich in omega-3 fatty acids, particularly alpha-linolenic acid (ALA), which has numerous health benefits, including promoting heart health and reducing inflammation.[180] It is also a great source of dietaryfiber, particularly soluble fiber, which aids digestion and can help regulate blood sugar levels. Additionally, flaxseeds are packed with lignans, plant compounds that have antioxidant properties and may help reduce the risk of certain cancers, particularly breast cancer. Due to its high nutrient density, flaxseed is often incorporated into diets in the form of ground seeds, oil, or supplements. However, it's important to note that whole flaxseeds may pass through the digestive system undigested, so grinding them is recommended for maximum nutrient absorption.[181]

Alfalfa (*Medicago sativa*)

Alfalfa (*Medicago sativa*) is a perennial flowering plant in the legume family, known for its high nutritional value and versatility as a forage crop. It is widely cultivated for its leaves, which are rich in protein, vitamins, and minerals, making it a staple in animal feed, particularly for livestock such as cattle, horses, and sheep. Alfalfa is also used in human consumption in the form of sprouts and is sometimes incorporated into herbal supplements due to its potential health benefits, such as promoting digestion and providing antioxidants. The plant thrives in well-drained soils and requires a temperate climate for optimal growth, often reaching heights of 24 to 36 inches. Alfalfa has deep roots, which

help it to withstand drought conditions and improve soil fertility by fixing nitrogen through its symbiotic relationship with rhizobial bacteria. Its distinctive purple or blue flowers attract pollinators like bees. Alfalfa's ability to enrich soil, combined with its high yield of nutrient-dense forage, makes it an important crop in sustainable agriculture systems.[182]

Ginger (*Zingiber officinale*)

Ginger (*Zingiber officinale*) is a flowering plant native to Southeast Asia, widelyrecognized for its aromatic rhizomes, which are commonly used as both a spice and a medicinal herb. The plant belongs to the Zingiberaceae family, and its rhizome has a sharp, spicy, and slightly sweet flavor. It is cultivated for its underground stem, which is typically harvested fresh, dried, or ground into powder. Ginger has been used for thousands of years in traditional medicine, prized for its anti-inflammatory, antioxidant, and digestive properties.[183] The active compounds in ginger, particularly gingerol, are thought to contribute to its ability to alleviate nausea, reduce pain, and support immune function. Beyond its medicinal benefits, ginger is a key ingredient in various culinary dishes and beverages worldwide, ranging from savory foods to drinks like ginger tea and ginger ale. Cultivation of ginger requires a warm, humid climate and rich, well-drained soil, making it an important crop in countries like India, China, and Indonesia. [184]

Conclusion:

Obesity, both hereditary and non-genetic in origin, is a significant global health issue with numerous causes and implications. Non-genetic obesity is frequently caused by lifestyle factors such as sedentary behavior, poor food, and environmental effects. Still, genetic obesity is caused by hereditary and molecular changes that affect metabolism, appetite regulation, and energy expenditure. Effective prevention and treatment plans must be both broad and customized. The cornerstone of non-genetic obesity treatment is lifestyle adjustment, which includes balanced nutrition, frequent physical activity, and behavioral therapy. Public health programs that promote healthy surroundings, limit the promotion of unhealthy foods, and increase access to healthier alternatives are also critical. Genetic obesity, on the other hand, frequently necessitates a more tailored strategy. Advances in genomics and molecular medicine have enabled the identification of gene variations associated with obesity, paving the way for precision medicine. Pharmacological therapy, bariatric surgery, and targeted gene-based treatments are being investigated for both monogenic and syndromic obesity. Despite advancements, there are still hurdles in closing the research-to-clinical-application gap, ensuring fair access to therapies, and eliminating the obesity stigma.

Future Prospective:

Precision medicine holds the key to the future of obesity therapy, as individual genetic, metabolic, and behavioral profiles inform tailored interventions. Gene editing techniques like CRISPR-Cas9 have the ability to fix harmful genes in monogenic obesity. New research on the gut microbiota reveals that it plays an important role in obesity development. Probiotics, prebiotics, and fecal microbiota transplantation could provide new treatment alternatives. Artificial intelligence and digital health platforms are rapidly being used in obesity prevention and management. Wearables, smart phone apps, and machine learning algorithms can be used to monitor activities, forecast risks, and deliver real-time interventions. Epigenetic studies may shed light on how environmental variables alter gene expression related to obesity. Interventions targeting epigenetic alterations could supplement conventional treatments. Future initiatives must consider broader societal reforms, such as food policy reform, urban planning to promote active living, and socioeconomic support systems to address health disparities. More long-term studies are required to assess the efficacy, safety, and sustainability of present and developing obesity treatments, particularly in varied populations.

Declaration:

Ethics approval and consent to participate: This manuscript is a review. Hence, no experiments in animals or humans are included in this study, so ethical approval and consent are not required.

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