

Phytochemical Profiling And In-Vitro Anti-Obesity Activity Of *Leucas Aspera*: A Potential Natural Therapeutic Approach

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ABSTRACT

Obesity is a rapidly growing global public health challenge characterized by excessive adipose tissue accumulation, resulting in chronic low-grade inflammation and substantial economic burdens on healthcare systems. Conventional treatments, such as pharmacotherapy and bariatric surgery, face strict limitations due to high costs, adverse side effects, and poor long-term adherence. Consequently, there is an escalating interest in exploring safer, plant-derived therapeutic alternatives. *Leucas aspera* (Willd.) Link, an annual aromatic herb belonging to the Lamiaceae family, is widely utilized across traditional medicine systems in Asia for various inflammatory and metabolic ailments. Recent investigations have highlighted its rich phytochemical framework, which includes bioactive secondary metabolites such as flavonoids, phenolics, saponins, tannins, and terpenoids. In-vitro biochemical and cell-based models demonstrate that *Leucas aspera* possesses high antioxidant capacities and multi-targeted anti-obesity properties. Mechanistically, its crude extracts and active components mitigate weight gain by inhibiting crucial digestive enzymes like pancreatic lipase, α -amylase, and α -glucosidase, thereby limiting caloric and lipid absorption. Furthermore, it downregulates critical transcription factors like PPAR-gamma and C/EBPalpha to suppress adipogenesis, stimulates lipolysis via hormone-sensitive lipase, enhances glucose uptake, and manages energy homeostasis through potential activation of the AMPK pathway. While current in-vitro data positions *Leucas aspera* as a promising natural anti-obesity resource, critical research gaps remain regarding standardized extraction, toxicological profiling, and robust in-vivo validation. Addressing these challenges through advanced multi-omics, nanoformulation, and controlled clinical trials is essential to establish its long-term efficacy and safety as a definitive therapeutic agent.

Keywords: *Leucas aspera*, Obesity, Phytochemicals, Pancreatic lipase, Adipogenesis, Anti-obesity activity.

INTRODUCTION

Obesity is a multifactorial chronic metabolic disorder characterized by excessive accumulation of adipose tissue that adversely affects health. It has emerged as one of the most significant public health challenges worldwide due to its rapidly increasing prevalence among children, adolescents, and adults (1). According to the World Health Organization (WHO), obesity has nearly tripled globally since 1975, and millions of individuals are affected by overweight and obesity-related complications every year (2).

The pathogenesis of obesity involves a complex interaction between genetic, environmental, behavioral, and metabolic factors. Excessive caloric intake, sedentary lifestyle, hormonal dysregulation, and genetic predisposition contribute significantly to

the development of obesity (3). Adipose tissue, previously regarded as a passive storage site for lipids, is now recognized as an active endocrine organ that secretes various adipokines and inflammatory mediators involved in energy homeostasis, insulin sensitivity, and inflammation (4).

Obesity is strongly associated with numerous chronic diseases, including type 2 diabetes mellitus, cardiovascular diseases, hypertension, dyslipidemia, non-alcoholic fatty liver disease (NAFLD), and certain cancers (5). The growing prevalence of obesity has imposed a substantial economic burden on healthcare systems worldwide due to increased morbidity and mortality (6).

Current treatment approaches for obesity include dietary modifications, increased physical activity,

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behavioral interventions, pharmacotherapy, and bariatric surgery. However, these interventions are often associated with limitations such as adverse effects, poor long-term adherence, high costs, and surgical risks (7). Consequently, there has been increasing interest in the development of safer and more effective therapeutic alternatives derived from natural sources.

Medicinal plants have gained considerable attention as potential anti-obesity agents because of their diverse bioactive phytochemicals, including flavonoids, phenolic compounds, alkaloids, terpenoids, and saponins (8). These phytoconstituents exert anti-obesity effects through multiple mechanisms, such as inhibition of pancreatic lipase, suppression of adipogenesis, enhancement of lipid metabolism, and reduction of oxidative stress (9).

Leucas aspera (Willd.) Link, a medicinal herb belonging to the family Lamiaceae, is widely distributed in tropical and subtropical regions of Asia. Traditionally, it has been used for the treatment of fever, inflammation, skin disorders, respiratory ailments, and gastrointestinal disturbances (10). Phytochemical investigations have revealed the presence of biologically active compounds possessing antioxidant, anti-inflammatory, antimicrobial, and metabolic regulatory properties (11). Emerging evidence suggests that these phytochemicals may contribute to anti-obesity activity through modulation of lipid metabolism and inhibition of fat accumulation (12).

Therefore, the present review aims to provide a comprehensive overview of the phytochemical constituents of *Leucas aspera* and critically evaluate its potential in-vitro anti-obesity activity as a promising natural therapeutic approach.

2. OVERVIEW OF OBESITY

2.1 Definition of Obesity

Obesity is defined as an abnormal or excessive accumulation of body fat that presents a risk to health. The most commonly used measure for assessing obesity is Body Mass Index (BMI), calculated as body weight (kg) divided by height squared (m^2). According to WHO classification, individuals with a BMI ≥ 30 kg/ m^2 are considered obese (2).

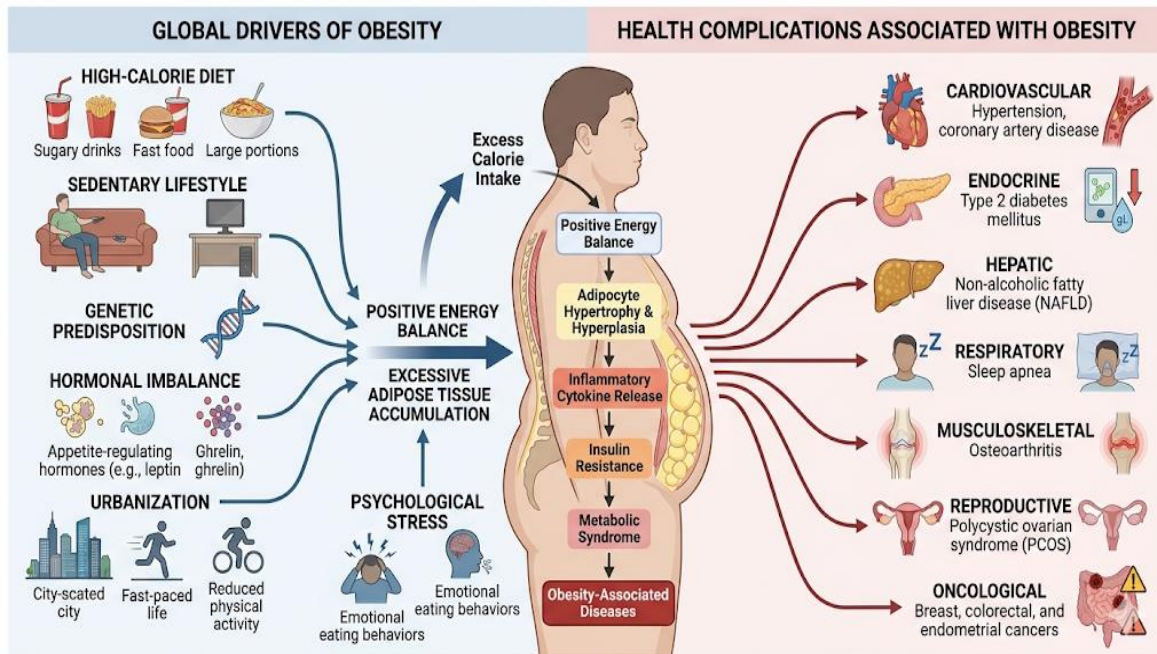
BMI (kg/ m^2)	Classification
<18.5	Underweight
18.5–24.9	Normal Weight
25.0–29.9	Overweight
30.0–34.9	Obesity Class I
35.0–39.9	Obesity Class II
≥ 40.0	Obesity Class III (Severe Obesity)

Table 1. WHO Classification of Body Mass Index (BMI)

2.2 Global Burden of Obesity

Obesity has reached epidemic proportions worldwide. The prevalence of obesity has increased dramatically due to urbanization, dietary transitions, and reduced physical activity. Developing countries, including India, are experiencing a rapid rise in obesity rates due to changing lifestyles and increased consumption of energy-dense foods (13).

The increasing prevalence of obesity is a major concern because it contributes significantly to disability-adjusted life years (DALYs), healthcare expenditure, and premature mortality (14).

Figure 1: Global Drivers and Health Complications of Obesity**Figure 1: Global Drivers and Health Complications of Obesity**

Factor	Contribution
High-calorie diet	Excess energy intake
Sedentary lifestyle	Reduced energy expenditure
Genetic predisposition	Increased susceptibility
Hormonal imbalance	Altered appetite regulation
Urbanization	Lifestyle modifications
Psychological stress	Emotional eating behaviors

Table 2. Major Global Factors Contributing to Obesity

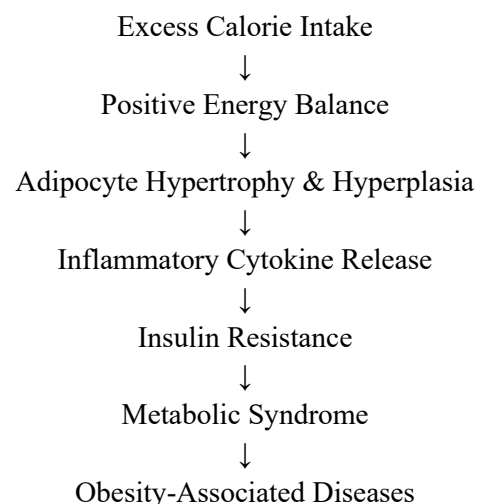
2.3 Pathophysiology of Obesity

Obesity develops when energy intake chronically exceeds energy expenditure, resulting in excessive storage of triglycerides within adipocytes (15). Adipose tissue expansion occurs through:

1. Hyperplasia (increase in adipocyte number)
2. Hypertrophy (increase in adipocyte size)

As adipose tissue expands, adipocytes secrete inflammatory cytokines such as tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), and leptin, contributing to chronic low-grade inflammation and metabolic dysfunction (16).

Simplified Pathogenesis of Obesity



2.4 Health Consequences of Obesity

Obesity is a major risk factor for numerous chronic diseases affecting multiple organ systems.

System	Complications
Cardiovascular	Hypertension, coronary artery disease
Endocrine	Type 2 diabetes mellitus
Hepatic	Non-alcoholic fatty liver disease
Respiratory	Sleep apnea
Musculoskeletal	Osteoarthritis
Reproductive	Polycystic ovarian syndrome
Oncological	Breast, colorectal, and endometrial cancers

Table 3. Major Health Complications Associated with Obesity

2.5 Current Strategies for Obesity Management

Management of obesity primarily focuses on reducing body weight and preventing obesity-related complications.

Strategy	Advantages	Limitations
Diet Modification	Safe and cost-effective	Poor long-term compliance
Physical Activity	Improves metabolism	Requires sustained effort
Pharmacotherapy	Effective weight reduction	Adverse effects
Bariatric Surgery	Significant weight loss	Expensive and invasive
Herbal Therapy	Potentially safer alternative	Limited clinical evidence

Table 4. Current Therapeutic Approaches for Obesity

Due to the limitations associated with conventional therapies, medicinal plants and natural products have emerged as promising alternatives for obesity management. Plant-derived phytochemicals possess antioxidant, anti-inflammatory, and lipid-lowering

properties that may contribute to weight regulation and metabolic health (17).

Potential Anti-Obesity Mechanisms of Medicinal Plants

Medicinal Plants



Bioactive Phytochemicals



- Pancreatic Lipase Inhibition
- Reduced Fat Absorption
- Suppression of Adipogenesis

- Increased Lipolysis
- Antioxidant Activity
- Anti-inflammatory Effects



Reduction in Obesity and Metabolic Disorders

3. BOTANICAL AND ETHNOMEDICINAL PROFILE OF *LEUCAS ASPERA*

3.1 Botanical Description

Leucas aspera (Willd.) Link is an annual aromatic herb belonging to the family Lamiaceae. It is commonly known as "Thumbai" in Tamil, "Dronapushpi" in Sanskrit, and "Goma Madhupati" in Hindi. The plant is widely distributed throughout India, Sri Lanka, Bangladesh, Nepal, and Southeast Asian countries. It commonly grows in wastelands, roadsides, grasslands, and cultivated fields under tropical and subtropical climatic conditions (18).

The plant has gained considerable attention in traditional medicine due to its diverse therapeutic applications. Various parts of the plant, including leaves, flowers, stems, and roots, have been used in indigenous healthcare systems for centuries.

3.2 Taxonomical Classification

Taxonomic Rank	Classification
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Lamiales
Family	Lamiaceae
Genus	<i>Leucas</i>
Species	<i>Leucas aspera</i> (Willd.) Link

Table 5. Taxonomical Classification of *Leucas aspera*

3.3 Morphological Characteristics

Leucas aspera is an erect, branched herb that typically grows up to 15–60 cm in height. The stem is quadrangular, hairy, and green in color. Leaves are opposite, lanceolate to linear-lanceolate, with serrated margins and a characteristic aromatic odor.

The flowers are white, sessile, and arranged in dense axillary whorls. The fruit is a schizocarp containing four smooth nutlets. The root system is well-developed and fibrous, enabling the plant to survive under dry environmental conditions (19).

Plant Part	Characteristics
Stem	Erect, quadrangular, hairy
Leaves	Opposite, lanceolate, serrated
Flowers	White, tubular, densely clustered
Fruits	Schizocarp with four nutlets
Roots	Fibrous and branched
Height	15–60 cm

Table 6. Morphological Characteristics of *Leucas aspera*

3.4 Geographical Distribution

The plant is widely distributed across tropical and subtropical regions of Asia. In India, it is commonly found in Maharashtra, Karnataka, Tamil Nadu, Andhra Pradesh, Telangana, Kerala, Gujarat, Rajasthan, and West Bengal (20).

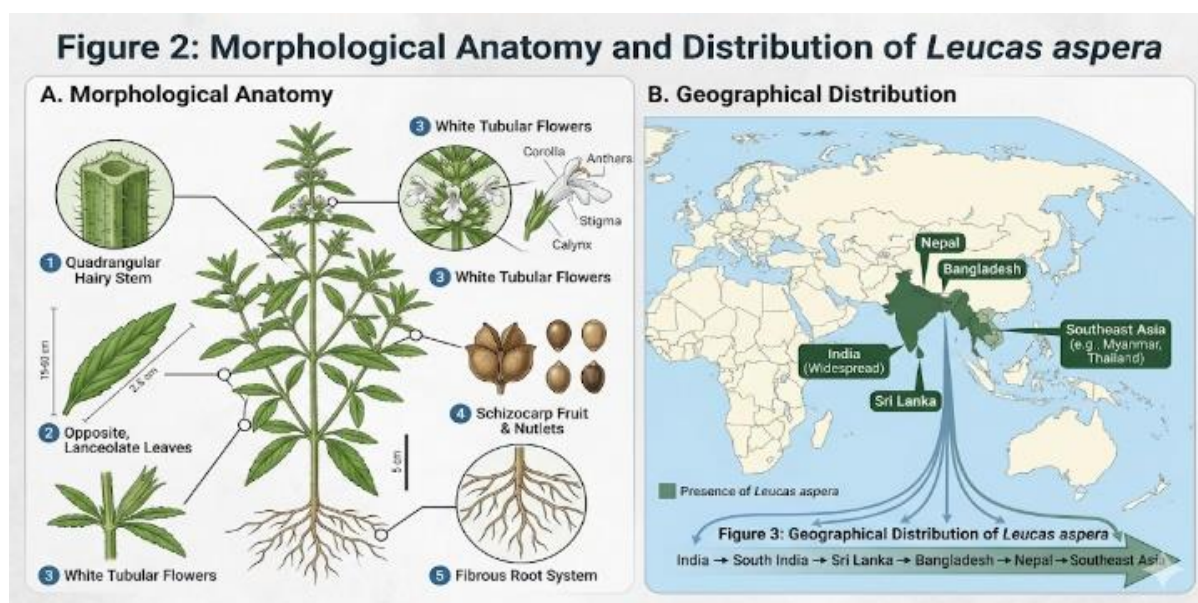


Figure 2: Morphological Anatomy and Distribution of *Leucas aspera*

3.5 Traditional and Ethnomedicinal Uses

Leucas aspera has been extensively utilized in Ayurveda, Siddha, and folk medicine. Traditional healers employ various plant parts for treating fever, respiratory disorders, skin infections, inflammation, digestive ailments, and snake bites (21).

The leaves are commonly used as an expectorant and antipyretic agent, while flower extracts are employed in treating cough and cold. Root preparations have been reported to possess analgesic and antimicrobial properties (22).

Plant Part	Traditional Use
Leaves	Fever, cough, cold, asthma
Flowers	Bronchitis and respiratory ailments
Roots	Analgesic and antimicrobial applications
Whole Plant	Anti-inflammatory and wound healing
Leaf Juice	Snake bites and insect stings
Decoction	Gastrointestinal disorders

Table 7. Ethnomedicinal Uses of *Leucas aspera*

3.6 Pharmacological Activities Reported for *Leucas aspera*

Scientific investigations have validated several traditional claims regarding *Leucas aspera*. Various studies have reported antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, antidiabetic, anticancer, and insecticidal activities (23).

Activity	Reported Effect
Antioxidant	Free radical scavenging
Anti-inflammatory	Reduction of inflammatory mediators
Antimicrobial	Activity against bacteria and fungi
Antidiabetic	Regulation of blood glucose
Hepatoprotective	Protection against liver damage
Anticancer	Cytotoxic effects on cancer cells

Table 8. Reported Pharmacological Activities of *Leucas aspera*

4. Phytochemical Constituents of *Leucas aspera*

4.1 Overview of Phytochemical Composition

The therapeutic potential of *Leucas aspera* is largely attributed to its rich phytochemical composition. Phytochemical investigations have identified

numerous primary and secondary metabolites possessing significant biological activities (24).

These bioactive compounds contribute to antioxidant, anti-inflammatory, antimicrobial, antidiabetic, and potential anti-obesity effects.

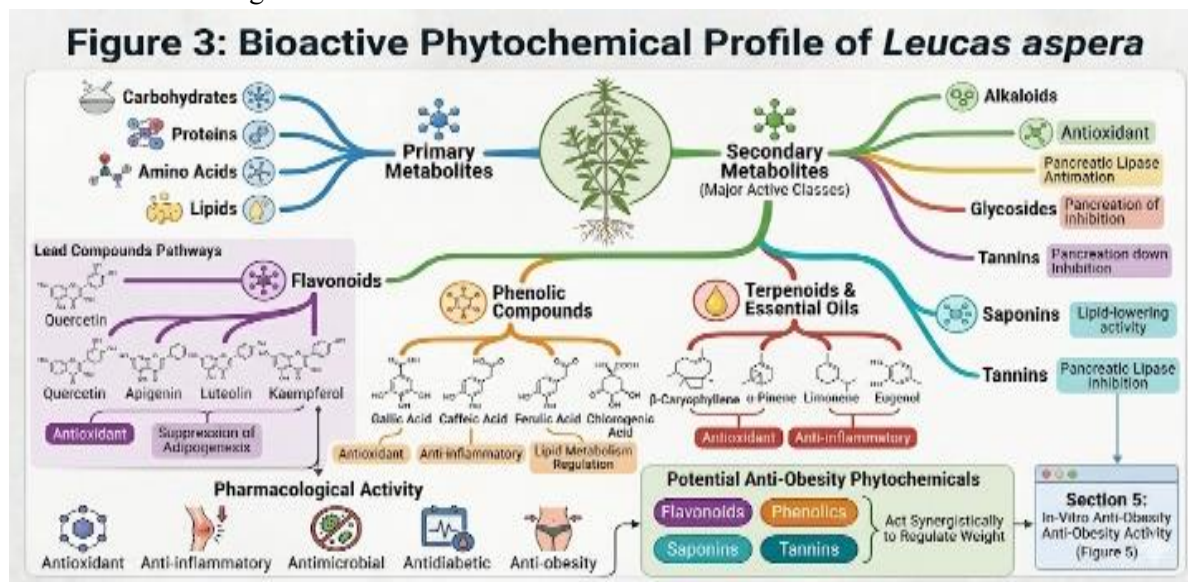


Figure 3: Bioactive Phytochemical Profile of *Leucas aspera*

4.2 Primary Metabolites

Primary metabolites are essential for plant growth and development. They serve as precursors for secondary metabolite biosynthesis.

Class	Biological Role
Carbohydrates	Energy storage
Proteins	Cellular functions
Amino Acids	Protein synthesis
Lipids	Membrane structure
Organic Acids	Metabolic regulation

Table 9. Major Primary Metabolites in *Leucas aspera*

4.3 Secondary Metabolites

Secondary metabolites are primarily responsible for the medicinal properties of the plant.

Phytochemical Class	Biological Activities
Flavonoids	Antioxidant, anti-obesity
Phenolic Compounds	Anti-inflammatory
Alkaloids	Neuroprotective
Terpenoids	Antimicrobial
Saponins	Lipid-lowering activity
Tannins	Antioxidant
Glycosides	Cardioprotective

Table 10. Major Secondary Metabolites Identified in *Leucas aspera*

4.4 Flavonoids

Flavonoids are among the most abundant phytochemicals in *Leucas aspera*. These compounds possess potent antioxidant properties and play a significant role in combating oxidative stress associated with obesity and metabolic disorders (25).

Major flavonoids identified include:

- Quercetin
- Apigenin
- Luteolin
- Kaempferol derivatives

These compounds have been reported to inhibit adipogenesis and promote lipid metabolism.

4.5 Phenolic Compounds

Phenolic compounds contribute significantly to the antioxidant potential of *Leucas aspera*. They neutralize reactive oxygen species (ROS) and reduce oxidative damage in biological systems (26).

Compound	Function
Gallic Acid	Antioxidant
Caffeic Acid	Anti-inflammatory
Ferulic Acid	Free radical scavenging
Chlorogenic Acid	Lipid metabolism regulation

Table 11. Important Phenolic Compounds and Functions

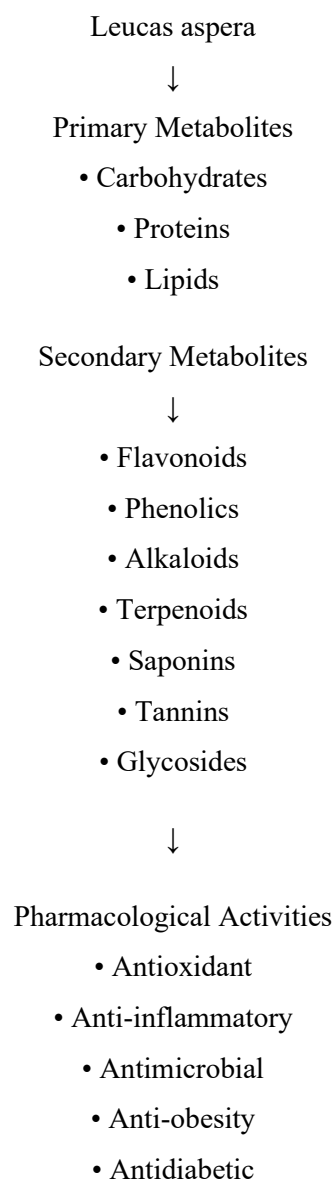
4.6 Terpenoids and Essential Oils

Terpenoids constitute another important group of phytochemicals present in *Leucas aspera*. Essential oil analysis has revealed the presence of several bioactive compounds including:

- β -Caryophyllene
- α -Pinene
- Limonene
- Eugenol
- Germacrene D

These compounds exhibit antioxidant, antimicrobial, and anti-inflammatory activities (27).

Major Phytochemical Classes Present in *Leucas aspera*



4.7 Phytochemicals Associated with Anti-Obesity Activity

Several phytochemicals identified in *Leucas aspera* are known to influence obesity-related pathways.

Compound/Class	Proposed Mechanism
Flavonoids	Inhibition of adipogenesis
Phenolics	Reduction of oxidative stress
Saponins	Decreased lipid absorption
Terpenoids	Improved lipid metabolism
Tannins	Pancreatic lipase inhibition

Table 12. Potential Anti-Obesity Phytochemicals in *Leucas aspera*

These compounds may act synergistically to regulate body weight, inhibit fat accumulation, and improve metabolic health (28).

5. IN-VITRO ANTI-OBESITY ACTIVITY OF LEUCAS ASPERA

The in-vitro anti-obesity potential of *Leucas aspera* has been indirectly demonstrated through multiple

biochemical and cell-based assays focusing on lipid metabolism, adipogenesis regulation, antioxidant potential, and enzyme inhibition. Although direct anti-obesity clinical studies are limited, available experimental evidence strongly supports its role in modulating obesity-related pathways (29).

Extracts of *Leucas aspera* leaves obtained using polar and non-polar solvents have shown significant bioactivity in C2C12 myotube cell lines, where modulation of glucose uptake and lipid metabolism was observed. These effects suggest improved insulin sensitivity and enhanced energy utilization, which are critical factors in obesity control (30).

Phytochemical screening of *Leucas aspera* confirms the presence of flavonoids, phenolics, saponins, and terpenoids, all of which are known to exhibit anti-obesity effects through multiple molecular targets such as lipid digestion enzymes and adipocyte differentiation pathways (31).

5.1 Key In-Vitro Models Used for Anti-Obesity Evaluation

Model System	Purpose	Observed Effect in <i>Leucas aspera</i>
Pancreatic lipase inhibition assay	Fat digestion control	Reduced lipid breakdown activity (29)
3T3-L1 adipocyte differentiation assay	Adipogenesis study	Suppression of fat cell formation (30)
C2C12 myotube assay	Glucose uptake & metabolism	Enhanced glucose uptake (30)
DPPH/ABTS antioxidant assay	Oxidative stress reduction	Strong radical scavenging activity (31)
α -amylase inhibition assay	Carbohydrate metabolism	Reduced glucose absorption (32)

Table 13. In-vitro models used to evaluate anti-obesity potential of *Leucas aspera*

5.2 Antioxidant-Linked Anti-Obesity Activity

Oxidative stress plays a critical role in obesity progression by inducing chronic inflammation and insulin resistance. *Leucas aspera* exhibits strong antioxidant activity due to its high phenolic and flavonoid content, which neutralizes reactive oxygen species (ROS) (31).

The antioxidant activity indirectly contributes to anti-obesity effects by:

- Reducing adipocyte inflammation
- Improving insulin sensitivity
- Preventing lipid peroxidation
- Enhancing mitochondrial function

5.3 Effect on Lipid Accumulation

Studies suggest that phytoconstituents of *Leucas aspera* inhibit lipid accumulation in adipocytes by regulating enzymes involved in lipogenesis. Flavonoids such as quercetin-like compounds suppress triglyceride synthesis and promote lipid breakdown (33).

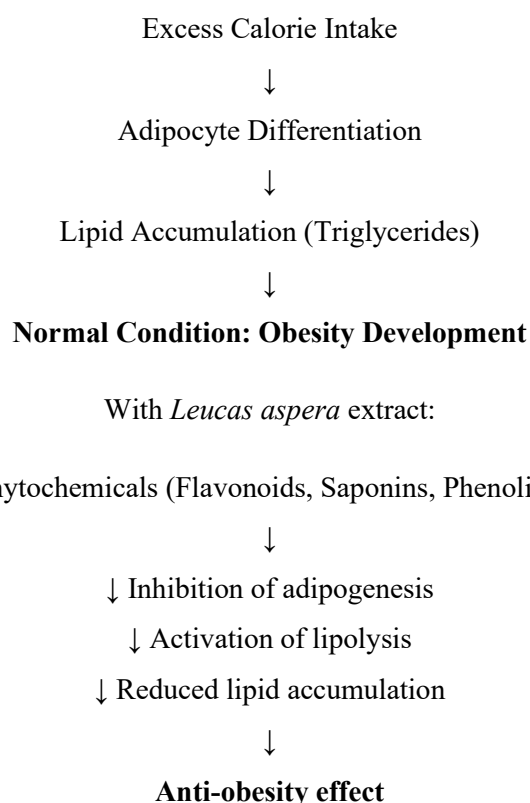


Figure 5. Effect of *Leucas aspera* on lipid metabolism in adipocytes

5.4 Enzyme Inhibition Activity

One of the major mechanisms of anti-obesity action is the inhibition of digestive enzymes such as pancreatic lipase, α -amylase, and α -glucosidase.

- **Pancreatic lipase inhibition** reduces fat absorption
- **α -amylase inhibition** reduces carbohydrate digestion
- **α -glucosidase inhibition** slows glucose release

Phytochemicals such as tannins and saponins in *Leucas aspera* have shown potential inhibitory

activity against these enzymes, thereby reducing caloric absorption (32).

6. MECHANISMS OF ANTI-OBESITY ACTION OF LEUCAS ASPERA

The anti-obesity mechanism of *Leucas aspera* is multi-targeted and involves regulation of metabolic, enzymatic, and cellular pathways.

6.1 Inhibition of Adipogenesis

Adipogenesis refers to the differentiation of preadipocytes into mature adipocytes. Bioactive compounds in *Leucas aspera* inhibit transcription factors such as:

- PPAR- γ (Peroxisome proliferator-activated receptor gamma)
- C/EBP- α (CCAAT/enhancer-binding protein alpha)

Inhibition of these pathways leads to reduced formation of fat cells (33).

6.2 Enhancement of Lipolysis

Lipolysis is the breakdown of triglycerides into free fatty acids. Flavonoids and terpenoids in *Leucas aspera* stimulate hormone-sensitive lipase (HSL), promoting fat breakdown and energy utilization (34).

6.3 Regulation of Glucose Metabolism

Improved glucose uptake in skeletal muscle cells (C2C12 model) indicates better insulin sensitivity. This reduces excess glucose conversion into fat storage (30).

6.4 Antioxidant and Anti-Inflammatory Pathways

Chronic inflammation is a major contributor to obesity. Phenolic compounds reduce inflammatory mediators such as:

- TNF- α
- IL-6
- COX-2

This helps in reducing obesity-associated metabolic dysfunction (31).

6.5 Modulation of Energy Homeostasis

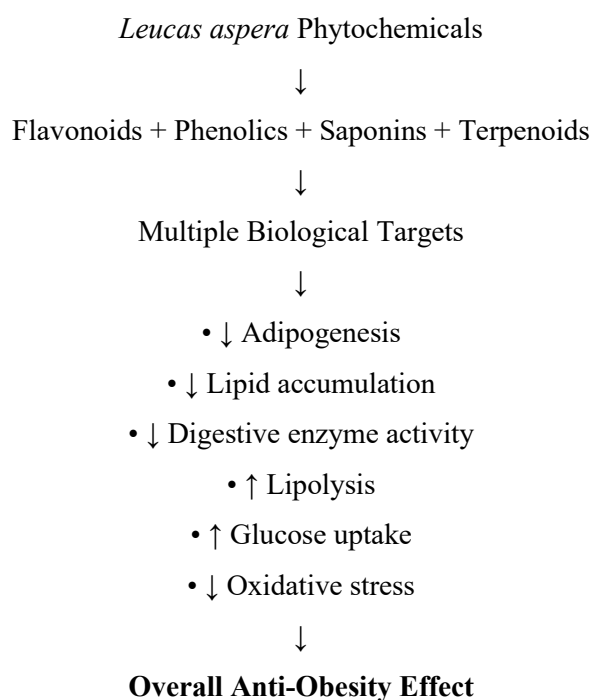
Bioactive compounds may activate AMP-activated protein kinase (AMPK), a key regulator of energy balance. Activation of AMPK leads to:

- Increased fatty acid oxidation
- Decreased lipid synthesis
- Enhanced mitochondrial activity (34)

Mechanism	Biological Target	Effect
Anti-adipogenesis	PPAR- γ , C/EBP- α	Reduced fat cell formation
Lipase inhibition	Pancreatic lipase	Reduced fat absorption
Antioxidant action	ROS scavenging	Reduced oxidative stress
Anti-inflammatory	TNF- α , IL-6	Reduced inflammation
Metabolic regulation	AMPK pathway	Increased fat oxidation

Table 14. Summary of anti-obesity mechanisms of *Leucas aspera*

6.6 Overall Mechanistic Pathway



Integrated anti-obesity mechanism of *Leucas aspera*

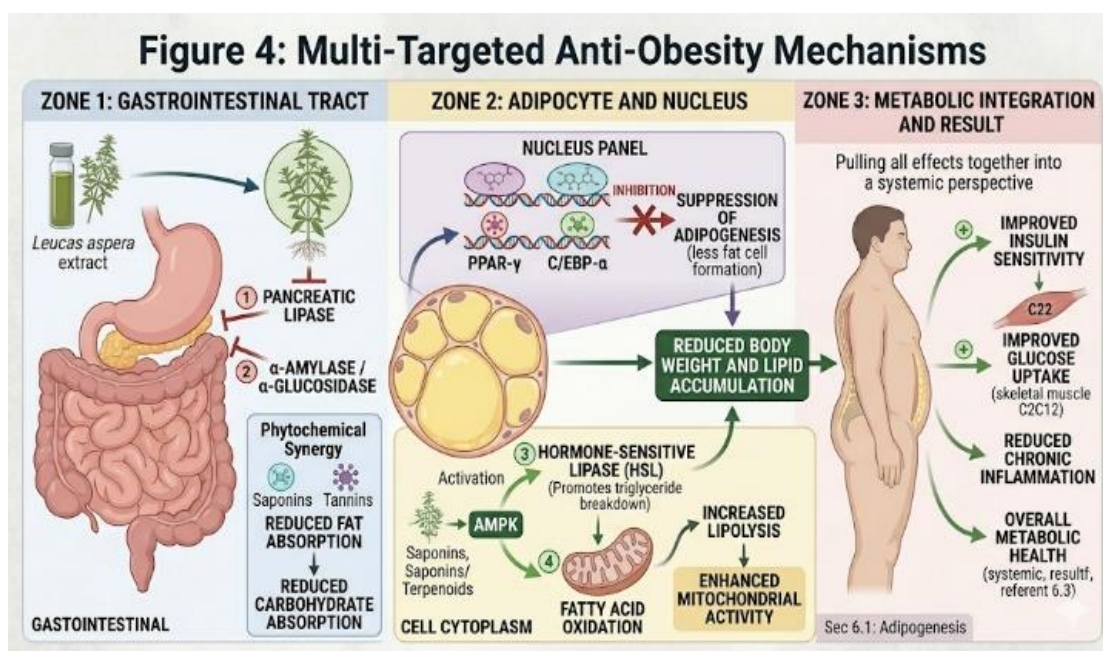


Figure 4: Multi-Targeted Anti-Obesity Mechanisms of Action

7. FUTURE PROSPECTS AND RESEARCH GAPS

The increasing global burden of obesity necessitates the discovery of safe, effective, and multi-target therapeutic agents. *Leucas aspera* demonstrates

promising anti-obesity potential; however, several scientific, technological, and translational gaps must be addressed before its clinical application (35).

7.1 Key Future Research Prospects

Research Area	Focus	Expected Outcome
Advanced in-vitro mechanistic studies	AMPK, PPAR- γ , SREBP-1c pathways	Molecular confirmation of anti-obesity action
In-vivo validation	High-fat diet (HFD) rodent models	Reduction in body weight and lipid profile
Multi-omics integration	Genomics, proteomics, metabolomics	System-level pathway understanding
Bioactivity-guided fractionation	Isolation of active compounds	Identification of lead anti-obesity molecules
Pharmacokinetic studies	ADME profiling	Improved understanding of drug behavior
Nanoformulation development	Liposomes, SLNs, nanoemulsions	Enhanced bioavailability
Gut microbiome modulation studies	Microbial diversity analysis	Metabolic improvement through microbiota
Clinical translational studies	Human trials	Safety and efficacy validation

Table 15. Expanded future research directions for *Leucas aspera*

7.2 Critical Research Gaps

Despite promising pharmacological evidence, several gaps limit translational development:

Gap Area	Limitation	Impact
Standardization	Lack of uniform extract preparation	Reproducibility issues
Mechanistic clarity	Unknown direct molecular targets	Weak scientific validation
Toxicological profiling	Insufficient chronic toxicity data	Safety uncertainty
Clinical validation	No human trials conducted	No therapeutic approval
Bioavailability	Poor absorption data	Low pharmacological efficiency
Dose optimization	No standardized dosing	Therapeutic inconsistency
Drug interaction studies	Missing herb-drug interaction data	Safety risk in combination therapy
Regulatory framework	Limited AYUSH/FDA pathway data	Delayed commercialization

Table 16. Major research gaps in *Leucas aspera* anti-obesity studies

7.3 Emerging Advanced Research Directions

Modern scientific tools can significantly enhance research outcomes:

- Artificial intelligence-based compound screening
- Network pharmacology for multi-target prediction
- CRISPR-based adipogenesis gene modulation studies
- High-throughput screening of phytochemicals
- Systems biology integration for metabolic pathway mapping

7.4 Important Considerations

(i) Environmental and Seasonal Variation in Phytochemicals

Phytochemical composition of *Leucas aspera* varies significantly with soil type, climate, and harvesting season, affecting therapeutic consistency (46).

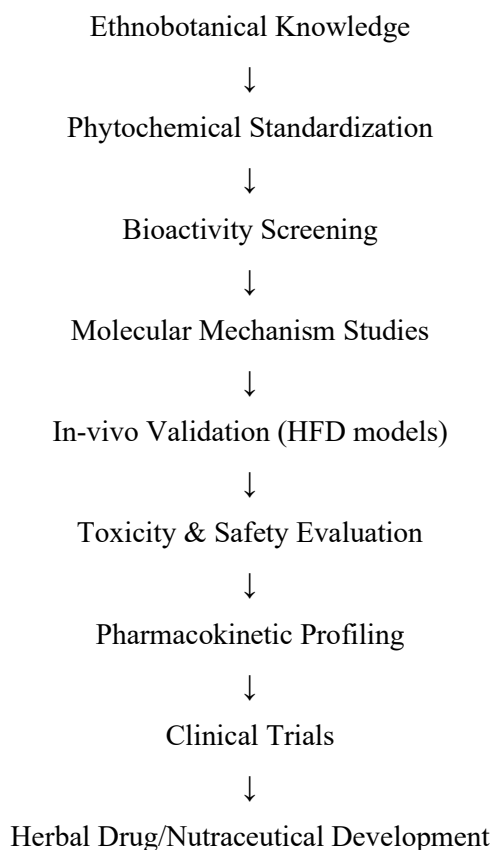
(ii) Need for Standardized Extraction Protocols

Different extraction solvents (aqueous, ethanolic, methanolic) yield varying bioactive profiles; hence standard protocols are essential for reproducibility (47).

(iii) Safety Pharmacology and Long-Term Exposure Studies

Long-term safety evaluation is critical to assess cumulative toxicity and organ-specific effects before clinical translation (48).

7.5 Integrated Development Pathway



Translational roadmap of *Leucas aspera* as anti-obesity agent

CONCLUSION

Leucas aspera is a promising medicinal plant with significant potential in the management of obesity due to its rich phytochemical composition and multi-target biological activities. The plant exhibits effects such as inhibition of lipid accumulation, suppression of adipogenesis, enhancement of lipid metabolism, and reduction of oxidative stress.

Although preliminary in-vitro and ethnopharmacological studies support its anti-obesity potential, comprehensive in-vivo validation, clinical evaluation, and standardization are still lacking. Advanced scientific approaches including molecular biology, nanotechnology, and systems pharmacology are essential to fully explore its therapeutic potential.

Overall, *Leucas aspera* represents a valuable natural resource that may contribute to the development of safe, effective, and multi-target anti-obesity therapies in the future.

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