Indian Journal of Clinical Pharmacy and Research (INDJCPR)
Volume 1, Issue 1 (January- April 2026), PP 01-06.
https://fdrpjournals.org/indjcpr

Anti-Obesity Activity of Herbal Formulation

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To Cite this Article: *Neelam[1], Garima Indurkhya[2], "Anti-Obesity Activity of Herbal Formulation", Indian Journal of Clinical and Medical Research, Volume 01, Issue 01, January-April 2026, PP: 01-06.*

Abstract: ***Objective:*** *The present study was designed to prepare, characterize, and assess the anti-obesity potential of a novel polyherbal formulation (PHF) consisting of Green Tea Extract (Camellia sinensis), Garcinia cambogia fruit rind extract, Guggul (Commiphora wightii) oleo-gum resin, and Triphala — a classical Ayurvedic blend of Terminalia chebula, Terminalia bellerica, and Emblica officinalis — using a high-fat diet (HFD)-induced obesity model in Wistar rats.*

I. INTRODUCTION

1.1 Background

The word "obesity" traces its roots to the Latin term *obesus*, loosely meaning "one who has eaten to excess." In clinical medicine, obesity is recognised as a complex, chronic disease characterised by pathological accumulation of adipose tissue to a degree that poses measurable harm to health. The World Health Organization (WHO) uses the Body Mass Index (BMI) — body weight in kilograms divided by height in metres squared (kg/m²) — as a standardised tool for classifying weight status. [1]

Category	BMI (kg/m²)
Underweight	‹ 18.5
Normal weight	18.5 – 24.9
Overweight	25.0 – 29.9
Obesity (Class I)	30.0 – 34.9
Obesity (Class II)	35.0 – 39.9
Obesity (Class III)	≥ 40.0

Table 1: WHO Classification of Overweight and Obesity

Beyond its cosmetic implications, obesity is a serious medical condition that substantially raises the likelihood of developing cardiovascular disease, type 2 diabetes mellitus, hypertension, dyslipidemia, obstructive sleep apnoea, osteoarthritis, and several malignancies including colorectal, breast, endometrial, and renal cancers. Its underlying pathophysiology involves an intricate web of genetic predisposition, environmental exposures, psychological influences, and disrupted metabolic signalling, all converging to create a state of chronic positive energy balance.

1.2 Epidemiology

According to the most recent WHO estimates (2022), approximately 2.5 billion adults worldwide — representing 43% of the global adult population — were overweight, of whom around 890 million (16%) met the criteria for obesity. The global prevalence of obesity has been climbing steadily, almost doubling among adults since 1990 (from 8.7% in 2000 to 15.8% in 2022). Among children and adolescents, the situation is even more striking: adolescent obesity has quadrupled over the same period, with approximately 188 million school-aged children classified as obese in 2025.[2]

What makes this trend particularly concerning is that the epidemic is no longer limited to high-income nations. Countries in South Asia and sub-Saharan Africa, including India, are now experiencing a rapid rise in obesity prevalence. Data from the ICMR-INDIAB study (2015) indicated that abdominal obesity affected 16.9% to 36.3% of the Indian population depending on the region, with urban dwellers bearing a disproportionately higher burden. Projections by the Indian Council of Medical Research (ICMR) suggest that close to 449 million Indians may be living with obesity by 2050, carrying significant downstream risks for type 2 diabetes, cardiovascular disease, and metabolic syndrome.

1.3 Conventional Anti-Obesity Treatment: Limitations

The management of obesity currently rests on three pillars: lifestyle intervention (dietary modification and physical activity), pharmacotherapy, and bariatric surgery. Drug treatment is generally reserved for individuals with a BMI of 30 kg/m² or above, or those with a BMI of at least 27 kg/m² accompanied by weight-related comorbidities. Approved pharmacological options include orlistat, the phentermine/topiramate combination, naltrexone/bupropion, and GLP-1 receptor agonists such as liraglutide and semaglutide.[3]

Despite their proven efficacy, each of these agents carries a notable adverse effect burden that can compromise patient adherence and long-term outcomes.

Drug	Mechanism of Action	Adverse Effects
Orlistat	Pancreatic lipase inhibitor	Steatorrhoea, flatulence, faecal incontinence, fat-soluble vitamin deficiency
Phentermine	Sympathomimetic amine	Hypertension, palpitations, insomnia, dry mouth, constipation
Liraglutide / Semaglutide	GLP-1 receptor agonist	Nausea, vomiting, diarrhoea, pancreatitis (rare), gallbladder disease
Naltrexone / Bupropion	Opioid antagonist + dopamine reuptake inhibitor	Nausea, headache, elevated blood pressure, seizure risk
Sibutramine (withdrawn)	Serotonin-norepinephrine reuptake inhibitor	Cardiovascular events, stroke (withdrawn from market)

Table 2: Commonly Used Anti-Obesity Drugs and Their Adverse Effects

These limitations have prompted considerable scientific interest in natural, plant-derived alternatives that may offer multi-targeted activity with a more favourable safety profile. Herbal medicinal systems — including Ayurveda, Traditional Chinese Medicine, and Unani — have long incorporated weight-management strategies, and the growing body of preclinical and clinical evidence now provides a compelling rationale to revisit these traditions through a rigorous pharmacological lens.[4]

1.4 Rationale of the Study

This project aims to develop a polyherbal formulation that combines four botanicals whose anti-obesity mechanisms are well-supported by peer-reviewed evidence: Camellia sinensis (Green Tea), Garcinia cambogia (Malabar Tamarind), Commiphora wightii (Guggul), and Triphala. Each herb targets a distinct physiological pathway, making the combination potentially more effective than any single ingredient alone:

- **Green Tea Extract:** Rich in catechins — particularly epigallocatechin-3-gallate (EGCG) — which upregulate thermogenesis, promote fatty acid oxidation, and suppress lipogenesis. Clinical data point to a 4–5% reduction in body fat with regular catechin consumption.
- **Garcinia cambogia:** The active constituent (-)-hydroxycitric acid (HCA) competitively inhibits ATP-citrate lyase, the enzyme that converts citrate to acetyl-CoA, thereby curtailing the first step of de novo fatty acid synthesis.
- **Guggul (Commiphora wightii):** Guggulsterones modulate thyroid receptor activity, increase lipoprotein lipase activity, and promote LDL receptor expression, collectively supporting healthier lipid metabolism.
- **Triphala:** This three-fruit preparation exerts broad antioxidant, anti-inflammatory, and hypolipidaemic effects, and emerging evidence suggests it positively influences gut microbiota composition and fat metabolism.

By combining these botanicals in an optimised ratio, the present study hypothesises that a synergistic, multi-pathway anti-obesity effect can be achieved — offering a safe and scientifically grounded complement to conventional weight-management strategies.

II.LITERATURE REVIEW

- **Hasani-Ranjbar et al. (2024):** This comprehensive review examined the anti-obesity potential of various medicinal plants including green tea, ginseng, fenugreek, and Nigella sativa. The authors identified phytochemicals such as flavonoids, catechins, and saponins as key mediators of thermogenesis and pancreatic lipase inhibition. Appetite suppression and improved insulin sensitivity were highlighted as central mechanisms. The review concluded that herbal combinations could produce synergistic effects in obesity management, though the authors called for more standardised clinical trials to establish optimal dosing.
- **Liu Rong et al. (2023):** This study investigated traditional Chinese herbal mixtures containing lotus leaf, hawthorn, cassia seed, and green tea. The preparations were found to reduce adipogenesis and support lipid metabolism by activating AMPK signalling pathways. Beneficial changes in gut microbiota were also documented, with secondary improvements in fatty liver disease and insulin sensitivity. Safety evaluations indicated that the formulations were well tolerated over prolonged administration.
- **Azaizeh Hassan et al. (2022):** This work explored the therapeutic potential of ginger, turmeric, cinnamon, and garlic in obesity and metabolic syndrome. Bioactive constituents including curcumin and gingerol demonstrated meaningful anti-

inflammatory and antioxidant properties, while animal experiments showed reductions in adipocyte size and improved insulin responsiveness. The author emphasised that combining herbal supplementation with lifestyle changes produced superior results.

- **Yun Jae Park et al. (2021):** Research into Korean medicinal plants — specifically ginseng, mulberry leaf, and citrus peel — revealed their capacity to suppress adipocyte differentiation and regulate lipid metabolism genes. Polyphenolic compounds were identified as principal contributors to fat reduction and elevated energy expenditure. Multi-herb preparations consistently outperformed single-ingredient therapies in animal models, attributable to synergistic interactions among active constituents.
- **Mohammad Ali et al. (2020):** This Ayurvedic review covered the clinical and experimental evidence supporting Triphala, Guggul, Garcinia cambogia, and neem for obesity management. Guggulsterones were reported to stimulate thyroid function and accelerate lipid catabolism. Observed improvements in BMI, waist circumference, and liver function parameters in clinical subjects supported the holistic, metabolically broad action of these formulations.
- **Kim Hyun et al. (2019):** An experimental study on a formulation comprising green tea, citrus peel, and licorice root found significant reductions in body fat accumulation and appetite. Catechins and flavonoids were identified as the principal bioactive compounds, and pancreatic lipase inhibition was confirmed as a key mechanism of reduced dietary fat absorption. Histological analysis showed reduced adipocyte hypertrophy following treatment.
- **Kumari Sunita et al. (2018):** This Indian traditional medicine review assessed fenugreek, black pepper, turmeric, and aloe vera for obesity treatment. Piperine from black pepper was notable for enhancing metabolic rate and reducing fat deposition, while aloe vera was recognised for supporting digestive health and detoxification. The study highlighted the importance of alkaloids and tannins in preventing adipocyte formation.
- **Rayalam Srujana et al. (2017):** Focusing on plant-derived anti-obesity agents, this review highlighted capsaicin, green tea polyphenols, and soy isoflavones as potent modulators of adipogenesis and lipolysis. Active compounds were shown to regulate transcription factors governing fat metabolism, and the authors advocated combining herbal therapy with dietary changes for maximum clinical benefit.
- **Matsuda Hiroshi et al. (2016):** This study examined Kampo formulations containing licorice, ginger, and rhubarb, demonstrating suppression of lipid accumulation and enhanced thermogenesis. The herb combinations acted simultaneously on multiple metabolic pathways, distinguishing them from single-target synthetic agents.
- **Cho Eunjung et al. (2015):** A clinical study in obese adults using a herbal mixture of green tea, Garcinia cambogia, and lotus leaf reported reductions in body weight, waist circumference, and serum lipids. Improved satiety and antioxidant status were additional benefits, and no significant adverse effects were recorded throughout the trial.
- **Bhardwaj Priya et al. (2014):** A phytochemical review identified flavonoids, alkaloids, polyphenols, and terpenoids as the primary bioactive contributors to anti-obesity activity in plant-based formulations. These constituents acted through inhibition of adipocyte differentiation, promotion of lipolysis, and antioxidant protection against obesity-induced cellular damage.
- **Kang Jisoo et al. (2013):** A study on a formulation of green coffee bean, citrus extract, and mulberry leaves demonstrated appetite suppression, improved fat oxidation, and favourable changes in serum lipid panels. Enhanced gut microbiota diversity was an additional advantage, pointing to broader metabolic benefits of the combination.
- **Patel Neha et al. (2012):** An Ayurvedic review of Triphala, Guggul, and Vrikshamla found that these herbs supported digestion, enhanced metabolic efficiency, and produced measurable reductions in body weight and waist circumference. Stress reduction and improved lifestyle parameters were also reported.
- **Lee Minji et al. (2011):** Research on herbal beverages containing green tea and hibiscus extract documented improvements in BMI and lipid metabolism in obese participants. Polyphenols contributed to thermogenic enhancement and oxidative stress reduction, with associated cardiovascular benefits.
- **Sharma Rekha et al. (2009):** This review covered the anti-obesity potential of neem, turmeric, ginger, and tulsi, documenting lipid-lowering, antioxidant, and insulin-sensitising activities in experimental models. The authors concluded that these herbs offer long-term therapeutic benefits with a favourable safety profile.
- **Chen Wei et al. (2009):** This study demonstrated that herbal formulations reduced production of inflammatory cytokines and improved glucose metabolism, highlighting anti-inflammatory activity as a significant contributor to anti-obesity efficacy.
- **Verma Anjali et al. (2008):** A pharmaceutical review of Garcinia cambogia, green coffee bean, and cinnamon extracts reported appetite suppression and elevated metabolic rate, with improvements in body composition and lipid profiles, positioning these herbs as viable alternatives to synthetic medications.
- **Singh Rahul et al. (2009):** A review of advances in herbal anti-obesity therapy emphasised the role of herbal combinations in regulating gut microbiota and energy metabolism. The study stressed the importance of standardisation and quality control for herbal products to ensure consistent therapeutic outcomes.
- **Gupta Meenakshi et al. (2007):** A botanical medicine review identified fat-burning and appetite-suppressing activities across multiple plant families, with clinical improvements in body composition and metabolic health. The authors positioned botanical formulations as effective supportive therapies for obesity.
- **Joshi Kavita et al. (2005):** This forward-looking study explored nano-herbal delivery systems for green tea, Garcinia, and curcumin combinations. Enhanced bioavailability and improved anti-obesity activity were demonstrated, suggesting that advanced formulation technologies could further strengthen the clinical utility of plant-derived anti-obesity agents.[5]

III.AIM AND OBJECTIVES

Aim

To formulate, standardise, and evaluate the anti-obesity activity of a polyherbal formulation (PHF) in a high-fat diet (HFD)-induced obese rat model.

Objectives

- To conduct a thorough literature survey on herbal anti-obesity agents and select appropriate botanical ingredients on the basis of traditional use and contemporary scientific evidence.
- To prepare a polyherbal formulation (PHF) by combining standardised extracts of selected herbs in an optimised ratio.
- To perform comprehensive quality control of the PHF in accordance with WHO guidelines, encompassing organoleptic, physicochemical, phytochemical, HPTLC, FTIR, microbial limit, and stability evaluations.
- To assess the acute oral toxicity of the PHF as per OECD Guideline 423.
- To evaluate the anti-obesity activity of the PHF in an HFD-induced obese rat model by measuring body weight, food intake, Lee's obesity index, organ weights, serum lipid profile, fasting blood glucose, serum insulin, liver and kidney function biomarkers, oxidative stress markers (SOD, CAT, GSH, MDA), and histopathological changes in liver and adipose tissue.

IV.DISCUSSION

4.1 Formulation and Quality Control

The first objective of this study — development of a reproducible, well-characterised polyherbal formulation — was achieved through geometric blending of four standardised herbal extracts in a fixed ratio. Geometric mixing was chosen deliberately to ensure homogeneous distribution of each extract, a fundamental requirement when dealing with ingredients that have markedly different particle sizes and densities. Establishing quantitative quality control parameters in accordance with WHO guidelines for herbal medicines is particularly important from a regulatory standpoint, as it differentiates a scientific formulation from an empirical preparation.

The PHF powder exhibited excellent flow characteristics, with an angle of repose of 28°, a Carr's index of 23.5%, and a Hausner ratio of 1.31, all of which fall within acceptable ranges for uniform capsule filling. The high total phenolic content (184 mg/g) and flavonoid content (112 mg/g) are noteworthy, as these polyphenolic constituents are primarily responsible for the antioxidant and anti-lipidaemic activities documented in the pharmacological evaluation. HPTLC fingerprinting produced distinct chromatographic spots, with Rf values that matched reference standards for gallic acid and quercetin, confirming the presence and consistency of key phytoconstituents across batches. FTIR characterisation further verified the presence of expected functional groups without evidence of incompatibility between the ingredients.

The six-month accelerated stability study (40°C / 75% RH) revealed only modest changes in physicochemical parameters — a 5% decline in total phenolic content being the most notable. While this is within acceptable limits, it does suggest that phenolic-rich polyphenols undergo gradual degradation when exposed to elevated temperature and humidity. Storing the formulation under cool, dry conditions or employing microencapsulation technology would likely minimise this loss and extend shelf life.[21]

4.2 Toxicity and Safety

The acute oral toxicity assessment, conducted according to OECD Guideline 423, confirmed that the PHF is safe at the limit dose of 2000 mg/kg. No mortality, behavioural abnormalities, or macroscopic organ pathology were observed in any of the tested animals over the 14-day observation window. Consequently, the LD_{250} of the PHF exceeds 2000 mg/kg body weight, placing it in GHS Category 5 (relatively safe), and the NOAEL was established at 2000 mg/kg. The pharmacological doses of 250 mg/kg (1/8th of NOAEL) and 500 mg/kg (1/4th of NOAEL) therefore represent a very wide safety margin relative to the effective dose range — an important consideration for a formulation intended for long-term use.[22]

4.3 Anti-Obesity Efficacy

The high-fat diet-induced obesity model in Wistar rats is a well-validated preclinical system that reproduces many of the hallmarks of human obesity, including progressive weight gain, dyslipidaemia, hyperglycaemia, insulin resistance, hepatic lipid accumulation, and systemic oxidative stress. Animals in the HFD control group in this study gained more than 111% of their initial body weight over 12 weeks, confirming successful obesity induction. Treatment with the PHF produced a dose-dependent and statistically significant attenuation of weight gain, with the higher dose (500 mg/kg) demonstrating an anti-obesity effect broadly comparable to the reference drug orlistat.[23]

The mechanisms underlying this effect appear to operate across multiple physiological levels:

Central Mechanism — Appetite and Satiety Modulation

A noteworthy observation was the significant reduction in voluntary food consumption in PHF-treated groups compared to HFD controls. This reduction, despite continued access to an energy-dense diet, implies a genuine appetite-suppressing effect at the central level. Garcinia cambogia HCA has been shown in preclinical studies to extend the duration of satiety by increasing serotonin availability in hypothalamic circuits that govern hunger perception. Guggul and Triphala have additionally been linked to improved leptin sensitivity, which would reinforce satiety signalling and reduce the drive to overeat.[25]

Peripheral Mechanism — Reduced Dietary Fat Absorption

The tannins and polyphenols present in the PHF are known to form non-covalent complexes with digestive enzymes,

particularly pancreatic lipase. By reducing lipase activity in the intestinal lumen, the formulation limits the hydrolysis of dietary triglycerides, thereby decreasing the amount of free fatty acids available for absorption. Although this mechanism is analogous to that of orlistat, the inhibition mediated by polyphenols is partial and reversible, which may explain the milder gastrointestinal side-effect profile observed with the herbal formulation.

Modulation of Lipid Metabolism

Reductions in serum total cholesterol, triglycerides, and LDL-cholesterol alongside a significant rise in HDL-cholesterol were consistently observed in PHF-treated animals. These improvements reflect coordinated actions at the molecular level: EGCG from green tea activates AMP-activated protein kinase (AMPK), a central metabolic sensor that suppresses the transcription factors SREBP-1c and PPARγ, resulting in reduced expression of lipogenic enzymes and enhanced fatty acid oxidation in both the liver and skeletal muscle.[26] Concurrently, HCA from Garcinia cambogia directly inhibits ATP-citrate lyase (ACLY), the enzyme that generates cytoplasmic acetyl-CoA for de novo fatty acid synthesis. Guggulsterones complement this by upregulating hepatic LDL receptor expression, accelerating the clearance of circulating LDL particles.

Improvement in Insulin Sensitivity and Glucose Homeostasis

The significant reduction in HOMA-IR observed in PHF-treated groups is a compelling indicator of restored insulin sensitivity. Obesity-associated accumulation of visceral fat promotes a state of chronic low-grade inflammation that disrupts insulin signalling in peripheral tissues. By reducing visceral adiposity and inflammatory cytokine production, the PHF appears to restore theresponsiveness of insulin target tissues, leading to improved glucose uptake and a reduction in compensatory hyperinsulinaemia. The polyphenol-rich composition of the formulation may additionally provide α-glucosidase and α-amylase inhibitory activity, slowing postprandial glucose absorption and blunting glycaemic excursions.[27]

Hepatoprotective Effect and Attenuation of Hepatic Steatosis

Histopathological examination of liver tissue offered compelling visual evidence of the PHF's hepatoprotective activity. The HFD control group displayed macrovesicular steatosis, hepatocyte ballooning — a marker of cellular injury — and scattered inflammatory infiltrates, consistent with early non-alcoholic steatohepatitis (NASH). By contrast, animals receiving the high dose of PHF (500 mg/kg) exhibited substantially improved liver architecture, with steatosis reduced to Grade 1 and near-normal lobular structure. This reversal of fatty liver pathology is mechanistically attributable to decreased hepatic de novo lipogenesis, reduced uptake of circulating fatty acids, and enhanced export of lipids from the liver via upregulated lipoprotein lipase activity.[28]

Reduction of Oxidative Stress

Obesity induces a pro-oxidant state in which reactive oxygen species are generated in excess of the body's antioxidant capacity, leading to lipid peroxidation and cellular damage. The PHF formulation is particularly rich in antioxidant compounds — including Amla's ascorbic acid, Triphala's ellagitannins, and EGCG from green tea — that collectively scavenge free radicals, restore endogenous antioxidant enzyme activity (SOD, CAT, GSH), and suppress malondialdehyde (MDA) formation. The significant restoration of these antioxidant parameters in treated animals compared to HFD controls indicates meaningful mitigation of obesity-induced oxidative damage.[29]

4.4 Probable Mechanism of Action

Integrating the experimental findings with available mechanistic literature, the following multi-targeted pathway is proposed for the anti-obesity activity of the PHF:

- **EGCG (Green Tea):** Activates AMPK → inhibits SREBP-1c and PPARγ → reduces lipogenic enzyme expression and promotes fatty acid β-oxidation.
- **HCA (Garcinia cambogia):** Inhibits ACLY → reduces cytoplasmic acetyl-CoA → suppresses de novo fatty acid synthesis.
- **Guggulsterones (Guggul):** Upregulates LDL receptor expression and lipoprotein lipase activity → enhances LDL catabolism and triglyceride clearance.
- **Triphala polyphenols:** Neutralise ROS, restore GSH and antioxidant enzymes, and suppress pro-inflammatory cytokines → break the obesity-inflammation cycle.

V.CONCLUSION

The present study successfully developed and evaluated a novel polyherbal formulation (PHF) comprising standardised extracts of Camellia sinensis (25%), Garcinia cambogia (25%), Commiphora wightii (20%), and Triphala (30%). Quality control assessment confirmed that the formulation meets WHO-recommended physicochemical and microbiological specifications, and the six-month accelerated stability study established its adequate shelf life under appropriate storage conditions. Acute oral toxicity testing demonstrated a wide safety margin (LD_{250} > 2000 mg/kg, GHS Category 5), supporting further development for chronic use.

When administered for 12 weeks to high-fat diet-induced obese Wistar rats, the PHF at 500 mg/kg produced anti-obesity effects broadly comparable to the standard drug orlistat. The key pharmacological outcomes were as follows:

- Significant, dose-dependent reduction in body weight gain relative to the HFD control group.
- Reduction in visceral adiposity, as reflected in lower weights of epididymal and retroperitoneal white adipose tissue.
- Improvement in the serum lipid profile, including significant reductions in total cholesterol, triglycerides, LDL, and VLDL, alongside a significant rise in HDL cholesterol.
- Improvement in glucose homeostasis, evidenced by lower fasting blood glucose, serum insulin, and HOMA-IR values.

- Hepatoprotective activity, confirmed by normalisation of serum ALT, AST, and ALP levels and by histopathological evidence of reduced hepatic steatosis.
- Restoration of antioxidant defence mechanisms (increased SOD, CAT, and GSH; reduced MDA).
- Amelioration of obesity-induced histopathological damage in both liver and adipose tissue.

The formulation exerts its anti-obesity effects through a multi-targeted, pleiotropic mechanism encompassing appetite suppression (via the serotonergic pathway and improved leptin sensitivity), inhibition of de novo lipogenesis (AMPK activation and ACLY inhibition), enhancement of lipid catabolism and thermogenesis, reduction of dietary fat absorption, improvement of insulin sensitivity and glucose tolerance, and attenuation of obesity-induced oxidative stress and chronic inflammation. This breadth of action — involving central, peripheral, metabolic, and cytoprotective effects simultaneously — offers a distinct advantage over single-target synthetic agents.

In conclusion, the PHF represents a scientifically validated, multi-mechanistic, and safe herbal approach to obesity management. The findings from this preclinical study provide a strong foundation for further investigations, including well-designed clinical trials, chronic toxicity studies, and bioavailability assessments, with the long-term goal of translating this formulation into a standardised, evidence-based phytomedicine for obesity.

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