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FORSKOLIN AND METABOLIC HEALTH: A REVIEW OF *COLEUS FORSKOHLII'S* ROLE IN WEIGHT MANAGEMENT AND BEYOND

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ABSTRACT: *Coleus forskohlii* (syn. *Plectranthus barbatus*), a medicinal plant from the Lamiaceae family, has been traditionally used in Ayurvedic medicine. Its primary bioactive compound, forskolin, a labdane diterpene, is known for its metabolic and weight management effects. Forskolin activates adenylate cyclase, increasing cyclic AMP (cAMP) levels, which regulate lipid metabolism, thermogenesis, and energy expenditure. This review compiles information from databases such as Google Scholar, PubMed, Science Direct, and Research Gate. Preclinical studies suggest that *C. forskohlii* extract (CFE) reduces body weight, adiposity, and dyslipidemia in obese models, while clinical trials indicate its potential to prevent weight gain and improve body composition. Beyond weight management, forskolin shows promise in glaucoma, and metabolic disorders. Safety studies confirm CFE has low toxicity, with no significant adverse effects observed. Forskolin also influences hormone regulation and smooth muscle relaxation, contributing to its therapeutic applications. To establish the long-term efficacy and safety of forskolin, large scale placebo-controlled trials are required. This review highlights the pharmacological applications, mechanisms, and safety of *C. forskohlii*, emphasizing its potential as a natural therapeutic agent for metabolic health and obesity management.

INTRODUCTION: Over recent decades, the prevalence of obesity in the population has seen a drastic rise globally and ultimately it has become a major health concern affecting humans and animals both. By 2016, around 39% of the world's population was overweight or obese, nearly three times the rate recorded in 1975 [1]. Obesity, defined as a BMI of 30 or higher, and overweight, ranging from 25.0 to 29.9, contribute to more deaths than underweight.

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This issue is widespread globally, except in parts of sub-Saharan Asia, Africa, and countries with low obesity rates like Sri Lanka, Indonesia, Sudan, Singapore, and Djibouti [2]. Obesity primarily results from an imbalance between energy intake and expenditure, which involves basal metabolism, physical activity, and diet-induced thermogenesis. To address this, various weight management strategies are available, including botanical supplements such as *Coleus forskohlii* extract, which is marketed for its potential role in weight loss [3].

Coleus forskohlii (syn. *Plectranthus barbatus*) is a well-known medicinal herb from the Lamiaceae family, commonly referred to as the mint family [4]. The genus name *Coleus* was introduced by De Loureiro in 1970, signifying a "sheath encasing the

style." The species name *forskohlii* was assigned in honour of the renowned Swedish botanist Forsskåhl [5]. *Coleus forskohlii* is an herbaceous plant that typically grows at elevations of 600 to 1500 feet. This species thrives naturally in the lush, warm climates of tropical and subtropical regions. Its native range spans several countries, including India, Nepal, Myanmar, Sri Lanka, Thailand, and various parts of Africa [6]. Traditionally, the roots have been utilized as flavouring agents in pickles and for medicinal applications in Ayurvedic medicine. The juice extracted from the roots is administered to children experiencing constipation. The Kotha tribe, native to Trichigadi in the Nilgiri region of South India, regards a decoction made from the tuberous roots as a revitalizing tonic [7].

Taxonomic Status: *C. forskohlii* is a plant native to India and has been traditionally recognized in Ayurvedic "Materia Medica" under the Sanskrit names "Makandi" and "Mayani". The taxonomic classification of *C. forskohlii* (also known as *P. forskohlii*) is as follows.

Kingdom: Plantae

Class: Dicotyledons

Subclass: Gamopetalae

Series: Bicarpellatae

Order: Lamiales

Family: Lamiaceae

Genus: *Plectranthus*

Species: *Forskohlii*. (Syn: *C. forskohlii*) [8, 9]

Vernacular Names:

Sanskrit: Pashanbhed

Hindi: Patharchur

Kannada: Makandiberu

English: Coleus

Gujarati: Garmalu

Marathi: Maimnul

Tamil: Koorkankilangu

Geographical Distribution: *C. forskohlii* is believed to have originated in the Indian subcontinent and thrives in subtropical and warm temperate mountain regions across India, Nepal, Myanmar, Sri Lanka, Thailand, and Africa. It has also been introduced to Egypt, Arabia, Ethiopia, tropical East Africa, and Brazil. In India, its cultivation is widespread in Gujarat, Bihar, the Deccan Plateau, Rajasthan, Maharashtra, Karnataka, and Tamil Nadu. Tamil Nadu alone accounts for approximately 6000 acres of cultivation, mainly in Salem, Dharmapuri, Trichy, Erode, Coimbatore, and Dindigul districts. The plant predominantly grows on dry, rocky terrains, typically at altitudes between 600 and 800 meters [9, 10].

Botanical Description: *C. forskohlii* is a perennial aromatic plant that grows 45-60 cm tall with branched, four-angled stems and hairy nodes. Its leaves are 7.5-12.5 cm long, pubescent, and taper into petioles. The plant produces racemose inflorescences (15-30 cm), with blue or lilac bilabiate flowers pollinated by wind or insects. It has tuberous, thick, fibrous roots that are brown externally and orange-red inside, emitting a strong aroma. The leaves and tubers have distinct scents, and its growth habit varies from erect to trailing. Root morphology differs across populations, ranging from tuberous to semi-tuberous or fibrous forms [11, 12].

Active Constituents: The tuberous roots of *Coleus forskohlii* produce forskolin, a labdane diterpene compound recognized as its primary active constituent, along with minor diterpenoids like deacetyl forskolin and 9-deoxyforskolin [9]. Initially named coleonol, forskolin was later recognized as exclusive to *C. forskohlii*. Second-generation forskolin derivatives, such as HIL 568 and NKH 477 are also present in *C. forskohlii*. Forskolin remains in high demand, for medicinal and research purposes [13].

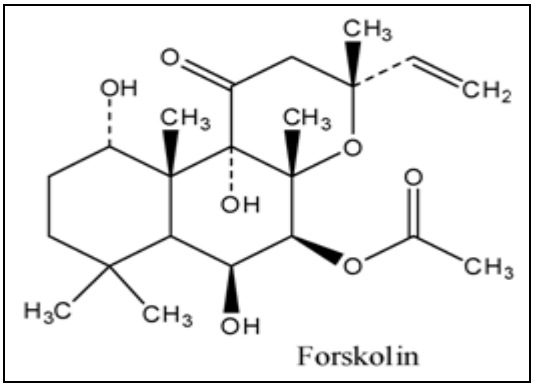

FIG. 1: STRUCTURE OF FORSKOLIN

***In-vitro* Regeneration:** The regeneration of *Coleus forskohlii* can be achieved using various explants such as leaves, nodal segments, and shoot tips, with nodal segments showing the highest survival rate. Optimal shoot regeneration occurs in MS medium supplemented with cytokinin's like BAP and kinetin, with combinations of auxins enhancing rooting. Callus formation and shoot multiplication depend on nutrient and hormone composition, with direct organogenesis being more effective for maintaining genetic stability. In vitro cultures using BA and NAA facilitate large-scale propagation, with successful soil establishment after hardening. Hairy root culture, induced by *Agrobacterium rhizogenes*, enhances forskolin production, with the highest yield from nodal explants. The addition of elicitors like methyl jasmonate and precursors like L-phenylalanine further improves forskolin synthesis. Proper sterilization and nutrient optimization are crucial for large-scale cultivation and conservation of this medicinal plant [14].

Pharmacological Application: *Coleus forskohlii*; native to tropical regions has been cherished in the traditional medicine for its medicinal value in addressing health related concerns. It is known for its potential benefits in promoting overall well-being [15].

Studies on Anti-obesity, and Glaucoma:

Preclinical Studies: In this study, cafeteria diet-induced obese rats were taken to evaluate the anti-obesity and metabolic effects of *Coleus forskohlii* extract (CFE). Rats were divided into five groups: normal diet, cafeteria diet, and cafeteria diet supplemented with different doses of CFE (50 mg/kg and 100 mg/kg) or orlistat (45 mg/kg). The cafeteria diet led to significant weight gain and metabolic disturbances, while CFE administration reduced food intake, weight gain, and dyslipidemia. Higher doses of CFE showed more pronounced effects in preventing obesity and metabolic disorders. The findings suggest that CFE may regulate appetite, improve lipid profiles, and mitigate obesity-related risks. This study supports the potential of CFE as a natural anti-obesity agent for managing metabolic disorders [16]. This study was aimed at evaluating the anti-obesity effects of *Coleus forskohlii* in ovariectomized (ovx) rats. A total of four groups were made in which Female Wistar rats were divided equally. Both control and treatment groups Received 50 g/kg of *Coleus forskohlii* extract. The study measured various parameters including body weight, cell diameter of adipose tissue after treatment. *Coleus forskohlii* administration led to reduced body weight, food intake, and fat accumulation in ovx rats. No adverse effects were reported. The findings suggest that *Coleus forskohlii* may help in obesity treatment [17].

In this particular study, *Coleus barbatus* water extract (WEB) was used in young Wistar rats with obstructive cholestasis to evaluate its potential in weight gain, food energy utilization, and lipid metabolism. Forty 21-day-old rats were divided into four groups, receiving either WEB or water with or without cholestasis. WEB and cholestasis both reduced food intake, weight gain, and energy utilization, but their effects were independent. Cholestasis increased liver weight, fat content, and cholesterol levels, while WEB reduced these values, with stronger effects in cholestatic rats. The findings suggest that WEB may help regulate lipid metabolism and body weight [18, 19].

Obesity and overweight pose significant health risks, requiring effective treatment approaches. This study investigated the anti-obesity effects of *Coleus forskohlii* in high-fat diet-induced obese mice. Thirty mice were divided into five groups and treated with different interventions, including *Coleus forskohlii* at two doses for 28 days. Body weight, food intake, and biochemical markers were assessed. Treatment with *Coleus forskohlii* significantly reduced fat accumulation, decreased cholesterol, triglycerides, and LDL levels, while increasing HDL levels, indicating effectiveness of *Coleus forskohlii* in the management of obesity [20].

Clinical Studies: A randomized, double-blind, placebo-controlled study was conducted in overweight individuals in order to examine the effects of *Coleus forskohlii* extract on obesity and metabolic health. Thirty participants received either 250 mg of the extract or a placebo twice daily for 12 weeks while following a reduced-calorie diet. Both groups experienced significant reductions in waist and hip circumference, along with an increase in HDL-C levels. The extract group showed notable improvements in insulin concentration and insulin resistance.

These results suggest that *C. forskohlii* extract, combined with a calorie-deficit diet, may help manage metabolic risk factors [21]. This clinical study was done to examine the safety, efficacy and therapeutic effect of *Coleus forskohlii* (CF) supplementation on body composition in overweight women. A total of 23 participants were randomly assigned to receive either 250 mg of CF extract or a placebo twice daily for 12 weeks. While CF did not significantly promote weight loss, it appeared to help prevent weight gain and reduce lean mass. Participants in the CF group also reported lower levels of fatigue, hunger, and fullness compared to the placebo group. No significant changes were found in metabolic markers, blood lipids, hormones, or other health parameters, further the findings suggested the safety of CF supplementation and its effectiveness in preventing weight gain rather than promoting weight loss [22].

This study examined the effects of forskolin supplementation on body composition, testosterone levels, metabolic rate, and blood pressure in overweight and obese men. A total of 30 participants were randomly assigned to either a forskolin (250 mg of 10% extract, twice daily) or a placebo group for 12 weeks. Forskolin was able to reduce the percentage of body and fat mass compared to the placebo group. Forskolin supplementation increased bone mass and showed a trend toward increasing lean body mass, also levels of serum free testosterone increased significantly while no significant increase in total testosterone level was observed. These findings suggest that forskolin may be a potential therapeutic agent for improving body composition and hormone balance in overweight and obese men, making it useful for obesity management [23].

This study was aimed at evaluating the effectiveness of *Coleus forskohlii* (CF) root extract in weight management. This was an 8-week open-label study in which fifteen healthy volunteers participated and received 500 mg of CF extract (10% forskolin) twice daily with meals. Results showed significant reductions in BMI, body weight, fat content, and basal metabolic rate, along with a slight decrease in lean body mass. The findings suggest that CF extract may aid in obesity management by promoting fat loss and metabolic health. However, further double-blind, placebo-controlled studies are required to confirm its effectiveness [24].

Safety Studies: This study assessed the acute, sub-acute, and chronic toxicity of *Coleus forskohlii* (CF) hydroethanolic root extract (10% forskolin) in Wistar rats. Acute toxicity was tested with a single dose of 2000 mg/kg, sub-acute toxicity with 100–1000 mg/kg for 28 days, and chronic toxicity with 500–1000 mg/kg for 180 days. No deaths, significant changes in haematology, serum biochemistry, or organ damage were observed. Body weight changes and necropsy results were normal. The Ames test confirmed no mutagenic potential. CF extract did not produce toxic effects at 1000 mg/kg. The NOAEL was established above 1000 mg/kg/day [25].

This study evaluated the toxic effects of *Coleus forskohlii* (CF) extract in Wistar rats. A single-dose oral toxicity study was conducted with 2000 mg/kg BW, and a sub-acute toxicity study was performed with 200, 400, and 800 mg/kg BW for 28 days. Behavioural, hematological, biochemical, and histological parameters were assessed. No deaths, significant toxicity, or organ damage were observed in any group. Body weight changes and necropsy results were normal. The study concluded that CF extract did not induce toxicity up to 2000 mg/kg BW. The No Observed Adverse Effect Level (NOAEL) was determined at 2000 mg/kg BW [26].

To assess the efficacy of Forskolin 1% w/v aqueous eye drops in open-angle glaucoma patients, this study was conducted. A total of 90 patients aged 18+ years having IOP >24 mm/Hg were recruited for this double-blind, randomized, controlled trial. Patients used two drops thrice daily for four weeks, with regular IOP assessments. The Forskolin group showed a greater reduction in IOP compared to the Timolol 0.5% group, achieving statistical significance ($p<0.05$). Forskolin was found to be safe and effective in managing glaucoma. The study concluded that Forskolin 1% eye drops could be a better alternative to Timolol for treating open-angle glaucoma [27]. *Coleus barbatus* has been traditionally used in folk medicine for its potential abortive effects. This study evaluated its impact on embryo implantation and fetal development in

pregnant Wistar rats. Increasing doses of hydroalcoholic extract of *C. barbatus* were given to rats either before (days 0–5) or after implantation (days 6–15). The highest dose (880 mg/kg) before implantation led to delayed fetal development and anti-implantation effects. Post-implantation exposure caused developmental delays linked to maternal toxicity. These findings support its traditional use for pregnancy interruption [28].

Role of Forskolin beyond Obesity and Glaucoma:

Cardiovascular Effects: Apart from anti-obesity and anti-glaucoma action, *Coleus forskohlii* also exhibits cardiovascular protection action. This property of *Coleus forskohlii* is directly linked with the stimulation of adenylate cyclase leading to reduction in cardiac pre-load and after load, also there is reduced pressure in the pulmonary artery [29]. In this study, effect of forskolin on patients with congestive cardiomyopathy was evaluated and it was observed that forskolin was able to reduce the cardiac preload and afterload in a dose dependent manner [30].

Antimicrobial Activity: Besides its role in obesity, glaucoma, and cardioprotection, *Coleus forskohlii* also exhibits antimicrobial activity against various bacteria and fungus also [29]. In this study, an extract of *Coleus forskohlii* containing fractions of ethanol, methanol, butanol, ethyl acetate was evaluated for antimicrobial activity. Results suggested that all fractions of extract showed significant antimicrobial action pathogens while the maximum antimicrobial action was shown by the fraction containing ethanol [31].

In this current investigation, the antifungal potential of *Coleus forskohlii* against *Colletotrichum gloeosporioides* was evaluated. Three solvents; hexane, ethyl acetate, and methanol containing extracts were obtained from the roots of *Coleus forskohlii*. The main chemical constituent responsible for showing dose dependent germination activity against *Alternaria solani* was found to be forskolin. All the extracts showed mycelial growth inhibition in *Colletotrichum gloeosporioides* [32].

Mechanism of Action: Forskolin is a diterpene known for its ability to directly activate adenylate cyclase, an enzyme that increases the levels of cyclic AMP (cAMP) in cells. cAMP serves as an essential second messenger that mediates various cellular responses to hormonal signals. When hormones bind to receptors on the cell membrane, adenylate cyclase is triggered, converting ATP into cAMP. This process activates cAMP-dependent enzymes, which regulate multiple physiological functions such as metabolism, cardiac function, and smooth muscle relaxation. Forskolin has been widely studied for its ability to modulate these pathways, making it useful in research and potential therapeutic applications. Hormones like catecholamines, adrenocorticotropic hormone, and vasopressin utilize this cAMP signalling mechanism to regulate bodily functions, including stress response, metabolism, and vascular control [33].

CONCLUSION: In conclusion, *Coleus forskohlii* has demonstrated pharmacological potential, particularly in metabolic regulation and obesity management. Preclinical and clinical studies indicate that forskolin, its primary bioactive diterpene, activates adenylate cyclase, leading to increased intracellular cyclic AMP (cAMP) levels, which regulate lipolysis, energy metabolism, and adipogenesis. Experimental evidence suggests that *C. forskohlii* supplementation may reduce adipose tissue accumulation, improve lipid profiles, and influence body composition. Additionally, *in-vitro* regeneration studies support its large-scale propagation for medicinal applications. Toxicological assessments indicate a high safety margin, with no significant adverse effects at therapeutic doses. However, further well-controlled clinical trials are required to establish its efficacy, optimal dosing strategies, and long-term safety. *C. forskohlii* remains a promising candidate for botanical interventions in metabolic disorders.

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