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Review Article

COLEUS (*PLECTRANTHUS BARBATUS*) – A MULTIPURPOSE MEDICINAL HERB

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ABSTRACT
Plectranthus barbatus Andr. (Syn. *Coleus forskohlii* Briq.) is a perennial herb, belonging to the family Lamiaceae. Its tuberous roots are found to be a rich source of forskohlin (coleonol) used as a potential drug for hypertension, congestive heart failure, eczema, colic, respiratory disorders, painful urination, insomnia, and convulsions. Clinical studies of the plant further support these traditional uses, indicating therapeutic benefit in asthma, angina, psoriasis and prevention of cancer metastases. Forskolin directly activates almost all hormone sensitive adenylate cyclases in intact cells, tissues and even solubilised preparation of adenylate cyclase. Stimulation of adenylate cyclase is thought to be the mechanism by which forskolin relaxes a variety of smooth muscles. Forskolin, by increasing cAMP level in turn, inhibits basophil and mast cell degranulation and histamine release, lowers blood pressure and intraocular pressure and it inhibits platelet aggregation, promotes vasodilation, bronchodilation, and thyroid hormone secretion. Coleus acts as a natural source of drug for many major diseases implying that there is a great demand for production and processing of the crop. The paper deals with botany, medicinal uses, phytochemistry, mechanism of action and case studies on coleus.
KEY WORDS: Coleus, cyclic AMP, forskolin, *Plectranthus barbatus*

INTRODUCTION

Plectranthus barbatus Andr. (Syn.*Coleus forskohlii* Briq.), that belongs to the family Lamiaceae. It is commonly known as Coleus, Pashanbhedi (Sanskrit), Patharchur (Hindi), Makandi beru or Mangani beru (Kannada) and is grown throughout the country. Its tuberous roots are found to be a rich source of forskohlin (coleonol) used as a potential drug for hypertension, congestive heart failure, eczema, colic, respiratory disorders, painful urination, insomnia, and convulsions[3]. Clinical studies of the plant and the forskolin constituent support these traditional uses, but also indicate it may have therapeutic benefit in asthma, angina, psoriasis, and prevention of cancer metastases[4].

Plectranthus barbatus Andr. is considered to be originated in Indian sub-continent. It occurs in the subtropical Himalayas from Kumaon to Nepal, Bihar and Deccan peninsula of South India as well as Sri Lanka. Apparently, it has been distributed to Egypt, Arabia, Ethiopia, tropical East Africa and Brazil. In India, the plant is found on dry, barren hills and at an altitude of about 2400m with moderate rainfall of 400-500mm and a mean annual temperature of 18-27^{0}C. The crop is being commercially grown in Rajasthan, Maharashtra, Karnataka and Tamil Nadu in an area of about 2500ha.

Botanical description

C. forskohlii is a perennial plant that grows to about 45 - 60 cm tall. It has four angled stems that are branched and nodes are often hairy. Leaves are 7.5 to 12.5 cm in length and 3 to 5 cm in width, usually pubescent, narrowed into petioles. Inflorescence is raceme, 15 – 30 cm in length; flowers are stout, 2 to 2.5 cm in size, usually perfect and calyx hairy inside. Upper lip of calyx is broadly ovate. The blue or lilac corolla is bilabiate. Lower lobes are elongated and concave so that they enclose the essential organs. The ovary is four parted and stigma is two lobed and the flower is cross-pollinated by wind or insects[5].

The root is typically golden brown, thick, fibrous and radially spreading. Roots are tuberous, fasciculated, 20 cm long and 0.5 to 2.5 cm in diameter, conical fusiform, straight, orange-red within and strongly aromatic. *C. forskohlii* is the only species of the genus to have fasciculated tuberous roots. The entire plant is aromatic. The leaves and tubers have quite different odours. However, the growth habit of *C. forskohlii* is strikingly variable being erect, procumbent or decumbent. Similarly, the root morphology in different populations is also fascinatingly diverse, being tuberous, semi tuberous or fibrous[40].

GENETIC VARIABILITY IN COLEUS

Reddy[34] reported that *C. forskohlii* is diploid with n = 14. However, Riley and Hoff[35] from their studies on

chromosome numbers in South African dicotyledons reported that *C. forskohlii* is diploid with basic chromosome number n=16. Bir and Saggoo[7,8] reported that Central Indian collections have basic number of n=17, while South Indian collections have n=15 and concluded that variability in base number of various members of the family could be due to aneuploidy at generic level which ultimately leads to morphological variations. Shah[40] reported that populations from different eco-geographic areas vary greatly in their morphology.

MEDICINAL USES

In India, the major medicinal species of *Coleus* is the tuberous *C. forskohlii*. *C. amboinicus*, *C. blumei*, *C. malabaricus* and *C. scutellaroides* are other species and are mainly used to treat dysentery and digestive disorders[16]. *C. forskohlii* is widely used in different countries for various ailments. In Egypt and Africa, the leaf is used as an expectorant, emmenagogue and diuretic. In Brazil, it is used as a stomach aid and in treating intestinal disorders[47]. It is used as a condiment in India and the tubers are prepared as pickle and eaten. In traditional Ayurvedic systems of medicine, *C. forskohlii* has been used for treating heart diseases, abdominal colic, respiratory disorder, insomnia, convulsions, asthma, bronchitis, intestinal disorders, burning sensation, constipation, epilepsy and angina[4]. The roots are also used in treatment of worms and to alleviate burning in festering boils. When mixed with mustard oil, the root extract is applied to treat eczema and skin infections. The plant is also used for veterinary purposes[15]. Forskolin is also used in the preparation of medicines preventing hair graying and restoring grey hair to its normal colour. Though grouped as a medicinal plant, it also contains essential oil in tubers, which has very attractive and delicate odour with spicy note[32]. Essential oil has potential uses in food flavouring industry and can be used as an antimicrobial agent[13].

PHYTOCHEMISTRY

The tuberous root extracts of *C. forskohlii* contain minor diterpenoids *viz.,* deactylforskolin, 9 - deoxyforskolin, 1, 9 -deoxyforskolin, 1, 9 - dideoxy - 7 - deacetylforskolin in addition to forskolin[3,15] (7 β- acetoxy - 8, 13-epoxy-1α, 6 β, 9 β- trihydroxylabd-14-en-11-one).

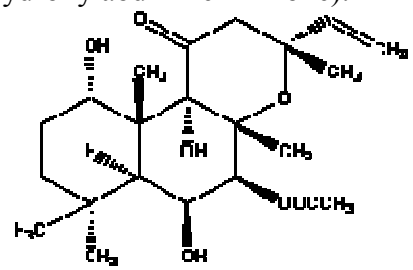

Fig.1: Structure of forskolin

Forskolin was discovered in the year 1974 and was initially referred to as coleonol. After the identification of other coleonols and diterpenoids the name was later changed to forskolin[38]. Shah *et al.*[41] reported that forskolin occurred exclusively in *C. forskohlii* and could not be detected in six other *Coleus* species *viz*., *C. amboinicus*, *C. blumei*, *C. canisus*, *C. malabaricus*, *C. parviflorus* and *C. spicatus* and six taxonomically related *Plectranthus* species *viz*., *P. coesta*, *P. incanus*, *P. melissoides*, *P. mollis*, *P. rugosus* and *P. stocksii*. Studies carried out using one hundred samples belonging to species of *Coleus*, *Orthosiphon* and *Plectranthus* of the sub family Ocimoideae at Japan also revealed the absence of forskolin in all the samples.

Second generation forskolin derivatives *viz*., _5-6-deoxy-7-deacetyl-7-methyl amino carbon forskolin (HIL 568), a potential anti-glaucoma agent and 6-(3-dimethylamino propionyl) forskolin hydrochloride (NKH 477), a potential cardio-tonic agent were developed[22]. Newer compounds are being identified from the root extracts of *C. forskohlii*. Xu *et al.*[50] obtained six compounds from the roots of *C. forskohlii* and identified structures as 14-deoxycoleon U, demethylcryptojaponol, alpha-amyrin, betulic acid, alpha-cedrol and betasitosterol and the compounds *viz*., alpha-amyrin and betulic acid were isolated from *C. forskohlii* for the first time. Two new diterpenoids forskolin I (1alpha, 6 betadiacetoxy- 7 beta, 9alpha-dihydroxy-8, 13-epoxylabd-14- en-11-one) and J, (1alpha, 9alpha-dihydroxy-6 beta, 7 beta-diacetoxy- 8, 13-epoxylabd-14-en-11-one) were isolated from *C. forskohlii* plants collected in Yunnan Province[44].

Recently, two more new labdane diterpene glycosides, forskoditerpenoside A, B were also isolated from the ethanol extract of the whole plant[42]. This was the first report about the occurrence of glycosides derived from labdane diterpene in the nature and these compounds showed relaxative effects on isolated guinea pig tracheal spirals *in vitro*. Later, three new minor labdane diterpene glycosides, forskoditerpenoside C, D and E and a novel labdane diterpene forskoditerpene A from the ethanol extract of the whole plant of *C. forskohlii* were isolated[43]. Forskoditerpenoside C, D and E showed relaxative effects on isolated guinea pig tracheal spirals *in vitro* and an unusual 8, 13-epoxy-labd- 14-en-11-one glycoside pattern. Forskoditerpene A is the first known labdane derivative with a spiro element. Forskolin is in great demand in Japan and European countries for its medicinal use and related research purposes.

MECHANISM OF ACTION

Forskolin being the major chemical constituent of the tuber, herbal preparations of it act on various multiple

pharmacologic mechanisms. The blood pressure lowering and antispasmodic effects of extracts of *C. forskohlii* roots were reported by Dubey *et al.*[18] based on the extensive screening of Indian plants for biological activity at the Central Drug Research Institute, Lucknow. De Souza[14] found that the methanol extracted from the root tuber is helpful in lowering blood pressure and positive inotropic activities in animal models. Singh and Tandon[46] compared physico-chemical properties of coleonol, forskolin and their derivatives and reported that the two compounds do not have the same structure and are stereoisomers that is, they differed only in the configuration of the acetate (-OAc) group at carbon-7. The pharmacological studies of forskolin and coleonol indicated that they had identical properties[39].

The principle mechanism by which forskolin exerts its hypotensive activity is by stimulation of adenylate cyclase and thereby increasing cellular concentrations of the second messenger cyclic AMP (cAMP) is presented in **Fig.2**. Forskolin directly activates almost all hormonesensitive adenylate cyclases in intact cells, tissues and even solubilised preparation of adenylate cyclase[29]. The unique feature of this activation is that the site of action for forskolin is the catalytic subunit of the enzyme or a closely associated protein[39]. Of the 9 types of adenylate cyclase in humans, forskolin can activate all except type IX, which is found in spermatozoa[23]. Stimulation of adenylate cyclase is thought to be the mechanism by which forskolin relaxes a variety of smooth muscles. This action of forskolin proved the potential use of the molecule, not only as an invaluable research tool for understanding cyclic – AMP dependent physiological processes, but also as a potential therapeutic agent for diseases like cardiac insufficiency, hypertension, glaucoma, thrombosis, asthma and metastatic condition[39].

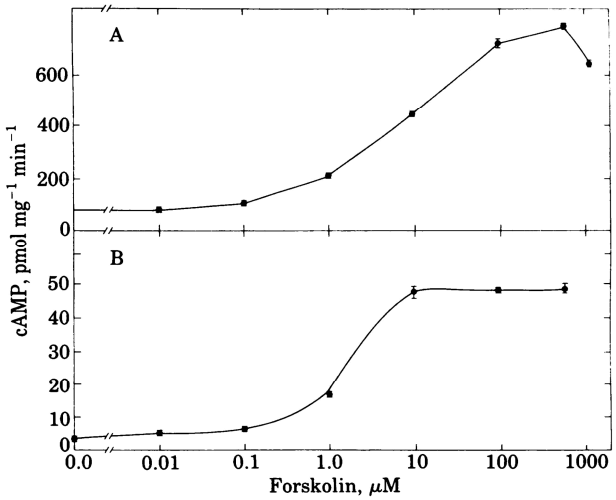

Fig. 2: Effect of forskolin on the activity of adenylate cyclase in rat cerebral cortical membranes with ATP as substrate

Forskolin, by increasing cAMP level in turn, inhibits basophil and mast cell degranulation and histamine release[28], lowers blood pressure[17] and intraocular pressure[12], inhibits platelet aggregation[2,48], promotes vasodilation[17,49],bronchodilation[26] and thyroid hormone secretion and stimulates lipolysis in fat cells[21,36].

Anti-obesity

Henderson *et al.*[20] suggested that *C. forskohlii* does appear to promote weight loss but may help mitigate weight gain in overweight females with apparently no clinically significant side effects. The antiobesity effects of *C. forskohlii* were investigated in ovariectomized rats[19] and the administration of *C. forskohlii* extracts reduced body weight, food intake and fat accumulation in those rats suggesting that *C. forskohlii* may be useful in the treatment of obesity.

Heart Disorder and Hypertension

Forskolin has a positive inotropic action on cardiac tissue via increased cAMP levels. Detailed pharmacological studies established that forskolin lowered normal or elevated blood pressure in different animal species through a vasodilatory effect and it had a positive inotropic action on the heart muscle[16,17].

Coleus forskohlii has traditionally been used to treat hypertension, congestive heart failure, and angina. Coleus's basic cardiovascular action is to lower blood pressure, while simultaneously increasing the contractility of the heart. This is believed to be due to forskolin's Cyclic AMP-elevating ability, which results in relaxation of the arteries, and increased force of contraction of the heart muscle. A preliminary trial found that coleus reduced blood pressure and improved heart function in people with cardiomyopathy. Coleus also

increases cerebral blood flow, indicating that it may be beneficial in cerebral vascular insufficiency, and in enhancing post-stroke recovery. The platelet aggregation-inhibiting effects of coleus also add to its value in cardiovascular disorders.

Glaucoma

Glaucoma is characterized by elevated intraocular pressure (IOP). Glaucoma is a condition in which the pressure in the eye is too high, due to an imbalance between the formation of aqueous humor in the eye and its absorption in or drainage out of the eye. Eventually, as the pressure builds up, the blood vessels nourishing the optic nerve are constricted, resulting in irreversible damage to the nerve and impaired vision culminating in blindness, if left untreated. Several animal and human studies have demonstrated the ability of forskolin to lower IOP, possibly via cAMP activation and a reduction in aqueous flow.

The effect of forskolin on aqueous humour dynamics and intraocular pressure was first described by Capriole and Sears[11]. The topical application of forskolin lowered the intraocular pressure in rabbits, monkeys and healthy human volunteers and it was associated with a reduction in aqueous inflow and no change in outflow facility indicating the potential of forskolin as a therapeutic agent in the treatment of glaucoma. However Lee *et al*.[25] reported that forskolin had no lasting effect on intraocular pressure in monkeys with glaucoma. It also showed no effect on humans in reducing aqueous flow when applied topically to the eye[9].

Asthma

Asthma and other allergic conditions are characterized by decreased cAMP levels in bronchial smooth muscle, as well as high levels of PAE In response to allergenic stimuli, mast cells degranulate, histamine is released and bronchial smooth muscle contracts. Forskolin's activation of cAMP inhibits human basophil and mast cell degranulation, resulting in subsequent bronchodilation.

Forskolin was studied as bronchodilator for its potential use in the treatment of asthma[10]. It blocked bronchospasm, the chief characteristic of asthma and bronchitis in guinea pigs caused by histamine and leukotriene C-4[24]. In human basophils and mast cells, forskolin blocked the release of histamine and leukotriene C-4[28]. A study involving human revealed that inhaled forskolin powder formulations were capable of causing broncho-dilation in asthma patients[6]. Forskolin seems to be a promising drug if used in an appropriate dosage for treatment of patients with congestive heart failure, glaucoma and asthma[15,37].

Cancer Metastases

Research has shown coleus to be a potent inhibitor of tumour colonization in mice. It is theoretically possible that coleus could be used in humans to prevent or inhibit tumour metastases. Many metastasizing tumour cell lines induce platelet aggregation both in vitro and in vivo. Upon aggregation, platelets release substances that promote tumour growth. Researchers have demonstrated forskolin's ability to block platelet aggregation via its stimulation of platelet adenylate cyclase and increase of intracellular cAME. 82 µg of forskolin to mice 30-60 minutes prior to injection with a highly metastatic melanoma cell line (B16 F10) reduced tumour colonization in the lungs by 70 percent[2].

Coleus and Psoriasis

In psoriasis, cells divide about 1,000 times faster than normal. Coleus helps to alleviate psoriasis by normalizing the cAMP /cGMP ratio. Like asthma, psoriasis is characterized by decreased levels of cAMP in the skin in relation to another regulating substance, cyclic guanosine monophosphate (cGMP). This imbalance results in a much higher rate of cell division--1,000 times greater than normal, resulting in psoriatic outbreaks. Although study details are not available, Ammon et al reported an improvement in symptoms of psoriasis in four patients supplemented with forskolin. The ability of forskolin to regulate cAMP levels in skin cells has been shown to have therapeutic benefit for sufferers of psoriasis[4].

Antithrombotic Effect

Forskolin inhibits platelet aggregation through adenylate cyclase stimulation, augmenting the effects of prostaglandins[1,45]. Its antithrombotic properties may be enhanced by cerebral vasodilation and it was observed in rabbits. This vasodilation was not potentiated by adenosine[49]. The use of crude *C. forskohlii* extract as a rational phyto-therapeutic antithrombotic has been proposed[14].

Depression

Depression is believed to be associated with an imbalance of neurotransmitters in the brain, serotonin and dopamine primarily. Where there is a shortage of serotonin, the supplements 5-HTP or tryptophan or the SSRI drugs like prozac or Zoloft may be beneficial. If the catecholamine neurotransmitters (epinephrine, norephinephrine) are deficient the amino acids L-Phenylalanine or L-Tyrosine, or monoamine oxidase inhibitors like GeroVital (GH3) or Deprenyl may be helpful. Recent research has also been evaluating drugs that increase Cyclic AMP as a means of elevating the catecholamines. Since forskolin elevates Cyclic AMP, it

may improve neurotransmitter function and thereby relieve depression. Clinical trials using coleus to treat depression have not been done.

Increasing Lean Body Mass

The health-promoting value of increasing lean body mass can be directly appreciated due to the known benefits derived from physical exercise in building lean body mass and stamina. Consider that lean body mass correlates positively with the performance of an incremental treadmill exercise test and that the percentage of fat in the abdomen is significantly less in athletes than non-exercising controls. Because abdominal fatty tissue is a significant risk factor for cardiovascular disease, exercise (as well as any other means) that results in increased lean body mass may have a positive impact on long-term cardiovascular health and life span. It has been postulated that by stimulating cyclic AMP, forskolin may increase the circulation of anabolic hormones and enhance their utilization which would theoretically lead to increased lean body mass.

Studies have shown that selective inhibitors of phosphodiesterase (PD) enzymes (group of enzymes inactivating cyclic AMP) and forskolin are potent activators of the hypothalamo-pituitary-adrenal (HPA) axis when given orally or intraperitoneally to rodents. The content of cyclic AMP in hypothalamic tissue increased in response to forskolin. At the same time CRH (corticotropin or ACTH releasing hormone) was released, and steroid hormones were synthesized. The selective inhibitors of PD enzymes worked synergistically with forskolin in increasing steroidogenesis. Forskolin also has a stimulatory effect on the cyclic AMP of testicular Leydig cells. This effect is similar to that of the LH (luteinizing hormone) which controls Leydig cell steroidogenesis by stimulation of the androgen pathways mainly through adenylate cyclase and cyclic AMP mediated mechanisms.

Other Uses

In addition to its cAMP stimulating activity, forskolin inhibits the binding of platelet-activating factor (PAF), independently of cAMP formation[48]. Forskolin also appears to have an effect on several membrane transport proteins and inhibits glucose transport in erythrocytes, adipocytes, platelets and other cells[31]. Forskolin also produces cyclic AMP independent effects through modulation of nicotinic acetylcholine receptor channel, desensitization, modulation of voltage dependent potassium channels, and reversal of multidrug resistance[33]. The safety of *C. forskohlii* and forskolin has not been fully evaluated. It should be avoided in people with ulcers, because it may increase stomach acid levels[39].

CASE STUDIES

Michael *et al*.[30] studied the effect of forskolin on body composition, testosterone, metabolic rate, and blood pressure in overweight and obese (BMI ≥26 kg/m^2) men. Thirty subjects (forskolin, n = 15; placebo, n = 15) were studied in a randomized, double-blind, placebo-controlled study for 12 weeks.

Forskolin was shown to elicit favourable changes in body composition by significantly decreasing body fat percentage (BF %) and fat mass (FM) as determined by DXA (Dual energy X-ray Absorptiometry) compared with the placebo group ($p \leq 0.05$). The average age, BMI, and body fat percent were 24.4 ±5.9 years, 32.5 ±4.1 kg/m^2, and 35.2 ±8.3% for the forskolin group and 28.7 ± 8.6 years, 32.6 ±3.8 kg/m^2, and 35.0 ±7.3% for the placebo group, respectively (**Table 1**). Additionally, forskolin administration resulted in a change in bone mass for the 12-week trial compared with the placebo group ($p \leq 0.05$). There was a trend toward a significant increase for lean body mass in the forskolin group compared with the placebo group ($p = 0.097$).

There was a significant difference among groups at pre–, mid–, and post–time-points for total testosterone ($p \leq 0.05$). A trend toward a significant increase in total testosterone existed within the forskolin group from pre- and post-time periods ($p = 0.051$). The percentage change for total testosterone for all time-points is presented in **Table 2**. Serum free testosterone levels were significantly increased in the forskolin group compared with the placebo group ($p \leq 0.05$). The actual change in serum total testosterone concentration was not significantly different among groups, but it increased 16.77 ±33.77% in the forskolin group compared with a decrease of 1.08 ±18.35% in the placebo group.

They observed that the oral ingestion of forskolin (250 mg of 10% forskolin extract twice a day) for a 12-week period was shown to favorably alter body composition while concurrently increasing bone mass and serum free testosterone levels in overweight and obese men. The results indicate that forskolin is a possible therapeutic agent for the management and treatment of obesity.

Henderson *et al*.[20] investigated the effects of *Coleus Forskohlii* (CF) on body composition, and determined the safety and efficacy of supplementation. In a double blind and randomized manner, 23 females supplemented their diet with ForsLean™ (250 mg of 10% CF extract, (n = 7) or a placebo [P] (n = 12) two times per day for 12-wks. Body composition (DEXA), body weight, and psychometric instruments were obtained at 0, 4, 8 & 12

weeks of supplementation. Fasting blood samples and dietary records (4-d) were obtained at 0 and 12-wks. Side effects were recorded on a weekly basis. Data were analyzed by repeated measures ANOVA and are presented as mean changes from baseline for the CF and placebo groups, respectively.

Significant differences were observed in caloric or macronutrient intake (**Table 3**). CF tended to mitigate gains in body mass (-0.7 ± 1.8, 1.0 ± 2.5 kg, p = 0.10) and scanned mass (-0.2 ± 1.3, 1.7 ± 2.9 kg, p = 0.08) with significant differences in fat mass (-0.2 ± 0.7, 1.1 ± 2.3 kg, p = 0.16), fat free mass (-0.1 ± 1.3, 0.6 ± 1.2 kg, p = 0.21), or body fat (-0.2 ± 1.0, 0.4 ± 1.4%, p = 0.40) (**Table 5 and Fig.3**). Subjects in the CF group tended to report less fatigue (p = 0.07), hunger (p = 0.02), and fullness (p = 0.04). No clinically significant interactions were seen in metabolic markers, blood lipids, muscle and liver enzymes, electrolytes, red cells, white cells, hormones (insulin, TSH, T3, and T4), heart rate, blood pressure, or weekly reports of side effects (**Table 4 and Table 6**). Results suggest that CF appears to promote weight loss and help mitigate weight gain in overweight females with apparently no clinically significant side effects.

Maioli *et al*.[27] assessed the antioxidant activity of the aqueous extract of *P. barbatus* leaves on Fe^{2+}-citrate-mediated membrane lipid peroxidation in isolated rat liver mitochondria, as well in non-mitochondrial systems. Male Wistar rats, weighing approximately 200 g, were used in this study. There was a significant DPPH (2, 2-diphenyl-1-picrylhydrazyl radical) reduction, OH scavenging activity, and iron chelation by prevention of formation of the Fe^{2+}-bathophenanthroline disulfonic acid (BPS) complex.

Within all the tested concentrations (15–75 µg/ml), *P. barbatus* extract presented significant free radical-scavenging activity (IC_{50} = 35.8 ± 0.27 µg/ml in the DPPH• assay and IC_{50} = 69.1 ± 0.73 µg/ml in the •OH assay) and chelated iron (IC_{50} = 30.4 ± 3.31 µg/ml). Over the same concentration range, the plant extract protected mitochondria against Fe^{2+}/citrate-mediated swelling and malondialdehyde production, a property that persisted even after simulation of its passage through the digestive tract.

These effects could be attributed to the phenolic compounds, nepetoidin – caffeic acid esters, present in the extract. Therefore, *P. barbatus* extract prevents mitochondrial membrane lipid peroxidation, probably by chelation of iron, revealing potential applicability as a therapeutic source of molecules against diseases involving mitochondrial iron overload which intern accounts for its hepatic protective action.

CONCLUSION

Coleus acts as a natural source of drug for hypertension, cardiovascular health, obesity, glaucoma and many other diseases without any side effects. The available evidence indicates that *C. forskohlii* is the only known natural source of the diterpenoid forskolin. The pharmacological and biochemical investigations established that forskolin possesses multifaceted biological activities. But most of the studies used concentrated extract of forskolin in a non-oral delivery form for treating various disorders in animal models only and the effect of oral forskolin in humans has not been well established. Moreover still, there is paucity for the mechanism of other bioactive principles present in the herb except forskolin. Further researches in view of applicability of forskolin for treating human ailments without side effects and activity of other bioactive principles other than forskolin are needed.Still there is paucity for the mechanism of other bioactive principles present in the herb except forskolin.

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Table 1. Body composition values -body weight, LBM, and fat mass at each time-point

	Pre	Post	Change (pre - post)	Percent change (pre - post)
Forskolin				
Body weight (kg)	103.98 ±14.89	103.91± 15.06	-0.07 ±2.39	-0.08 ±2.44
LBM (kg)	63.61± 5.94	67.32 ±8.29[†]	3.71 ±4.07	5.65 ±6.32
Fat mass (kg)	37.43± 12.65	32.91 ±11.29[†]	-4.52 ±5.74[*]	-11.23± 13.20[*]
Bone mass (kg)	3.41 ±0.43	3.68 ±0.43[†]	0.27 ±0.31[*]	8.63 ±10.46
Placebo				
Bodyweight (kg)	100.95± 9.30	102.15± 9.65	1.20 ±2.33	1.20 ±2.35
LBM (kg)	61.82± 6.44	63.39 ±7.07[†]	1.57 ±2.56	2.56 ±4.39
Fat mass (kg)	35.65± 9.99	35.14 ±10.56	-0.51 ±1.91	-1.73 ±5.64
Bone mass (kg)	3.41 ±0.55	3.60 ±0.51	0.20 ±0.53	7.46 ±18.78

Table 2.Total testosterone and free testosterone values

	Pre	Post	Change (pre - post)	Percent change (pre - post)
Forskolin				
Total testosterone (ng/mL)	5.06 ± 1.21[*]	5.75 ± 1.50[*]	0.69 ± 1.26	16.77 ± 33.77
Free testosterone (pg/mL)	15.90 ± 13.39	16.36 ± 13.32	0.46 ± 0.86[*]	3.47 ± 8.10
Placebo				
Total testosterone (ng/mL)	4.12 ± 0.82	4.00 ± 0.89	-0.11 ± 0.95	-1.08 ± 18.35
Free testosterone (pg/mL)	13.28 ± 7.26	12.77 ± 7.30	-0.51 ± 1.04	-4.11 ± 11.48

All values are presented as means ± SD.
[*] Significant difference between groups and
[†] significant difference within groups across time ($p \leq 0.05$).

Table 3: Four-day total dietary intake for the CF and P groups

Variable	Group	Week 0 (T1)	Week 8 (T3)	Week 12 (T4)	Significance	
Fat (g/kg/d)	CF	281.5 ± 87.5	243.2 ± 69.0	187.0 ± 55.8	Group	0.153
	P	337.0 ± 124.2	310.1 ± 99.1	219.0 ± 86.3	Time	0.002
					Group × Time	0.696
Carbohydrates (g/kg/d)	CF	959.1 ± 278.7	903.5 ± 227.9	777.5 ± 303.2	Group	0.719
	P	959.7 ± 253.6	953.3 ± 269.2	831.5 ± 184.1	Time	0.025
					Group × Time	0.676
Protein (g/kg/d)	CF	293.8 ± 112.0	270.8 ± 93.0	242.8 ± 80.7	Group	0.525
	P	318.5 ± 143.5	290.7 ± 129.9	282.1 ± 77.6	Time	0.213
					Group × Time	0.831
Energy Intake	CF	7458 ± 1920	6833 ± 1259	5690 ± 1927	Group	0.299
(kcal/kg/d)	P	8087 ± 2310	7772 ± 2165	6435 ± 1475	Time	0.007
					Group × Time	0.919

Table 4: Selected hematological markers for the CF and P groups

Variable	Group	Week 0 (T1)	Week 12 (T4)	Significance	
White Blood Cells (thous/cum)	CF	6.5 ± 1.8	7.9 ± 2.3	Group	0.030
	P	5.9 ± 1.7	5.1 ± 1.7	Time	0.366
Absolute Lymphocytes (cells/mcl)	CF	2161.2 ± 433.6	2771.0 ± 643.2	Group	0.051
	P	2084.4 ± 511.4	1945.8 ± 447.5	Time	0.043
Calcium (mg/dl)	CF	9.1 ± 0.1	9.3 ± 0.4	Group	0.894
	P	9.3 ± 0.2	9.1 ± 0.2	Time	0.904
ALT (SGPT) (U/L)	CF	11.8 ± 4.6	11.4 ± 3.4	Group	0.020
	P	22.5 ± 10.1	22.0 ± 13.8	Time	0.036
Uric Acid (mg/dl)	CF	4.2 ± 0.9	3.8 ± 1.0	Group	0.006
	P	3.9 ± 1.1	4.4 ± 1.4	Time	0.724
Absolute Neutrophils (cells/mcl)	CF	3791.9 ± 1273.0	4467.7 ± 1737.2	Group	0.042
	P	3270.7 ± 1251.3	2732.5 ± 596.0	Time	0.787

Table 5: Body composition and bone density values for the CF and P groups

Variable	Group	Week 0 (T1)	Week 12 (T4)	Significance	
Body Weight (kg)	CF	87.2 ± 12.4	86.6 ± 13.0	Group	0.987
	P	86.1 ± 12.5	87.4 ± 13.4	Time	0.492
				Group × Time	0.121
Bone Mineral Area (cm^2)	CF	1772 ± 94	1781 ± 130	Group	0.148
	P	1846 ± 116	1844 ± 120	Time	0.929
				Group × Time	0.756
Bone Mineral Content (g)	CF	1781 ± 202	1803 ± 223	Group	0.412
	P	1872 ± 237	1870 ± 242	Time	0.663
				Group × Time	0.601
Bone Mineral Density (g/cm^2)	CF	1.0 ± 0.08	1.0 ± 0.07	Group	0.923
	P	1.0 ± 0.08	1.0 ± 0.08	Time	0.367
				Group × Time	0.578
Fat Mass (kg)	CF	33.82 ± 8.00	33.61 ± 8.37	Group	0.638
	P	31.27 ± 7.22	32.36 ± 8.22	Time	0.336
				Group × Time	0.161
Lean Mass (kg)	CF	44.65 ± 5.75	44.59 ± 5.53	Group	0.446
	P	46.40 ± 6.18	47.05 ± 5.62	Time	0.168
				Group × Time	0.212
Lean + BMC (kg)	CF	46.43 ± 5.88	46.40 ± 5.66	Group	0.440
	P	48.27 ± 6.36	48.92 ± 5.81	Time	0.154
				Group × Time	0.211
Total Mass (kg)	CF	80.25 ± 12.42	80.017 ± 12.7	Group	0.948
	P	79.54 ± 12.70	81.28 ± 13.01	Time	0.139
				Group × Time	0.080
Body Fat (%)	CF	41.8 ± 4.7	41.6 ± 4.8	Group	0.243
	P	39.0 ± 3.7	39.3 ± 4.3	Time	0.923
				Group × Time	0.395
Body Water (%)	CF	43.9 ± 4.0	45.3 ± 4.3	Group	0.289
	P	46.1 ± 3.2	47.3 ± 5.2	Time	0.200
				Group × Time	0.802

Table 6: Appetite markers for the CF and P groups

Variable	Group	Week 0 (T1)	Week 8 (T3)	Week 12 (T4)	Significance	
Appetite	CF	4.8 ± 0.3	4.4 ± 1.1	4.5 ± 0.7	Group	0.829
	P	5.1 ± 0.8	4.3 ± 1.4	5.1 ± 1.1	Time	0.673
					Group × Time	0.581
Hunger	CF	4.0 ± 1.2	4.0 ± 1.8	3.1 ± 1.5	Group	0.054
	P	4.9 ± 1.1	4.1 ± 1.1	5.2 ± 1.0	Time	0.645
					Group × Time	0.165
Satisfaction from Food	CF	5.8 ± 1.7	4.4 ± 1.2	4.7 ± 1.9	Group	0.138
	P	6.1 ± 1.4	5.5 ± 1.9	5.8 ± 1.1	Time	0.026
					Group × Time	0.242
Feeling of Fullness	CF	5.8 ± 1.3	5.0 ± 2.1	4.1 ± 1.3	Group	0.040
	P	6.3 ± 1.3	6.1 ± 1.8	6.4 ± 1.5	Time	0.086
					Group × Time	0.042
Amount of Energy	CF	5.9 ± 2.0	5.5 ± 2.5	5.5 ± 1.9	Group	0.611
	P	5.8 ± 1.2	5.9 ± 1.4	5.8 ± 1.7	Time	0.781
					Group × Time	0.785

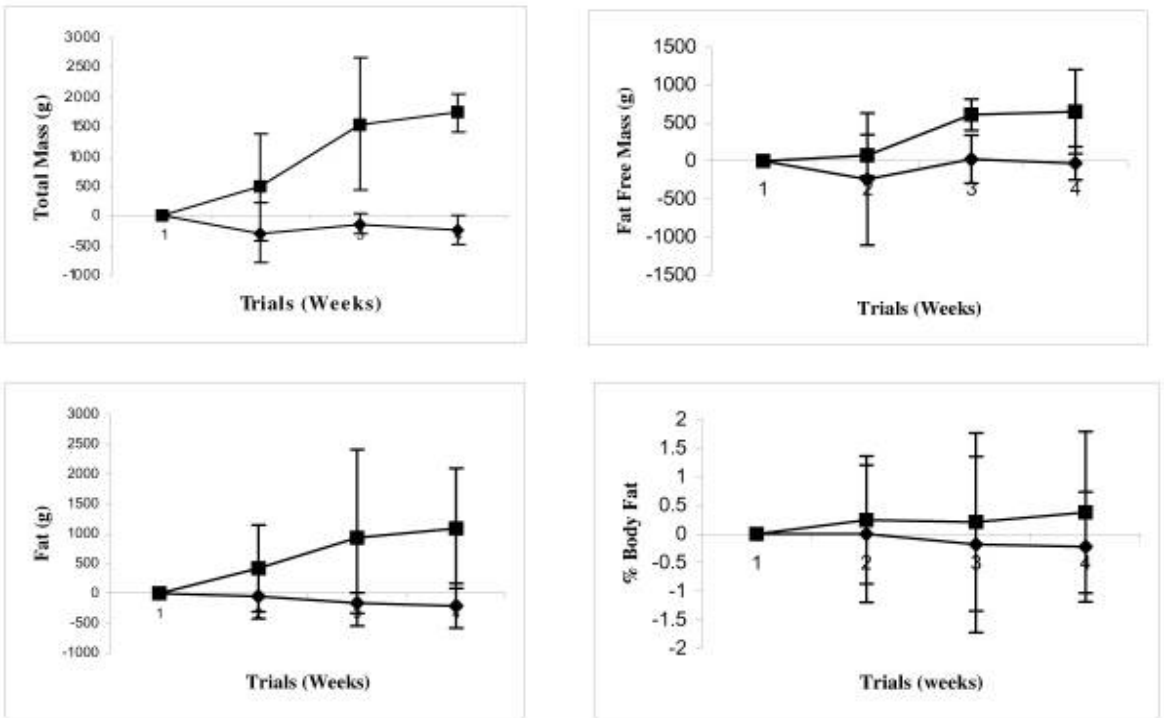

Fig.3 : The upper left panel depicts changes in DEXA total scanned mass (g), the upper right panel illustrates changes in DEXA fat-free mass (g), the lower left panel highlights differences in DEXA lean mass (g), and the lower right panel shows changes in DEXA % body fat from Week 0 to Week 12 for CF (◆) and P (■).

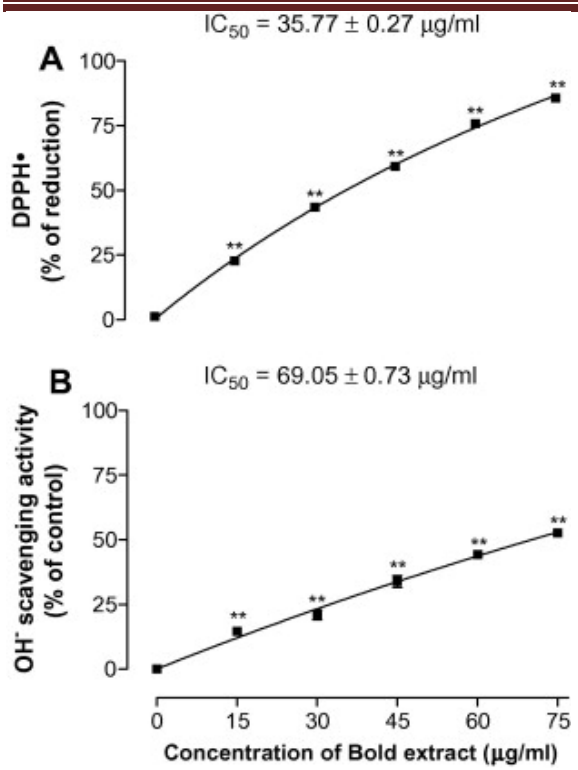

Fig.4: Effects of *Plectranthus barbatus* extract (Bold extract) on DPPH - (A) and hydroxyl radicals- (B) scavenging

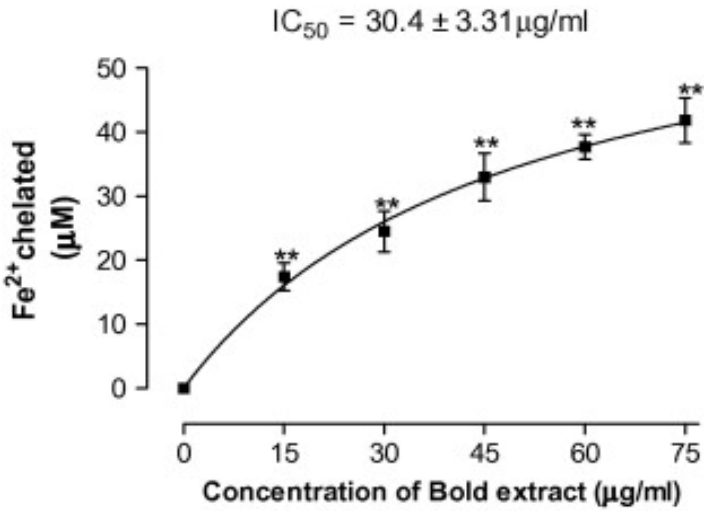

Fig. 5: Effects of *Plectranthus barbatus* extract (Bold extract) on iron chelation. **Significantly different ($P < 0.01$) from the control.