



On the High value Medicinal plant, *Coleus forskohlii* Briq.

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Abstract

Plan: To review literature on the medicinal value of *Coleus forskohlii*

Prologue: *Coleus forskohlii* is an aromatic plant belonging to the family Lamiaceae. The roots are fasciculate, thick, succulent and contain the unique chemical forskolin. Out of the 300 species of *Coleus*, only *Coleus forskohlii* contains the diterpene forskolin.

Outcome: *Coleus forskohlii* contains abietane diterpenoids, 8,13-epoxy-labd-14-en-11-one-diterpenoids, 8,13-epoxy-labd-14-en-11-one-diterpene glycosides and an essential oil with bornyl acetate as the major compound. Among them the most investigated compound forskolin has significant cardiovascular effects. Forskolin derivatives are used in cardiac care. Owing to the pharmaceutical value of forskolin, *Coleus forskohlii* is increasingly being cultivated all over India.

Keywords: *Coleus forskohlii*, forskolin, weight loss, cultivation

1. Introduction

Coleus forskohlii Briq is a perennial, branched, aromatic herb, belonging to the botanical family of Lamiaceae (Labiatae). It is called *Gandhamulika* in Sanskrit, *Pashanbhed* in Hindi, *Markandiberu* in Kannada and *Marunthu koorkankizhanku* in Tamil. It is one of the 10 species of the genus *Plectranthus*, having greatest number of synonyms and most number of uses. Its synonyms are *Coleus barbatus* Benth, *Plectranthus barbatus* Andrews, *Plectranthus forskohlii* Briq, *Plectranthus forskalaei* Willd, *Plectranthus kilimandschari* (Gürke) H.L. Maass., *Plectranthus grandis* (Cramer) R.H. Willemse, *Coleus kilimandschari* Gürke ex Engl, *Coleus comosus* A. Rich and *Coleus coerulscens* Gürke^{1, 2}. The genus *Coleus* was first described by the Portuguese naturalist, João de Loureiro (1717-1791). The generic name is derived from the Greek word *Coleos*, meaning “sheath”. The specific name is given in honor of the Swedish taxonomist Pehr Forsskål³.



A field of *Coleus forskohlii*

It is a herbaceous plant with a thick and perennial rootstalk. The stems grow up to 1-2 feet and become decumbent, when grown larger. The inflorescence and flowers are typical of the family Labiatae⁴.



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The roots are fasciculate, thick, succulent, and contain the unique chemical forskolin. There are about 300 species of *Coleus*. But it is only the species *Coleus forskohlii* that contains the diterpene, forskolin.

Srivastava et al (2002)⁵ carried out a detailed pharmacognostical study of roots procured from different geographical areas of India. All the samples showed similarity in macroscopic and microscopic characteristics. But there was considerable variation in the content of forskolin, sugars, protein and starch in the various samples.



An uprooted plant with the succulent roots

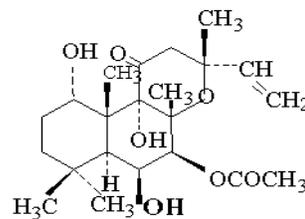
For example, forskolin content was higher in Salem (3.11%) and Vijayawada (2.20%), compared to Agrakhal (1.14%) and Tarikhet (0.73%). Similarly, there was four-fold increase in sugar and starch content of the southern samples, while protein content was twice higher in the northern samples. There was also a variation in heavy metal content of the samples. These variations are attributed to genetic or climatic factors⁶⁹.

2. Ethno botanical uses

In India the roots are traditionally used in the preparation of pickles. In Kenya it is used in the treatment of stomachache and as a purgative^{6, 1}, for nausea⁷ and in Brazil for gastritis and intestinal spasms⁸. In Kenya and the Democratic Republic of Congo, the plant is used in the treatment of wounds and ringworms^{9, 10}. In Yemen its leaves are cooked as vegetable¹¹. *Coleus forskohlii* is distributed widely in both Old and New World. Lukhoba et al (2006)¹ remark that the wide distribution of this frequently used species reflects the fact that it has been semi-cultivated as “herb” and carried by people from place to place, as they migrated across the world. Generally, the uses in the New World are quite similar to those in the Old World, though with some differences.

3. Chemistry

Coleus forskohlii contains many chemical compounds that are diterpenes in nature. They belong to two groups viz., abietane diterpenoids (abietanoids) and 8, 13-epoxy-labd-14 en-11-one diterpenoids. The most investigated compound is forskolin. Initially it was named colenol. However, after the identification of other colenols and diterpenoids, it was renamed as forskolin¹². Chemically it is 7 β -acetoxy-8, 13-epoxy-1 α , 6 β , 9 α -trihydroxy-labd-14 en-11-one (Figure 3). Forskolin is routinely assayed by HPLC using a mobile phase of water-acetonitrile (55:45)^{12a}. The diterpenoids isolated from *Coleus forskohlii* and the plant parts used are listed in Table 1



Chemical structure of forskolin

In addition to these compounds many minor constituents have also been reported from different tissues of *Coleus forskohlii*. They include coleoside⁶⁷, α -cedrol²⁴, 4 β ,7 β ,11-entioeudesmantriol⁶⁶, α -amyrin²⁷, coleonic acid⁶⁸, euscaphic acid, myrianthic acid⁶², uvaol³³, betulic acid²⁷,

arjunic acid, arjungenin⁶², crocetin dialdehyde⁶⁹, stigmasterol⁷⁰, β -sitosterol³³, genkwanin, guaicol glycerin ether²⁴, caffeic acid⁶⁷, coleoside B⁷¹, colexanthone⁶³, 2,6,10,14-tetramethylpentadecane; 2,6,10,14-tetramethylhexadecane, 2,6,10,14-tetramethylheptadecane¹³, monogalactosyl diacylglycerol, digalactosyldiacylglycerol, trigalactosyl diacylglycerol, tetragalactosyl diacylglycerol and sulfoquinovosyl diacylglycerol⁷².

4. Essential oil

Coleus forskohlii roots contain an essential oil, with an attractive and spicy note. It can find application in the food industry as a flavourant^{73,74}. The major constituents of the oil are 3-decanone (7%), bornyl acetate (15%), a sesquiterpene hydrocarbon (7.5%), β -sesquiphellandrene (13.15%) and γ -eudesmol (12.5%)⁷³. The essential oil extracted from the stems of the plant contains insignificant quantities of β -phellandrene, α -pinene, α -copaene, sabinene, caryophyllene oxide, limonene, β -caryophyllene and α -humulene⁷⁵. An essential oil has been isolated from the inflorescence also⁷⁶.

5. Physiological actions of minor constituents and forskolin analogues

Iso forskolin was found to stimulate cAMP^{48,77} and therefore, decrease blood pressure and produce an inotropic effect lesser than that produced by forskolin^{46,47,48}. Isoforskolin is also reported to relax guinea pig tracheal spirals⁶⁴ and at 1mg/loop to produce a comparable antidiarrhoeal activity against *E.coli*-induced secretory response in animal ileal loop models⁷⁸.

1-Acetylforskolin stimulates adenylyl cyclase mildly and suppresses rabbit ocular hypertension⁷⁷.

7-Deacetylforskolin displays a blood pressure lowering effect less intense than that of forskolin^{45,46,48}, but equipotent with forskolin in spontaneously hypertensive rats⁴⁵.

9-Deoxyforskolin exhibits some activity on cAMP generating systems. However, it is inactive in lowering blood pressure, even at high doses in anesthetized cats⁴⁸.

1,9-Dideoxyforskolin is able to produce several cAMP-related effects like inhibition of glucose transport and cytochalasin B binding in rat adipocyte plasma membranes⁷⁹, augmentation of low voltage-dependant Na⁺ channel activity in cardiac ventricular myocytes⁸⁰, inhibition of basal cardiac L-type Ca²⁺ current and inhibition of Ca²⁺ influx induced by K⁺ in rat phaeochromocytoma cell line PC12⁸¹.

FSK88. Li and Wang (2006)⁸² extracted FSK88, a forskolin derivative from cultured roots of *Coleus forskohlii*. They tested the compound for its anti-cancer property. It was observed that FSK88 caused apoptosis of human gastric cancer BGC823 cells in a dose-dependent manner. The FSK88-induced apoptosis was accompanied by the mitochondrial release of cytochrome-c and activation of caspase-3 in BGC823 cells. There was also up-regulation of Bax, Bad and down-regulation of Bcl-2. These results demonstrate clearly that the induction of apoptosis by FSK88 involves multiple cellular and molecular pathways.

Table 1 .The chemical compounds isolated from *Coleus forskohlii*

Sl. No.	Name of the compound	Plant part used*	Reference
Abietane diterpenoids			
1	Abietatriene (dehydroabietane)	R	13
2	7 β -Acetyl-12-deacetoxy-cyclobutatusin	L	14
3	(+)-Allylroyleanone (plectranthone J)	L	15
4	Barbatusin	L	14, 16, 17
5	Barbatusol	S	18
6	Carioical	S	19
7	Coleon C	WP	20
8	(16R)-Coleon E	L	15, 21
9	Coleon F	L	15, 22
10	Coleon O	L	23
11	Coleon S	L	24, 25
12	Coleon T	L	24, 25
13	Cyclobutatusin	L	14, 16, 26
14	Demethylcryptojaponol (11-hydroxysugiol)	R	27
15	20-Deoxocarnosol	S	28, 29
16	14-Deoxycoleon U	R	27
17	Ferruginol	S	18
18	6 β -Hydroxycarnosol	S	30
19	3 β -Hydroxy-3-deoxybarbatusin	L	16
20	Plectrin	L	15, 23
21	(16R)-Plectrinon A	L	15, 31
22	Plectrinon B	L	15
23	6,7-Secoabitanone diterpene I	S	32
24	6,7-Secoabitanone diterpene II	S	32
25	Sugiol	WP	33
8,13-Epoxy-labd-14-en-11-one-diterpenoids			
26	1-Acetoxy coleosol	R	34
27	6-Acetyl-1-deoxyforskolin	WP	35
28	1-Acetylforskolin	R, WP	36, 37, 38
29	6-Acetyl-1,9-dideoxyforskolin	WP	35
30	Coleol	R	39, 40, 41, 42
31	Coleonol E	R	43
32	Coleonol F	R	43
33	Coleosol	R	40, 44
34	7-Deacetylforskolin	R	36, 37, 38, 39, 45, 46
35	Deacetyl-1-deoxyforskolin	R	39
36	Deoxycoleonol	R	47
37	9-Deoxyforskolin	R	39, 45, 48
38	1,6-Diacetoxy-9-deoxyforskolin	R, WP	33, 35, 49
39	1,6-Di-O-acetylforskolin	R, WP	36, 37, 38
40	1,9-Dideoxy-7-deacetylforskolin	R	39, 45, 46
41	1,9-Dideoxyforskolin	R	39, 45, 46
42	1,9-Dideoxycoleonol B	R	34
43	Forskolin	R	39, 45, 46, 50, 51, 52
44	Forskolin E	R, WP	36, 53
45	Forskolin F	R, WP	36, 39, 40, 53, 54
46	Forskolin G	R, WP	53, 55, 56, 57, 58
47	Forskolin H	R, WP	53, 55, 56, 57
48	Forskolin I	R, WP	49, 55, 56, 59
49	Forskolin J	R	49, 55, 59
50	6 β -Hydroxy-8,13-epoxy-labd-14-en-11-one	R	39, 49, 55
51	Isoforskolin	R	24, 36, 37, 38, 40, 46, 52, 55, 56, 60
52	11-Oxomanoyloxide	R	39
8,13-Epoxy-labd-diterpenoids with some deviations			
53	Coleonol	R	47
54	Coleonone	R	41, 42
55	13-Epi-9-deoxycoleonol	R	61
56	3-Hydroxyforskolin	WP	62
57	3-Hydroxyisoforskolin	WP	62
58	Manoyl oxide	R	13
Miscellaneous labdane diterpenoids			
59	Coleolic acid	WP	63
60	Coleonic acid	WP	63
61	Forskoditerpene A	WP	64
62	12-Hydroxy-8,13E-labdadien-15-oic-acid	WP	35
63	13-Epi-sclareol	R	65
8,13-Epoxy-labd-14-en-11-one-diterpene glycosides			
64	Forskoditerpenoside A	WP	66
65	Forskoditerpenoside B	WP	66
66	Forskoditerpenoside C	WP	64
67	Forskoditerpenoside D	WP	64
68	Forskoditerpenoside E	WP	64

* L = leaf, R = root, S = stem, WP = whole plant

13-epi-sclareol showed antiproliferative activity in breast and uterine cancer cells *in vitro*. The antiproliferative activity of the compound was comparable to that of Tamoxifen⁶⁵.

Coleon C. The antiproliferative activity of this compound was investigated for the first time by Xing et al (2008)⁸³ on eight human tumour cell lines. Results indicate that A375 was the most sensitive of all the cell lines. Based on this and toxicity data, the authors suggest that *coleon C* could effectively inhibit tumour cell proliferation and growth by inducing apoptosis with low toxicity.

Barbatusin is reported to inhibit Lewis lung carcinoma and lymphocytic leukemia P 388 in mice¹⁶. *Barbatusol* induced a potent blood pressure lowering effect at a dose of 3 mg/kg, accompanied by discrete bradycardia¹⁸.

Plectrin is shown to exert antifeedant activity against the green bug *Schizaphis graminum* and the pink bollworm *Pectinophora gossypiella*²³. *Plectrinon A* inhibited the gastric H⁺,K⁺-ATPase, more effectively than the classic proton pump inhibitor omeprazole. This may be the mechanism underlying the anti-ulcer property of *Coleus forskohlii*³¹.

5.1 Forskolin derivatives in cardiac care

In spite of the multifaceted pharmacological actions of forskolin including positive inotropic, hypotensive, bronchospasmolytic and antiglaucoma activities, this molecule has not been available as an approved drug. This is due to its poor water solubility (0.001%). Thus forskolin is not used as intravenous or oral formulation. The nonspecific nature of forskolin activation of adenylyl cyclase raises the concern that it may be too toxic for clinical use. Therefore, forskolin has been used as a prototype for developing more potent compounds, with improved water solubility and selective activation of adenylyl cyclase. Many attempts have been made in this direction. However, the most potent water soluble forskolin derivative so far produced is 6-(3-dimethylaminopropionyl) forskolin hydrochloride or NKH477^{84, 85, 86, 87}. NKH477 produces several cAMP-dependant effects, is orally active, and has high affinity for adenylyl cyclase type V, major isoform of the enzyme in the myocardium, thus accounting for its cardiovascular effects. It is the first clinically available adenylyl cyclase activator for post-operative management of patients undergoing cardiac surgery. Iranami et al (2002)⁸⁸ published a report on how continuous infusion of NKH477 successfully weaned a neonate from cardiopulmonary bypass, after correction of a complex congenital cardiac anomaly. This was made possible under conditions in which better known inotropic agents like milrinone in combination with epinephrine and isoproterenol were ineffective. NKH477 [Colforsin daropate HCl (Adehl® Inj.)] is available in Japan, where it is used in the treatment of heart failure.

5.2. Adverse reactions of forskolin

Many of the side effects caused by forskolin are mild in nature and may include restlessness, coughing or tremors^{88a}. Gastrointestinal disturbances may develop some times.

This is because, cAMP-dependent secretagogues like forskolin generate a gradual, sustained secretory response compared to the remarkably fast and transient fluid secretion caused by calcium-dependent secretagogues like acetyl choline^{88b}.

6. Commercial cultivation of *Coleus forskohlii*

A research programme was initiated in the 1970s by the European pharmaceutical company Hoechst. The project was on the development of a hypotensive agent from herbal source. Forskolin, earlier named colenol was the outcome of this research⁸⁹. In spite of the many interesting biological properties attributed to it, the molecule was abandoned finally. A decade later Dr. Muhammed Majeed, the founder of Sabinsa Corporation, New Jersey, obtained a U.S. patent for the use of forskolin in promoting lean body mass. While forskolin was used parenterally in earlier studies, Majeed et al (1998)⁹⁰ demonstrated that when introduced into humans via oral route, forskolin is able to promote lean body mass. Armed with this patent, Sabinsa Corporation started aggressively promoting its forskolin-rich extract Forslean[®] in the North American and European nutraceutical markets. As a result of this commercial success, *Coleus forskohlii* has become a pharmaceutical crop, from the humble status of a weed. Presently about 40,000 acres are under *Coleus forskohlii* cultivation in India, Africa and South East Asia⁹¹.

Coleus forskohlii thrives well in porous and well-drained soils having a pH range of 5.5-7. It is cultivated widely in many parts of India, up to an altitude of 2400 metres. As it does not require very fertile soils, it can be grown with less expense in soils with marginal fertility. Experience shows that red, sandy loam is the ideal soil.

6.1 Seedlings

The plant can be propagated both from seeds and stem cuttings. Raising seedlings from seeds is a difficult process, as the viability of seeds is poor (8-10%). This method should be adopted only for breeding new varieties. For mass propagation of the plant, stem cuttings are found to be ideal. Generally, 10-12 cm long stem cuttings, consisting of 3-4 pairs of leaves, are planted in well-prepared nursery beds. The seedlings should be looked after well and watering should be regular. The cuttings develop roots within a week. The young plants should be transplanted to the main field, in about a month, when they will have developed sufficient number of roots.

In most of the areas, *Coleus forskohlii* is planted during June-July, when the south-west monsoon sets in. Soon after the monsoon showers the field is ploughed deep and brought to a fine filth. Farmyard manure (4 t/acre) should be applied evenly in the field. The field is further prepared into ridges and furrows, at a spacing of 60 cm. The rooted cuttings are planted 20 cm apart in a row. About 28,000 rooted cuttings are required for planting in a hectare⁹².

6.2 Application of fertilizers

Coleus forskohlii responds well to the application of N, P and K. A combination of 40 kg of N, 60 kg of P₂O₅ and 50 kg of KO₂/hectare is found to be optimum for getting maximum fresh (120 t/hectare) and dry (40 t/hectare) yield of tubers.

Half the dose of N, the whole of P and the entire K is to be applied as basal dose, followed by the remaining half of N, 30 days after planting, as top-dressing.

6.3 Irrigation

The first irrigation should be given immediately after transplanting. This can be avoided if there are rains during the period. Thereafter, the crop should be irrigated once in three days, for two weeks after transplanting. Only weekly irrigation is required afterwards. Good growth of plants and yield of tubers can be ensured thus.

6.4 Weeding

Because of the availability of good amount of water in the fields, there is intense competition from weeds. Frequent weeding is required in the early days to encourage growth of the young plants.

6.5 Pests

The common pests of *Coleus forskohlii* are leaf-eating caterpillars and root-knot nematodes. The caterpillars can be controlled by spraying the plants and drenching their roots with 0.1% methyl parathion. The nematodes can be controlled by the application of carbofuran granules in the soil, at the rate of 20 kg/hectare.

6.6 Diseases

Bacterial wilt is the most important disease attacking *Coleus forskohlii* plants. This is caused by the soil-borne pathogens *Fusarium chlamydosporum*, *Rhizoctonia bataticola* and *Sclerotium rolfsii*. Wilt by *Fusarium chlamydosporum* is characterized by gradual yellowing and drying of leaves, followed by loss of vigor and premature defoliation, leading to death of the plants. Roots get discolored and tap roots and lateral roots are destroyed⁹³. In the case of infection by *Rhizoctonia bataticola*, infection starts at the collar region of plants and the affected tissues turn into a watery mass. The roots are infected and eventually disintegrate. In advanced stage, the aerial parts also rot⁹³. Leaves turn flaccid and drop off, when plants are affected by *Sclerotium rolfsii*. White, fan-shaped mycelia strands creep over the stem and develop small, dark sclerotia on the affected parts. The sclerotia soon turn brown and the plants wither⁹³.

Wilt can be controlled by applying farmyard manure (10 t/hectare) and *Trichoderma harzianum* (25 kg/hectare). Equally effective is the drenching of soil with carboxin and thiram (0.1%). These measures reduce wilt and improve root growth⁹³.

Fernandes and Barreto (2003)⁹⁴ reported for the first time leaf spots caused on the leaves by the dematiaceous fungus *Corynespora cassiicola*. The lesions were initially brown and punctiform becoming elliptic, sub circular to irregular and pale brown. They were well-defined with a dark brown rim, having a diameter of up to 5 mm. No record of this disease could be found in the

Brazilian list of fungi on plants⁹⁵ or in the world literature. Therefore, this is the first record of the disease. *C. cassicola* has wide range of hosts and *Coleus forskohlii* is its new host.

6.7 Harvesting

To obtain more biomass of roots, flowers should be nipped off whenever they appear. The crop is ready for harvest, usually after 5-6 months after planting. It is advisable to irrigate the field a day before the harvest, as this measure loosens the soil, making the pulling of roots easier. The roots are pulled out manually, cleaned and washed. They are thereafter, chopped into small pieces, dried under shade and stored in gunny bags. A yield of 1500-2000 kg/hectare of dry tubers is obtained with satisfactory cultivation practices⁹⁶.

7. Conclusions

Coleus forskohlii is a medicinal plant containing a large number of bioactive compounds. The roots yield an essential oil which has antimicrobial properties and is therefore, put to use in cosmetics⁹⁷. The roots contain a wide spectrum of diterpenoid compounds. Many of them have cardiovascular and antiproliferative actions. *Coleus forskohlii* is the only source of forskolin, the analogues of which are of immense value in the treatment of cardiovascular diseases. Cultivation of this herb is therefore, gaining prominence.

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