Hygeia :: journal for drugs and medicines

April 2013 - September 2013
OPEN ACCESS
A half yearly scientific, international, open access journal for drugs and medicines
Research article section: Natural products/ review
Article ID- Hygeia.J.D.Med/90/13

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

Mariya Paul, A. Radha, D. Suresh Kumar*

CARe KERALAM Ltd, KINFRA Small Industries Park, Nalukettu Road, KINFRA Park P.O., Koratty-680 309, Trichur, Kerala, India.

Article history: Received: 24 November 2012, revised: 29 December 2012, accepted: 10 January 2013, Available online: 3 April 2013

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* (Gűrke) H.L. Maass., *Plectranthus grandis* (Cramer) R.H. Willemse, *Coleus kilimandschari* Gűrke ex Engl, *Coleus comosus* A. Rich and Coleus *coerulscens* Gűrke [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 Forsskål [3].

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 Labiatae [4].

For Correspondence: dvenu21@yahoo.com
Hygeia.J.D.Med. Vol.5 (1), April 2013

Article ID- Hygeia.J.D.Med/90/13

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

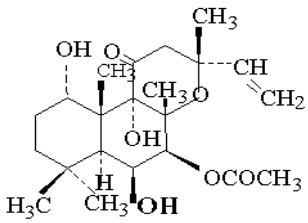
For example, forskolin content was higher in Salem (3.11%) and Vijayawada (2.20%), compared to Agrakhal (1.14%) and Tarikhet (0.73%). Similarly, there was four-fold increase in sugar and starch content of the southern samples, while protein content was twice higher in the northern samples. There was also a variation in heavy metal content of the samples. These variations are attributed to genetic or climatic factors [69].

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 nausea[7] and in Brazil for gastritis and intestinal spasms [8]. 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 vegetable [11].*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 forskolin [12]. Chemically it is 7β-acetoxy-8, 13-epoxy-1α, 6β, 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 coleoside [67], α-cedrol [24], 4β,7 β,11-enantioeudesmantriol [66], α-amyrin [27], coleonolic acid [68], euscaphic acid, myrianthic acid [62], uvaol [33], betulic acid [27],

arjunic acid, arjungenin [62], crocetin dialdehyde [69], stigmasterol [70], β-sitosterol [33], genkwanin, guaicol glycerin ether [24], caffeic acid [67] ,coleoside B [71], colexanthone [63], 2,6,10,14-tetramethylpentadecane; 2,6,10,14-tetramethylhexadecane, 2,6,10,14-tetramethylheptadecane [13], monogalactosyl diacylglycerol, digalactosyldiacylglycerol, trigalactosyl diacylglycerol, tetragalactosyl diacylglycerol and sulfoquinovosyl diacylglycerol [72].

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-humulene [75]. An essential oil has been isolated from the inflorescence also [76].

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 spirals [64] and at 1mg/loop to produce a comparable antidiarrhoeal activity against *E.coli*-induced secretory response in animal ileal loop models [78].

1-Acetylforskolin stimulates adenylyl cyclase mildly and suppresses rabbit ocular hypertension [77].

7-Deacetylforskolin displays a blood pressure lowering effect less intense than that of forskolin [45, 46, 48], but equipotent with forskolin in spontaneously hypertensive rats [45].

9-Deoxyforskolin exhibits some activity on cAMP generating systems. However, it is inactive in lowering blood pressure, even at high doses in anesthetized cats [48].

1,9-Dideoxyforskolin is able to produce several cAMP-related effects like inhibition of glucose transport and cytochalasin B binding in rat adipocyte plasma membranes [79], augmentation of low voltage-dependant Na^+ channel activity in cardiac ventricular myocytes[80], inhibition of basal cardiac L-type Ca^{2+} current and inhibition of Ca^{2+}influx induced by K^+ in rat phaeochromocytoma cell line PC12 [81].

*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	7β-Acetyl-12-deacetoxycyclobutatusin	L	14
3	(+)-Allylroyleanone (plectranthone J)	L	15
4	Barbatusin	L	14, 16, 17
5	Barbatusol	S	18
6	Cariocal	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	6β-Hydroxycarnosol	S	30
19	3β-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-Secoabitane diterpene I	S	32
24	6,7-Secoabitane 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-Dideoxyfoskolin	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	6β-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 Tamoxifen [65].

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 mice [16].*Barbatusol* induced a potent blood pressure lowering effect at a dose of 3 mg/kg , accompanied by discrete bradycardia [18].

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 research [89]. 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 Asia [91].

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 hectare [92].

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 P_2O_5 and 50 kg of KO_2/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 pants.

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 destroyed [93]. 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 rot [93]. 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 wither [93].

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 growth [93].

Fernandes and Barreto (2003)[94] reported for the first time leaf spots caused on the leaves by the dematiaceous fungus *Corynspora 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 plants [95]or in the world literature. Therefore, this is the first record of the disease. *C. cassiicola* 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 practices [96].

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 cosmetics [97]. 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.

Acknowledgements

The authors are thankful to Mr. Karimpuzha Raman, Managing Director of CARe KERALAM Ltd and Dr. Joy Varghese, Executive Director, for constant encouragement.

References

1. Lukhoba C.W., Simmonds M.S.J., Paton A.J. *Plectranthus*: a review of ethnobotanical uses. *J. Ethnopharmacol*. **2006**; 103, pp. 1-24.
2. Pulliah T. *Plectranthus barbatus* Andr. Encyclopaedia of World Medicinal Plants, Regency Publications, New Delhi. **2006**; Volume 3, pp. 1566-1567.
3. Friis I., Thulin M. The spelling of Pehr Forsskål's family name. *Taxon*. **1984**; 33, pp. 668-672.
4. Jaarsveld E. Lamiaceae, In Dicotyledons, Springer Verlag, Heidelberg, **2004**; (Edited by U. Eggli), p. 293.
5. Srivastava S.K., Chaubey M., Khatoon S., Rawat A.K.S., Mehrotra S. Pharmacognostic evaluation of *Coleus forsksohlii*. *Pharm. Biol*. **2002**; 40, pp.129- 134.
6. Johns T., Kokwaro J.O., Kimani E.K. Herbal remedies of the Luo of Siya district, Kenya: quantitative criteria for consensus. *Econ. Bot*. **1990**; 44, 369-381.
7. Hamill F.A., Apio S., Mubiru N.K., Bukenya-Ziraba R., Mosango M., Maganyi O.W., Soejarto D.D. Traditional herbal drugs of Southern Uganda II). Literature analysis and antimicrobial assays. *J. Ethnopharmacol*. **2003**; 84, pp. 57-78.
8. Camara C.C., Nascimento N.R., Macedo-Filho C.L., Almeida F.B., Fonteles M.C. Antispasmodic effect of the essential oil of *Plectranthus barbatus* and some major constituents on the guinea-pig ileum. *Planta Medica*. **2003**; 69, pp. 1080-1085.
9. Githinji C.W., Kokwaro J.O. Ethnomedical study of major species in the family Labiatae from Kenya. *J. Ethnopharmacol*. **1993**; 39, pp. 197-203.
10. Chifundera K. Contribution to the inventory of medicinal plants from the Bushi area, South Kivu Province, Democratic Republic of Congo. *Fitoterapia*. **2001**; 72, pp. 351-368.
11. Fleurentin J., Mazars G., Pelt J.M. Cultural background of the medicinal plants of Yemen. *J. Ethnopharmacol*. **1983**; 7, pp. 183-203.
12. Saksena A.K., Geen M.J., Shue H.J. Identity of colenol with forskolin: structure revision of a base-catalysed rearrangement product. *Tetrahedron Lett*. **1985**; 26, pp. 551-554.

12a. Amit A., Murali B. Quality Assessment of Selected Indian Medicinal Plants, NMPB & Natural Remedies Pvt Ltd, Bangalore. **2010**; pp. 208-228.

13. Mathela D.K., Kharkwal H.B., Mathela C.S. Terpenoids of roots of *Coleus forskohlii*. *Fitoterapia*. **1986**; 57, pp.299-301.
14. de Albuquerque R.L., Kentopff M.R., Machado M.I.L., Silva M.G.V., Matos F.J. de A., Morais S.M., Braz-Filho R. Abietane diterpenoids isolated *from Plectranthus barbatus* Andrews. *Quim. Nova* . **2007**; 30, pp. 1882-1886.
15. Ruedi P. Novel diterpenoids from leaf glands of *Plectranthus barbatus* (Labiatae). The absolute configuration of the 2-hydroxypropyl group in coleon E. *Helv. Chim. Acta*. **1986**; 69, pp. 972-984.

16. Zelnik R., Lavie D., Levy E.C., Wang A.H.J., Paul I.C. Barbatusin and cyclobutatusin, two novel diterpenoids from *Coleus barbatus* Bentham. *Tetrahedron* . **1977**; 33, pp.1457-1467.
17. Wang A.H.J., Paul I. C., Zelnik R., Mizuta K., Lavie D. Structure and absolute stereochemistry of the diterpenoid barbatusin. *J. Am. Chem. Soc*. **1973**; 95, pp.598- 600.
18. Kelecom A. Isolation, structure determination and absolute configuration of barbatusol, a new bioactive diterpene with a rearranged abietane skeleton from the labiate *Coleus barbatus*. *Tetrahedron*. **1983**; 39, pp.3603-3608.
19. Kelecom A., Dos Santos T.C. Cariocal, a new seco-abietane diterpenoid from the labiate *Coleus barbatus*. *Tetrahedron Lett*. **1985**; 26, pp.3659-3662.
20. Liu Y., Wu H., Wang X.M.,Liu J., Xing X. Use of coleon C extracted from Coleus as inhibitor for tumour growth and tumour cell proliferation.*Chinese Patent*. **2007**; CN 1899273 A.
21. Ruedi P., Eugster C.H. Structure of coleon e, a new diterpenoid methylenequinone from *Coleus barbatus* species (Labiatae). *Helv. Chim. Acta* .**1972**; 55, pp. 1994- 2014.
22. Ruedi P., Eugster C.H. Structure of coleon F. *Helv. Chim. Acta*. **1973**; 56, pp. 1129-1132.
23. Kubo I., Matsumoto T., Tori M., Asakawa Y. Structure of plectrin, an aphid antifeedant diterpene from *Plectranthus barbatus*. *Chem. Lett*. **1984**; 9, pp.1513- 1516.
24. Yao C.S., Shen Y.H., Xu Y.L. The chemical constituents of *Coleus forskohlii*. *Nat. Prod. Res. Dev*. **2002**; 14, pp. 1-6.
25. Yao C.S., Xu Y.L. The diterpenoid quinones from *Coleus forskohlii*. *Chin.Chem. Lett.* **2001**; 12, pp. 339-342.
26. Wang A.H.J., Paul I.C., Zelnik R., Lavie D., Levy E.C. Structure and stereochemistry of cyclobutatusin, a diterpenoid containing a four-membered ring. *J. Am. Chem. Soc*. **1974**; 96, pp.580-581.
27. Xu L.L., Lu J., Li W.J., Kong L.Y. Studies on the chemical constituents in root of *Coleus forskohlii*. *Zhongguo Zhong Yao Za Zhi*. **2005**; 30, pp.1753-1755.
28. Kelecom A., Dos Santos T.C., Madeiros W.L.B. On the structure and absolute configuration of (-)20-deoxocarnesol. *Ann. Acad. Bras. Cienc*. **1986**; 58, pp. 53-59.
29. Kelecom A. An abietane diterpene from the labiate *Coleus barbatus*. *Phytochemistry*. **1984**; 23, pp.1677-1679 .
30. Kelecom A. 6-β-Hydroxycarnosol, a new minor diterpene from the false boldo *Coleus barbatus* Bentham (Labiatae). *Quim Nova* . **1983**; 6, pp. 117-118.
31. Schultz C., Bossolani M.P. Torres L.M.B., Lima-Landman M.T.R., Lapa A.J., Souccar C Inhibition of the gastric H+,K+- ATPase by plectrinone A, a diterpenoids isolated from *Plectranthus barbatus* Andrews. *J. Ethnopharmacol*. **2007**; 111, pp.1- 7.
32. Kelecom A., Dos Santos T.C., Medeiros W.L.B. Secoabietane diterpenes from *Coleus barbatus*. *Phytochemistry*. **1987**; 26, pp. 2337-2340.
33. Li S., Yang Q.R., Wang X.M., Zou G.A., Liu Y.W. Chemical constituents of *Coleus forskohlii* replanted to Tongcheng. *Zhongcaoyao*. **2006**; 37, pp. 824-826.
34. Roy R., Mishra A., Varma N., Tandon J.S., Saux M., Carpy A. Minor diterpenes from *Coleus forskohlii*. *Phytochemistry* . **1993**; 34, pp. 1577-1580.
35. Xu L.L., Kong L.Y. Labdane diterpenoids from *Coleus forskohlii* (Willd.)Briq. *J. Integr. Plant Biol*. **2006**; 48, pp.478-481.
36. Jin Q.D., He B.H. Minor constituents from *Coleus forskohlii*. *Acta Bot. Yunn*. **1998**; 20, 469-473.
37. Wu M., Lai G.F., Jin Q.D., Xu Y.L. spectral characteristic property of forskolins (2). *Nat. Prod. Res. Dev*. **2005**; 17 (Suppl.), pp. 17-19, 22.
38. Jin Q.D., Xie X.H., Mu Q.Z. Study on the chemical constituents from *Coleus forskohlii* Briq. *Nat. Prod. Res. Dev*. **1990**; 2, 6-9.
39. Gabetta B., Zini G., Danieli B. Minor diterpenoids of *Coleus forskohlii*. *Phytochemistry* . **1989**; 28, pp. 859-862.
40. Prakash O., Roy R., Tandon J.S., Dhar M.M. Carbon-13 and proton two-dimensional NMR study of diterpenoids of *Coleus forskohlii*. *Magn. Reson. Chem*. **1988**; 26, pp. 117-119.
41. Singh S., Painuly P., Tandon J.S. Diterpenes from *Coleus forskohlii*:stereochemistry of the carbonyl chromaphore. *Indian J. Chem. Sect. B, Org. Chem. Inc. Med. Chem.* **1984**; 23B, pp. 952-955.
42. Katti S.B., Jauhari P.K., Tandon J.S. New diterpenes from *Coleus forskohlii*: structures of the diterpenes, coleonol-D, coleol and coleonone. *Indian J. Chem. Sect. B, Incl. Med. Chem*. **1979**; 17B, pp.321-323.
43. Painuly P., Katti S.B., Tandon J.S. Diterpenes from *Coleus forskohlii*: structures of coleonol-E and Coleonol-F. *Indian J. Chem, Sect B, Org. Chem. Incl. Med. Chem*. **1979**; 18B, pp. 214-216.
44. Jauhari P.K., Katti S.B., Tandon J.S., Dhar M.M. Coleosol- a new diterpene from *Coleus forskohlii*. *Indian J. Chem. Sect. B, Org. Chem. Incl. med. Chem*., **1978**; 16B, pp. 1055-1057.
45. de Souza N.J., Dohadwalla A.N., Reden J. Forskolin: a labdane diterpenoid with antihypertensive , positive inotropic, platelet aggregation inhibitory and adenylate cyclase activating properties. *Med. Res. Rev*. **1983**; 3, pp.201-219.
46. Bhat S.V., Bajwa B.S., Dornauer H., de Souza N.J., Fehlhaber H.W. Structures and stereochemistry of new labdane diterpenoids from *Coleus forskohlii* Briq. *Tetrahedron Lett*. **1977**; 19, pp. 1669-1672.
47. Tandon J.S., Jauhari P.K., Singh R.S., Dhar M.M. Structures of three new diterpenes , coleonol B, coleonol C and deoxycoleonol isolated from *Coleus forskohlii*. *Indian J. Chem. Sect.B, Org. Chem. Incl. med. chem*. **1978**; 16B, pp. 341-345.
48. Bhat S.V., Dohadwalla A.N., Bajwa B.S., Dadkar N.K., Dornauer H., de Souza N.J. The antihypertensive and positive inotropic diterpene forskolin: effects of structural modifications on its activity. *J. Med. Chem*. **1983**; 26, pp. 486-492.
49. Yang W.M., Jin Q.D., Xu Y.L. Spectral characteristics of forskolins (4). *Nat. Prod. Res. Dev*. **2007**; 19, pp. 991-994.
50. Shah V., Bhat S.V., Bajwa B.S., Dornauer H., De Souza N.J. The occurrence of forskolin in Labiatae. *Planta Medica* . **1980**; 39, pp. 183-185.
51. Liu C., Yao W., Meng K., Liu Y., Zhang S., Zeng S., Lu S., Li H. Isolation and purification of forskolin and identification of its chemical structure and biological activity. *Shengwu Huaxe Yu Shengwu Wuli Jinzhan*.**1992**; 19, pp.74-76.
52. Zhang X.H., Zhang W., Jin Q.D., Xu Y.L. Spectral characteristics of forskolins (1). *Nat. Prod. Res. Dev*. **2005**; 17, pp. 163-165.
53. Xu Y.L., Jin Q.D., Liu J. Spectral characteristics of forskolins (3). *Nat. Prod. Res. Dev*. **2006**; 18 (Suppl.), pp. 79-81, 97.
54. Khandelwal Y., Jotwani P.K., Inamdar P.K., de Souza N.J., Rupp R.H. Isolation, structure elucidation and synthesis of 1-deoxyforskolin. *Tetrahedron*. **1989**; 45, pp. 763-766.
55. Xu L.L., Kong L.Y. Isolation and identification of labdane diterpenoids from the roots of *Coleus forskohlii*. *China J. Nat. Med.* **2004**; 2, pp. 344-347.
56. Yang Q.R., Wu H.Z., Wang X.M., Zou G.A., Liu Y.W. Three new diterpenoids from *Coleus forskohlii* Briq. *J. Asian Nat. Prod. Res*. **2006**; 8, pp.355-360.
57. Shen Y.H., Yao C.S., Xu Y.L. New diterpenoids from *Coleus forskohlii*. *Chin. Chem. Lett*. **2002**; 13, pp.740-743.
58. Shan Y.P., Wang X.B., Kong L.Y. Forskolin G. *Acta Crystallogr. Sect. E, Struct*. **2006**; Re. Online; E62:02408-02410. Available at http://journals.iucr.org/e/issues/2006/06/00/hk2036/index.html
59. Shen Y.H., Xu Y.L. Two new diterpenoids from *Coleus forskohlii*. *J. Asian Nat. Prod. Res*. **2005**; 7, pp. 811-815.
60. Carpy A., Leger J.M., Tandon J.S., Saksena A.K. Molecular and crystal structure of colenol-B, C22H3O7. *Z. Kristallogr*. **1991**; 194, pp. 229-233.

61. Tandon J.S., Roy R., Balachandran S., Vishwakarma R.A. Epi-deoxycoleonol, a new antihypertensive labdane diterpenoid from *Coleus forskohlii*. *Bioorg. Med. Chem. Lett.* **1992**; 2, pp. 249-254.
62. Shan Y.P., Kong L.Y. Isolation and identification of terpenes from *Coleus forskohlii*. *Chin. J. Nat. Med.* **2006**; 4, pp. 271-274.
63. Liu Y., Wang X.M., Wu H. Main components of *Coleus forskohlii* extract and relevant extraction method. *Chinese Patent*. **2007**; CN 1944384A.
64. Shan Y., Xu L., Lu Y., Wang X., Zheng Q., Kong L., Niwa M. Diterpenes from *Coleus forskohlii*. *Chem. Pharm. Bull*. **2008**; 56, pp. 52-56.
65. Sashidhara K.V., Rosiah J.N., Kumar A., Bid H.K., Konwar R., Chattopadhyay N. Cell growth inhibitory action of an unusual labdane diterpene, 13-epi-sclareol in breast and uterine cancers in vitro. *Phytother. Res*. **2007**; 21, pp. 1105-1108.
66. Shan Y., Wang X., Zhou X., Kong L., Niwa M. Two minor diterpene glycosides and an eudesman sesqiterpene from *Coleus forskohlii*. *Chem. Pharm. Bull*. **2007**; 55, pp.376-381.
67. Ahmed B., Vishwakarma R.A. Coleoside, a monoterpene glycoside from *Coleus forskohlii*. *Phytochemistry*. **1988**; 27, pp. 3309-3310.
68. Roy R., Vishwakarma R.A., Varma N., Tandon J.S. Coleonolic acid, a rearranged ursane triterpenoid from *Coleus forskohlii*. *Tetrahedron Lett*. **1990**; 31, pp.3467-3470.
69. Tandon J.S., Katti S.B., Ruedi P., Eugster C.H. Crocetin dialdehyde from *Coleus forskohlii*. Briq. , Labiatae. *Helv. Chim. Acta*.**1979**; 62, pp. 2706-2709.
70. Shah V.C., D'sa A.S., deSouza N.J. Chonemorphine, stigmasterol and ecdysterone: steroids isolated through bioassay-directed plant screening programs. *Steroids*. **1989**; 53, pp. 559-565.
71. Ahmed B., Merotra R. Coleoside-B, a new phenolic glycoside from *Coleus forskohlii*. *Pharmazie*. **1991**; 46, pp.157-158.
72. Mendes B.G., Machado M.J., Falkenberg M. Screening of glycolipids in medicinal plants. *Rev. Bras. Farmacognosia* . **2006**; 16, pp. 568-575.
73. Misra L.N., Tyagi B.R., Ahmad A., Bahl J.R. Variability in the chemical composition of the essential oil of *Coleus forskohlii* genotypes. *J. Essent. Oil Res*.**1994**; 6, pp. 243-247.
74. Chowdhary A.R., Sharma M.L. GC-MS investigations on the essential oil from *Coleus forskohlii* Briq. *Indian Perfumer*. **1998**; 42, pp. 151-16.
75. Kerntopf M.R., de Albuquerque R.L., Machado M.I.L., Matos F.J.A., Craveiro A.A. Essential oils from leaves, stems and roots of *Plectranthus barbatus* Andr. (Labiatae) grown in Brazil. *J. Essential Oil Res*. **2002**; 14, pp.101-102.
76. Khare P., Sashidhara K.V., Yadav A., Garg S.N., Khanuja S.P.S. Chemical composition of the inflorescence essential oil of *Coleus forskohlii*. *India Perfumer*. **2007**; 51, pp. 47-48.
77. Yang W., Li X., Chen Z., Nie L., Wang B., Shen Z. Adenylate cyclase stimulation and ocular hypertension inhibition by forskolin analogs. *Yanke Yangiu* . **2001**; 19, pp. 1-4.
78. Yadava J.N.S., Gupta S., Ahmad I., Varma N., Tandon J.S. Neutralization of enterotoxins of Escherichia coli by colenol (forskolin) in rabbit and guinea pig ileal loop models. *Indian J Anim. Sci.* **1995**; 65, pp. 1177-1181.
79. Joost H.G., Habberfield A.D., Simpson I.A., Laurenza A., Seamon K.B. Activation of adenylate cyclase and inhibition of glucose transport in rat adipocytes by forskolin analogues: structural determinants for distinct sites of action. *Mol. Pharmacol*. **1988**; 33, pp. 449-453.
80. Ono K., Fozzard H.A., Hanck D.A. A direct effect of forskolin on sodium channel bursting. *Pflugers Arch*. **1995**; 429, pp. 561-569.
81. Park T.J., Kim K.T. Cyclic AMP-independent inhibition of voltage-sensitive calcium channels by forskolin in PC12 cells. *J. Neurochem*. **1996**; 66, pp. 83-88.
82. Li Z., Wang J.A. Forskolin derivative , FSK88 induces apoptosis in human gastric cancer BGC823 cells through cspase activation involving regulation of Bcl-2 family gene expression, dissipation of mitochondrial membrane potential and cytochrome c release. *Cell Biol. Int*. **2006**; 30, pp. 940-946.
83. Xing X., Wu H., Wang X., Hung Y., Li Q., Li C., Yang Y., Liu Y., Liu J. Inhibition of tumour cell proliferation by coleon C. *J. Chemother*. **2008**; 20, pp. 238-245.
84. Hosono M., Takahira T., Fujita A., Fujihara R., Ishizuka O., Ohoi I., Tatee T., Nakamura K. Cardiovascular effects of NKH477, a novel potent water-soluble forskolin derivative. *Eur. J.Pharmacol*. **1990**; 183, p. 2110.
85. Laurenza A., Khandelwal Y., de Souza N.J., Rupp R.H., Metzger H., Seamon K.B. Stimulation of adenylate cyclase by water-soluble analogues of forskolin. *Mol Pharmacol*. **1987**; 32, pp.133-139.
86. Khandelwal Y., Rajeshwari K., Rajagopalan R., Swamy L., Dohadwalla A.N., de Souza N.J., Rupp R.H. Cardiovascular effects of new water-soluble derivatives of forskolin. *J. Med. Chem*. **1988**; 31, pp. 1872-1879.
87. Tatee T., Narita A., Narita K., Izumi G., Takahira T., Sakurai M., Fujita A., Hosono M.,Yamashita K., Enomoto K., Shiozawa A. Forskolin derivatives. I. Synthesis and cardiovascular and adenylate cyclase stimulating activities of water-soluble forskolins. *Chem. Pharm. Bull*. **1996**; 44, pp. 2274-2279.
88. Iranami H., Okamoto K., Kimoto Y., Maeda H., Kakutani T., Hatano Y. Use of colforsin daropate following cardiac surgery in a neonate. *Anesthesiol*. **2002**; 97, pp. 503- 504.

88a. Powell M. http://www.wisegeek.com/what-are-the-most-common-forskolin-side- effects.htm **2012**: Accessed on 24 .12.2012.

88b. Reynolds A., Parris A., Evans L.A., Lindqvist S., Sharp P., Lewis M., Tighe R.Williams M.R. Dynamic and differential regulation of NKCC1 by calcium and cAMP in the native human colonic epithelium. *J. Physiol*. **2012**; pp.507-524.

89. Rupp R.H., de Souza N.J., Dohadwalla A.N. Forskolin: Its Chemical, Biological and Medical Potential, Hoechst India Ltd., Bombay, **1985**; pp. 1-191.
90. Majeed M., Badmaev V., Rajendran R. Method of preparing a forskohlin composition from forskohlin extract and use of forskolin for promoting lean body mass and treating mood disorders . *U.S.Patent*. **1998**; No. 5,804,596.
91. Anonymous. http://www.samilabs.com/services/farming/ **2012**; Accessed on 22 June, 2012.
92. Anonymous. Agro-Techniques of Selected Medicinal Plants, National Medicinal Plants Board, New Delhi, **2008**; Volume 1, pp. 59-62.
93. Hegde Y.R., Ammajamma R., Venugopal C.K., Ashoka S., Chavhan T.L. Novel approaches for management of wilt complex of *Coleus forskohlii* (Willd.) Briq. , University of Agricultural Sciences, Dharwad, **2009**; pp. 1-27.
94. Fernandes R.C., Barreto R.W. *Corynespora cassiicola* causing leaf spots on *Coleus barbatus*. *New Disease Reports*. **2003**; Volume 7, p. 8.
95. Mendes M.A.S., Silva V.L., Dianses J.C., Ferreira M.A.S.V., Santos C.E.N., Gomes Neto E., Urben A.F., Castro C. Fungos em Plantas no Brasil, Embrapa, Brasilia, **1998**; pp. 1- 558.
96. Farooqi A.A ., Sreeramu B.S. *Coleus*, In Cultivation of Medicinal and Aromatic Crops, Universities Press, Hyderabad, **2004**; pp. 85-89.
97. Majeed M., Prakash S. Composition and methods containing an antimicrobial essential oil extracted from *Coleus forskohlii*. *U.S. Patent*. **2003**; No. 6,607,712.

Mariya Paul, A. Radha, D. Suresh Kumar. On the High value Medicinal plant, *Coleus forskohlii Briq*. *Hygeia.J.D.Med*. **2013**; 5(1):69-78. Available from http://www.hygeiajournal.com / Article ID- Hygeia.J.D.Med/90/13