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Medicinal Coleus (*Coleus forskohlii* Briq): A phytochemical crop of commercial significance - Review

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Abstract
Coleus forskohlii is an important medicinal plant native to India. It has been used in traditional Ayurvedic medicine for curing various disorders and this is the only source of diterpenoid forskolin. A 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 benefits in asthma, angina, psoriasis and prevention of cancer metastases, where decreased intracellular cAMP level is believed to be a major factor in the development of the disease process. This article gives a comprehensive look on Coleus as a natural product and aims to present it in a brief manner for the researchers, scientist, botanists, pharmacognosists and herbalists to refresh their knowledge about coleus. This paper also comprehensive account of the plant classification, Phytochemistry, mechanism of action, medicinal and other uses, cytogenetic, botanical distribution, crop improvements and varieties, biotechnological approaches, complete cultivation aspects and postharvest technology for higher forskohlin production reports are included in view of the many recent findings.

Keywords: Medicinal coleus, diterpenoid forskolin, phytochemistry, medicinal use, crop improvement and cultivation aspects

1. Introduction
*Coleusforskohlii*Briq.is an important medicinal plant family of lamiaceae, growing wild in the subtropical climate of India, Nepal, Bhutan, Thailand, Burma and Sri Lanka. India is considered to be native place of the plant (Valdes *et al.* 1987; Patil *et al*. 2001) [47, 77]. In India the plant grows in the Himalayan region extending from Shimla to Kumaon and Garhwal hills (600-2300 altitude). The plant has been described in Ayurveda by the name 'Mayani' or 'Makandi' (Shah, 1996) [65]. Generally the plant is found in agricultural fields, wastelands, dry and barren hills. Coleus is a perennial herb with a height up to 45-60cm with four angled branched stem having hairy nodes. The roots are radially spreading, thick, fibrous and golden brown in color (Thorne research article 2006) [76]. *C. forskohlii* is the only species having fasciculate roots. The root morphology is quite variable indifferent populations (Kavitha *et al*., 2010) [35]. Tamil Nadu has great potential for development of medicinal plants as a commercially viable venture. Its rich bio-diversity and varied agro-climate provide a conducive atmosphere for promotion of medicinal plants as a successful commercial venture. In Tamil Nadu, Medicinal and Aromatic plants are cultivated in an area of 11684 hectares. Out of total areas coleus only cultivating 3869 hectares. (DHPC, 2018). In Tamil Nadu Salem, Tiruvannamalai, Villuppuram and velloredistricts are the major medicinal coleus production centres. The 'coleus' is cultivated on about 700 hectares in Salem district. Attur, Thalaivasal and Kallakurichi are the major coleus production centres in the district. In Attur region, contract farming of coleus gained popularity among small and marginal farmers. It is easy to grow and a profitable crop for the farmers (The Hindu 2016) [75]. The plant has been used by the tribal population of this region since old times for the various treatments *viz*., psoriasis, eczema, skin infections, leucorrhea and asthma. In general the roots and leaves of the plant are used as an economic part. The tuberous roots are found to be rich source of the labdane diterpenoid forskolin. However the whole plant has been a rich source of various phytochemicals as roots also contains Coleonol and Coleosolwhile the leaves containbarbatusin, cyclobarbatusin, methylene quinine and coleon. The diterpenoids are found in almost all parts of the plant but the roots are major source (Chandel *et al*., 1991) [14]. Many other phytochemicals also found in the plant as Terpinoids, monoterpenes, sesquiterpenes glycosides and phenolic glycosides. The plant has been used in treatment of various diseases worldwide, in Egypt and Africa leaves are used asemmenogauge and Diuretuic.

In Brazil it is used intreatment of intestinal disorders (Valdes *et al.*, 1987) [77]. In Central India the plant roots are used as condiments and for making pickles also. The plant also used for veterinary purposes (De Souza and Shah, 1988) [19]. The decoction of the plant is given with honey for the treatment of asthma and leucorrhea. Powdered roots are given for cardiac complaints, piles and urinary complaints.

2. Taxonomical classification

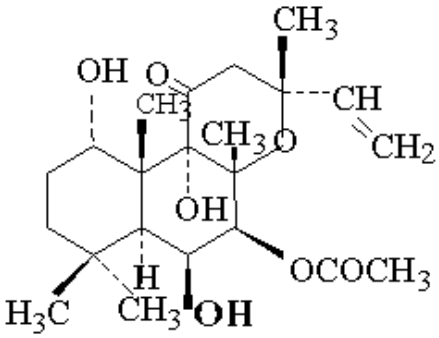
The plant belongs to family Lamiaceae and the genus Coleus. Commonly known as the mint family, Lamiacese includes a number of potent medicinal plants. It consists of 236 genera and 7000 species, the largest family of the order Lamiales. The plants are generally aromatic with colorful leaves, and have been used since ancient times for their pharmaceutical properties The genus coleus was first described by Flourier in 1790; from the greek word 'COLEOS' meaning sheath. There 150 species belonging to this genus, having showy, colorful leaves and have been used as ornamentals. The major medicinal species of Coleus in India are tuberous *C. for skohlii, C. scutellaroides, C. malabaricus, C. zeylanicus and C. amboinicus*, other species are mainly used to treat dysentery and digestive disorders (De Souza *et al.* 1983) [20].

The taxonomies position of *Coleus forskali* is as follows:

Kingdom - Plantae
Division - Magnolophyta
Class - Magnoliopsid
Order - Lamiales
Family - Lamiaceae
Genus - Coleus
Species – For skohlii

3. Phytochemistry

Forskolin was found to be the main active constituent of the roots. It is a labdane diterpenoid assumed to be synthesized via non-mevalonate pathway in the root cork cells of the plant and it reduces blood pressure. For skol in activates an enzyme, adenylate cyclase, which increases cyclic adenosine monophosphate (cAMP) levels in cells, which is the most important cell-regulating compound (Seamon and Daly, 1981; Dubey *et al.*, 1981) [23, 63]. Activation of cAMP results in inhibition of platelet activation, increased force of contraction of heart muscle, relaxation of smooth muscle, increased insulin secretion and increased thyroid function. The compound is generally extracted from the root tubers of the plant. Kavitha *et al*. (2010) [35] observed that the 0.5cm thick slices of the root tubers dried at 40°C when kept in gummy polythene bag yield a high amount of for skolin. The major hurdle faced at present is that the level of for skolin is very low and it seems difficult to produce economically. Moreover, the growth rhythm of the plant is comparatively slow and the alkaloid accumulation pattern is influenced by environmental and geographical conditions (Chandel *et al*., 1991) [14]. 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 (7β - acetoxy - 8, 13-epoxy-1α, 6 β,9α - trihydroxylabd-14-en-11-one) (Ammon and Kemper 1982; De Souza and Shah, 1988) [5, 19]. 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 (Saksena *et al*., 1985) [60]. Shah *et al.* (1980) [67] 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. Mathela *et al.* (1986) [41] had identified seven monoterpenes and nine sesquiterpene hydrocarbons and five oxygenated compounds in the steam distillate from the roots of *C. forskohlii*.



Chemical Structure of forskolin

Second generation forskolin derivatives *viz.*, Δ5-6-deoxy-7-deacetyl-7-methyl amino carbon forskolin (HIL 568), a potential ant glaucoma agent and 6-(3-dimethylamino propionyl) forskolin hydrochloride (NKH 477), a potential cardio tonic agent were developed (Hosono *et al*., 1990) [31]. Tandon and his colleagues isolated antihypertensive labdenediterpenoid 13-epi-9- deoxycoleonol (13-epi-9deoxyforskolin) from *C. forskohlii* and the stereo structure of the diterpenoid ascertained by various 2D NMR techniques (Tandon *et al*. 1979) [74]. The structure of two new minor diterpenes 1,9 dideoxy coleonol-B and 1- acetoxy coleosol, isolated from the roots of *C. forskohlii* have been shown to be 7- hydroxyl-6-acetoxy, 13-epoxy labd-14- en-11-one and 1-acetoxy-6, 9-dihydroxy, 13-epoxy labd-14-en-11-one, respectively, mainly through the interpretation of 2D NMR data and X ray analysis (Roy *et al*. 1993) [57]. Yao and Shen (2002) [83] isolated two new diterpenoids, forskolin G and H from the chloroform extract of the roots of the *C. forskohlii* and based on the spectroscopic data their structures were identified as 1α-hydroxy-6β,7β-diacetoxy-8,13-epoxylabd-14-ene-11-one and 1α,6β- diacetoxy-8,13-epoxylabd-14-ene-11-one. Newer compounds are being identified from the root extracts of *C. forskohlii*. Two new diterpenoids forskolin I (1 α, 6 β diacetoxy- 7 β, 9 α -dihydroxy-8, 13-epoxylabd-14- en-11-one) and J, (1 α, 9 α -dihydroxy-6 β, 7 β diacetoxy- 8, 13-epoxylabd-14-en-11-one) were isolated from *C. forskohlii* plants collected in Yunnan Province (Shen and Xu, 2005) [70].

Recently two more new labdane diterpene glycosides, forskoditerpenoside A, B were also isolated from the ethanol extract of the whole plant (Shan *et al*. 2007) [69]. 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 for skoditerpene A from the ethanol extract of the whole plant of *C. forskohlii* were isolated (Shan *et al*., 2008) [68]. 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.

4. 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.* (1974) [23] based on the extensive screening of Indian plants for biological activity at the Central Drug Research Institute, Lucknow. De Souza (1977) [17] 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 (1982) [72] 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 (Seamon and Daly, 1981) [63]. The principle mechanism by which forskolin exerts its hypotensive activity is by stimulation of adenylate cyclase and thereby increasing cellular concentrations of the secondary messenger cyclic AMP (cAMP) (Seamon *et al*., 1981) [63]. Forskolin directly activates almost all hormone sensitive adenylate cyclases in intact cells, tissues and even solubilized preparation of adenylate cyclase (Metzger and Lindner, 1981) [42]. 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 (Seamon and Daly, 1981) [63]. Of the 9 types of adenylate cyclase in humans, forskolin can activate all except type IX, which is found in spermatozoa (Iwatsubo *et al.,* 2003) [33]. 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 cAMP dependent physiological processes, but also as a potential therapeutic agent for diseases like cardiac insufficiency, hypertension, glaucoma, thrombosis, asthma and metastatic condition (Seamon, 1984) [62]. Forskolin, by increasing cAMP level in turn, inhibits basophil and mast cell degranulation and histamine release, (Marone *et al.,* 1987) [40] lowers blood pressure (Dubey *et al*., 1981) [22] and intraocular pressure, (Caprioli *et al*., 1984) [13] inhibits platelet aggregation, (Agarwal and Parks, 1983; Wong, 1993) [2, 80] promotes vasodilation, (Dubey *et al.,* 1981; Wysham *et al*., 1986) [22, 81] bronchodilator, (Lichey *et al*., 1984) [38] and thyroid hormone secretion (Haye *et al.,* 1985; Roger *et al*., 1987) [28, 56] and stimulates lipolysis in fat cells (Haye*et al.,* 1985; Roger *et al.,*1987) [28, 56].

5. Medicinal uses

Intraditional Ayurveda systems of medicine, *C. for skohlii*has been used for treating heart diseases, abdominal colic, respiratory disorder, insomnia, convulsions, asthma, bronchitis, intestinal disorders, burning sensation, constipation, epilepsy and angina (Ammon and Muller,1985) [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 (De Souza and Shah, 1988) [19]. Forskolin is also used in the preparation of medicines preventing hair graying and restoring grey hairto 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 (Misra *et al*., 1994) [44]. Essential oil has potential uses in food flavoring industry and can be used as an antimicrobial agent (Chowdhary and Sharma, 1998) [15].

5.1. Heart disorder

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 (De Souza *et al*., 1983; Dubey *et al*., 1981) [20, 22].

5.2. Glaucoma

The effect of forskolin on aqueous humour dynamics and intraocular pressure was first described by Capriole and Sears (1983) [12]. 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*. (1987) 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 (Brubaker *et al*., 1987) [87].

5.3. Asthma

Forskolin was studied as bronchodilator for its potential use in the treatment of asthma (Bruka, 1986) [11]. It blocked bronchospasm, the chief characteristic of asthma and bronchitis in guinea pigs caused by histamine and leukotriene C-4 (Kreutner *et al.,* 1985) [36]. In human basophils and mast cells, forskolin blocked the release of histamine and leukotriene C-4 (Marone*et al*., 1987) [40]. A study involving human revealed that inhaled forskolin powder formulations were capable of causing Broncho dilation in asthma patients (Bauer *et al.,* 1993) [8]. Forskolin seems to be a promising drug if used in an appropriate dosage for treatment of patients with congestive heart failure, glaucoma and asthma (Rupp *et al*., 1986; De Souza and Shah, 1988) [19, 58].

5.4. Antithrombotic effect

Forskolin inhibits platelet aggregation through adenylate cyclase stimulation, augmenting the effects of prostaglandins (Siegl *et al*., 1982; Adnot *et al*., 1982) [1, 71]. Its antithrombotic properties may be enhanced by cerebral vasodilation and it was observed in rabbits. This vasodilation was not potentiated by adenosine (Wysham *et al*., 1986) [81]. The use of crude *C. forskohlii* extract as a rational phyto therapeutic antithrombotic has been proposed (De Souza, 1993) [18].

A. Anti-obesity

Henderson *et al*. (2005) [30] suggested that *C. forskohlii* does not appear to promote weight loss but may help mitigate weight gain in overweight females with apparently no clinically significant side effects. The anti-obesity effects of *C. forskohlii* were investigated in ovariectomized rats (Han *et al*., 2005) 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.

B. Other uses

In addition to its cAMP stimulating activity, forskolin inhibits the binding of platelet-activating factor (PAF), independently of cAMP formation (Wong, 1993) [80]. Forskolin also appears to have an effect on several membrane transport proteins and inhibits glucose transport in erythrocytes, adipocytes, platelets and other cells (Mills *et al.*, 1984) [43]. Forskolin also produces cAMP independent effects through modulation of nicotinic acetylcholine receptor channel, desensitization, modulation of voltage dependent potassium channels, and reversal of multidrug resistance (Morris *et al*., 1991) [45]. The safety of *C. forskohlii* and forskohlin has not been fully evaluated. It should be avoided in people with ulcers, because it may increase stomach acid levels (Seamon *et al*., 1981) [63].

C. Cosmetic uses

Forskolin extracted from Coleus plant increases isoform selectivity via acting on adenylyl cyclase to enhance the intracellular levels of cyclic adenosine monophosphate (cAMP). The mechanism of increasing and maintaining lean body mass is link to the availability of cyclic AMP. By facilitating hormonal action, cyclic AMP may control the thermo genic response of the body to food, increase the utilization of body fat and enhance the metabolic rate of the body. Forskohlin in combination with hydroxycitric acid (HCA) can be used for body fat and body shape management (Gupta, 2004) [26].

D. For skin problems

Coleus oil is useful in topical preparations, due to its antimicrobial properties. Coleus oil is particularly effective against Propionibacterium acnes, the microorganism responsible for acne, and it has been found active against other microorganism known to be responsible for skin infections and eruptions. Laboratory studies suggest that Coleus oil inhibit the growth of different skin pathogens. It has also been found effective against yeast culture (Majeed and Prakash, 2007) [39].

E. Antioxidant activity

Plant extract of *C. forskohlii* shows high amount of polyphenols and higher antioxidant activity in comparison to other Coleus species. Leaf extract of this plant exhibited significantly high amount of total polyphenols, flavonols and flavones and high antioxidant activity. High performance liquid chromatography (HPLC) profiling of stem and leaf tissues exhibited the presence of standard antioxidative polyphenols and more potent polyphenols. Rasineni *et al*. (2008) [52] suggest that Coleus can be used as an important source of phenolic compounds with significantly high antioxidant activity (Rasineni *et al*., 2008) [52]. Coleus is a rich source of diterpenoids with different oxygen patterns, and six diterpenoids are isolated from whole plant up to the year 2001. Yao and Xu (2001) [82] isolated two new diterpenoidquinones and named them coleon S and T.

F. Perfumery uses

Over forty compounds belonging to four different classes of aroma compounds have been isolated from oils obtained from different indigenous genotypes of *C. forskohlii*. These include monoterpenoids, diterpenoids, sesquiterpenes and sesquiterpenes alcohol. The presence of compounds like 3-decanone, bornyl acetate and g-eudesmol were identified in experimental studies (Majeed and Prakash, 2007) [39].

G. Miscellaneous uses

Coleus also works well in treating asthma, cancer, cardiopathy, congestive heart failure, convulsions, cramp, depression, dermatosis, dyspepsia, dysuria, eczema, glaucoma, high blood pressure, hypothyroidism, infertility, insomnia, ischemia, myocardosis, obesity, psoriasis, respirosis, thrombosis and water retention (Duke *et al*., 2002) [24].

H. Cytogenetic

Reddy (1952) [53] reported that *C. forskohlii* is diploid with n = 14. However, Riley and Hoff (1961) 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 (1985) [9] 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 (1989) [66] reported that populations from different ecogeographic areas vary greatly in their morphology. Chromatographic analysis of *C. forskohlii* extracts from Brazil, Africa and India revealed that plants from each country produced different compounds in different quantities and the differences were attributed to genetic or climatic factors (Tandon *et al*., 1979) [74]. A comparative assessment of the performance of two varieties of *C. forskohlii* revealed that the variety 'Maimul' exhibited significantly superior per cent of establishment and highertuber yield per plant to variety 'Garmai' under Tamil Nadu conditions (Veeraragavathatham *et al*., 1985). Similarly, wide variation for morphological and yield parameters among the genotypes of *C. forskohlii* was observed by several workers (Vishwakarma *et al*., 1988; Shah, 1989; Prakash and Krishnan, 1994; Patil *et al*., 2001; Kavitha *et al*., 2007) [34, 47, 48, 66, 79].

6. 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 bivariate. 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 (Bailey, 1942) [7]. The root is typically golden brown, thick, fibrous and radially spreading.

Full plant of coleus

Coleus flowers

Carrot shaped coleus roots

Roots are tuberous, fasciculate, 20 cm long and 0.5 to 2.5 cm in diameter, conical fusiform, straight, orangish 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 was also fascinatingly diverse, being tuberous, semi tuberous or fibrous (Shah, 1989) [66].

7. Crop improvements

7.1. Hybridization

Attempting many hybridization study in coleus. Hybrid populations raised from eleven different crosses were screened for root traits. Ten selections were made from the hybrid population based on root traits (root diameter, number of tuberous roots, root length, collar diameter) and dry root yield. Among the selections dry tuber yield ranged from 58.0 to 112.0 g /plant. OP seedlings raised from open pollinated seed of six different tuberous hybrids were field planted and screened for tuber traits. Fifteen selections with good tuber traits were selected for further evaluation. Dry root yield plant in these selections ranged from 55 to 130g/plant. Ten hybrids which recorded forskolin content above 0.6% were selected for further evaluation. Eight good tuberous rooted plants selected based on root traits were evaluated for root yield in a yield trial with three replications along with the check K-8. Out of them, dry root yield of the hybrids Hy08-7 (85.50 g) recorded higher root yield over check K8 (63.00g), whereas the dry root yield of remaining hybrids were on par with the check. (IIHR Annual report, 2008)

7.2. Mutation breeding

Srinivasappa *et al*. (2010) [73] standardize the best plant material for mutation study with maximum variation. Based on the study they chose the three different type of plant parts viz. (i) Tissue cultured plant (TC) (ii) rooted cutting (RC) and (iii) unrooted cuttings (UC) of *Coleus forskholii* were subjected to gamma irradiation (1 to 15 kR), and evaluated for three generations (M1 to M3) under field conditions for various quantitative and qualitative traits. Remarkable variations were observed in the leaf shape, plant height, leaf colour, tuber yield and forskolin content. The mutant M3RC-2-3 recorded the highest tuber yield (168.64 g/plant) and forskolin content (1.74%), amounting to 155.88 per cent increase over the control K-8 (0.68%). The other three mutants M3UC-5-2, M3RC-1-4 and M3UC-1-3 closely followed the M3RC-2-3 with regard to dry tuber yield per plant (139.48, 122.98 and 141.00 g, respectively), and forskolin content (1.63, 1.69 and 1.51% respectively), resulting in 139.71, 148.53 and 122.06 per cent increase over the control.

7.3. Morphological and molecular characterization

Morphological and molecular characterization of this herb will enhance our understanding in improving the optimal yields of forskolin through breeding. To assess the morphological and molecular genetic diversity in eighteen *C. forskohlii* genotypes collected from different places of central India, RAPD, ISSR, and AFLP marker systems were employed. Eleven RAPD, ten ISSRs and eight AFLP primers produced 101, 80, and 483 fragments, respectively. Among the three marker system used in this study, RAPD and ISSR showed 61.39 and 68.75% polymorphism, respectively, while eight AFLP primer combinations produced 70.81% polymorphism. UPGMA cluster analysis method group genotypes in two clusters with all marker systems separately and after combined analysis. Results show that both morphological and molecular factors are effective in observing variations. Our results also indicate that the RAPD, ISSR, and AFLP approaches, along with pharmaceutically important morphological trait analysis, seemed to be best-suited for assessing the genetic relationships among distinct *C. forskohlii* genotypes with high accuracy. (Niraj *et al*. 2013) [46]

8. Crop management

Medicinal coleus (*Coleus forskohlii*) is an important medicinal crop which contains forskolin in their roots. Because of continuous collection of roots from the wild sources, this plant has been included in the list of endangered species. The *Coleus forskohlii* root of the plant resembling a carrot in shape and brown in colour. In this part we have brief discussion on complete package and practices of coleus.

8.1. Varieties

1. **CO1**- This variety developed by Tamil Nadu Agricultural University Coimbatore which clonal selection from Periyakulam local. This variety released during the year of 1991. The variety yields 32.89 per cent increased yield over local type with 0.40 per cent forskohlin. Dry tuber yield about 2.5 t /ha. Moderately tolerant to root rot and wilt diseases under field conditions. Field tolerant to nematode and mealy bug infestation. Except Nilgiris all parts of Tamil Nadu, specifically suited to Salem, Erode, Namakkal, Coimbatore, Dindigul, Theni, Thiruvannamalai and Vellore districts

2. **K8** - it is released from IIHR, Bangalore and selection from Karnataka. It give 0.5% of forskolin and a higher tuber yield
3. **Aisiri** (Mutant-7) is a higher tuber and forskolinyielding variety developed and released by the University of Agricultural Science, Bangalore the variety mature in 180- 200 days and give a dry tuber yield of 7000 – 7500 kg/ha with a forskolin content of 0.76%.
4. **Manganiperu** - It is cultivated in and around Belgaum districts of Karnataka. The tubers are big, 30.00cm length. It is also commercially cultivated in Tamil Nadu.
5. **Garmai and Maimul** -It is cultivated in Gujarat state. The tubers are in medium size.

8.2. Soil and climate

It thrives better in porous and well drained soils with a pH ranging from 5.5 to 7. It does not require very fertile soils and can be economically grown even on the soils with marginal fertility. The red sandy are ideal for the cultivation of this crop. Coleus is a crop of tropics and is found growing well on barren hills at an altitude of about 2400m. It prefers humid climate with a RH ranging from 60 to 85 per cent and a temperature range between 10-25ºC for its successful growth. The annual rainfall in such areas ranges from 100 to 160 cm, mainly during June to September month spreferred.

8.3. Propagation

Coleus can be propagated by seeds as well as by stem cutting. However propagation through seeds it little difficult and slow and should be used only for the breeding of new varieties. Where, propagation by cutting is very easy and economical to raise this crop on large scale.

8.4. Nursery raising

The viability of the seeds being very poor (8-10%), a sufficient quantity of fresh seeds has to be sown in well-prepared nursery beds to obtain good germination. Regular care about watering weeding and plant protection of the nursery should be taken. In about 15 to 20 days, the germination is completed. When the seedling are 45 days old and have attained about 8-10 cm height, they are ready for transplanting.

8.5. Vegetative propagation

Vegetatively, the crop is propagated through terminal cutting. Normally, 10-12 cm long cutting, comprising of 3-4 pairs of leaves, are sown in already prepared nursery bed and regular care about shading and watering is taken. The cutting establish well in the nurseries and there is no problem in their rooting. After about a month's time, when the cutting have produced sufficient roots, they are transplanted to the main field.

8.6. Micro propagation

In vitro propagation is useful for mass multiplication and germplasm conservation of any plant species. *C. forskohlii* being succulent in nature responds well to *in vitro* propagation and various explants viz., nodal segments, shoot tip, leaf etc., are effectively used. Sen and Sharma (1991) [14] reported that nodal segments as explants on MS medium supplemented with Kinetin (2.0 mg/l) and IAA (1.0 mg/l) are rooted well and their plantlets were established successfully under field conditions. Shoot tip explants from 30 days old aseptically germinated seedlings are also used for multiplication using 2 mg/l of 6-benzylaminopurine (Sen and Sharma, 1991) [14]. Reddy *et al*. (2001) [54] developed a plant establishment protocol from leaf derived callus and found that the *in vitro* raised plants produce comparable quantity of forskolin with that of wild plants. Complete plantlets of *C. forskohlii* were developed within 35-40 days by culturing shoot tip explants in MS medium containing 0.57 M IAA and 0.46 M kinetin through direct multiplication at the rate of 12.5 shoots per explant (Rajasri and Sabita, 2001). The significance of the protocol is the formulation of growth regulators which affected very fast multiplication of the plant in less time that is, one-third time less of the hitherto known methods. Leaf explants of *C. forskohlii* induced callusing when cultured on MS media supplemented with 1 mg/L BAP with 2 mg/L NAA. Regeneration of shoot lets is observed after 7 weeks of initial culture (Anbazhagan *et al*., 2005) [6].

8.7. Planting

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.

8.8. Manure and fertilizers

The crop responds well to organic and inorganic fertilizers. Organic manure is required to the level of 140 kg on 30th day and 45th day of planting. A combination of 40 kg N, 60 kg P_2O_5 and 50 kg K_2O per ha is optimum for obtaining the maximum fresh (120 t/ha) and dry (3.982 t/ha) tuber yield. Half the dose of N, the whole P and whole K may be applied as the basal dose followed by the remaining half N, 30 days after planting as top dressing (Veeraragavathatham *et al*., 1985). Coleus plants raised in presence of the arbuscular mycorrhizal fungi *Glomus Bagyarajii*, showed an increase in plant growth and forskolin content over those grown in the absence of AM fungi (Sailo and Bagyaraj, 2005) [59]

8.9. Irrigation

The first irrigation is given immediately after transplanting, if there are no rains. During the first two week after planting, the crop is irrigated once in three day and thereafter, weekly irrigation is enough to obtain good growth and yield.

Due to frequent irrigation during the initial stages, there is a lot of competition from weeds. In order to obtain economic yield, frequent weeding during the early growth period is desirable.

8.11. Pests and Disease

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.

8.12. Disease

Bacterial wilt is the most important disease attacking *Coleus forskohlii* plants. This is caused by the soil-borne pathogens *Fusarium chlamydosporum, Rhizoctonia bataticola* and *Sclerotiumrolfsii.* 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 (Hegde *et al*., 2009) [29]. 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 (Hegde*et al.,* 2009) [29]. Leaves turn flaccid and drop off, when plants are affected by *Sclerotiumrolfsii*. 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 (Hegde *et al.*, 2009) [29].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 (Hegde *et al.*, 2009) [29].

Fernandes and Barreto (2003) [25] reported for the first time leaf spots caused on the leaves by the dematiaceous fungus *Corynspora cassiicola*. The lesions were initially brown and puncti form 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 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.

8.13. Harvesting and yield

The crop is ready for harvest four and half to five months after planting. The plants are uprooted, the tubers separated, cleaned and sun dried. On an average, a yield of 800 to 1000 kg/ha of dry tubers may be obtained. However, if proper cultivation practices are applied, a yield up to 2000 to 2200 kg/ha of dry tubers can be easily obtained (Rajamani and Vadivel, 2009) [49]. *C. forskohlii* is mainly cultivated under contract farming system in India. A study conducted by Agila *et al*. (2006) [3] concluded that minimum risk in farming, assured price for the harvested produce, reduction in price risk, elimination of middlemen, assured income and availability of financial support, technical guidance from the company, timely availability of inputs, awareness about appropriate technology are the major effective factors for better performance of the coleus contract farming.

9. Post-harvest technology

The harvested tubes are cutinto slices and dried in two methods viz., Sun drying and mechanical drying. Sun drying require more time for drying. Tubers are sliced by mechanical slicers into 0.5 to 1.0cm bits. The bits are dried under sun for 5-7 days until the moisture level drops to 7 percent. Dried coleus tuber packed in polyethylene lined gunny bag to retain the highest amount of essential oil, starch and forskolin. (Rajamani *et al*., 2009) [50]

10. Future research needs

Although *Coleus forskohlii* is a commercially grown medicinal plants, tubers are still collected from the wild leading to habitat loss. This species is vulnerable under wild and International Union for Conservation of Nature (IUCN) has affirmed the need for conserving the species. To reduce the pressure on wild habitat, protocol available for rapid propagation of this species (through micro propagation) should be effectively utilize to generate adequate planting material for the benefit of farmers. Genetic improvement in this species with desirable characters like better plant vigor, high root yield with high forskohlin content, tolerance to leaf eating caterpillars, mealy bugs, nematode, bacterial diseases and other abiotic stresses are considered important. Attempts on wide hybridization, mutation breeding, biotechnology approaches and advance cultivation aspects with post-harvest technology will provide answer for the above. Knowledge on supply and value chain, market information and future prospects need to be studied to benefit the farmers and the pyto-pharmaceutical industry.

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