

Review

***Coleus forskohlii*: A comprehensive review on morphology, phytochemistry and pharmacological aspects**

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***Coleus forskohlii* is an important indigenous medicinal plant in India. It has been used in traditional Ayurvedic medicine for curing various disorders and this is the only source of the diterpenoid forskolin. Forskolin is used for the treatment of eczema, asthma, psoriasis, cardiovascular disorders and hypertension, where decreased intracellular cAMP level is believed to be a major factor in the development of the disease process. A comprehensive account of the morphology, distribution, medicinal uses, phytochemistry, pharmacological activities, analytical methods, cultivation aspects and biotechnological approaches for forskolin production reported are included in view of the many recent findings of importance on this plant.**

Key words: *Coleus forskohlii*, forskolin, review.

INTRODUCTION

Plants are the first medicines for mankind and hundreds of plant species are harvested for their medicinal properties all over the world. In spite of modern development of sophisticated pharmaceutical chemicals to treat illnesses, medicinal plants remain an important tool for treating illness. In some regions, traditional medicines made from local plants are the only available and affordable source for treating various ailments. World Health Organization (2003) estimates that 80% of the world's population depends on traditional medicine for their health needs. In many developed countries, traditional herbal remedies are making a comeback as alternatives to modern medicine.

The existence of traditional medicine depends on plant diversity and the related knowledge of their use as herbal medicine. India is one of the twelve mega diversity hot spot regions of the world and one fifth of all plants found in India are used for medicinal purpose (Schippmann et al., 2002). Nearly 25,000 effective plant based

formulations are used in folk medicine by rural communities in India

(Ramakrishnappa, 2002). Both plant species and traditional knowledge are important to the herbal medicine trade and the pharmaceutical industry, whereby plants provide raw materials and the traditional knowledge prerequisite information (Tabuti et al., 2003).

Encompassing concepts and methods for the protection and restoration of health, traditional medicine has served as source of alternative medicine, new pharmaceuticals and healthcare products. Medicinal plants are important for pharmacological research and drug development, not only when constituents are used directly as therapeutic agents, but also as starting materials for the synthesis of drugs or as models for pharmacologically active compounds (Mukherjee, 2003). The world market for plant derived chemicals viz., pharmaceuticals, fragrances, flavours and colour ingredients exceeds several billion dollars per year. Classic examples of phytochemicals in biology and medicine include taxol, vincristine, vinblastine, colchicine as well as the Chinese antimalarial - artemisinin and the Indian ayurvedic drug - forskolin.

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Importance

The therapeutic properties of forskolin, the main diterpene constituent of this plant contributed to the emergence of *C. forskohlii* as a taxon of importance in modern medicine. Forskolin is used for the treatment of eczema, asthma, psoriasis, cardiovascular disorders and hypertension, where decreased intracellular cAMP level is believed to be a major factor in the development of the disease process (Rupp et al., 1986). The presence of yellowish to reddish brown cytoplasmic vesicles in cork cells of *C. forskohlii* tubers is unique character of this plant and these vesicles store secondary metabolites including forskolin (Abraham et al., 1988).

ORIGIN AND GEOGRAPHICAL DISTRIBUTION

Indian sub- continent is considered as the place of origin of *C. forskohlii* (Valdes et al., 1987). It grows wild in the subtropical temperate climates of India, Nepal, Burma, Sri Lanka and Thailand. Apparently, it has been distributed to Egypt, Arabia, Ethiopia, tropical East Africa and Brazil (Willemse, 1985). In India, the plant is found mostly on the dry and barren hills (Anon, 1950). Latitudinal and altitudinal range for the occurrence of the species is between 8° and 31° N and 600 – 800 m, respectively.

SPECIES STATUS

C. forskohlii Briq. is a member of the mint family, Lamiaceae. It is indigenous to India and is recorded in Ayurvedic *Materia Medica* under the Sanskrit name 'Makandi' and 'Mayani' (Shah, 1996). The taxonomic position of *C. forskohlii* is as follows:

Kingdom	- Plantae
Division	- Magnolophyta
Class	- Magnoliopsida
Order	- Lamiales
Family	- Lamiaceae
Genus	- <i>Coleus</i>
Species	- <i>forskohlii</i>

The genus *Coleus* was first described by Loureiro in 1790 and the generic name was derived from the Greek word 'COLEOS' meaning sheath. All the species of *Coleus* have four didynamous, dedinate stamens, and the filaments of the stamens unite at their base to form a sheath around the style. The species name *forskohlii* was given to commemorate the Finnish botanist, Forskel. The genus *Coleus* consists of 150 species and the following species viz., *C. amboinicus*, *C. forskohlii*, *C. spicatus* and *C. malabaricus* occur naturally.

GENETIC BASE WITH CHROMOSOME PLOIDY AND VARIABILITY

Reddy (1952) 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 (1982 and 1985) 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) 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). 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 higher tuber 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).

BOTANICAL DESCRIPTION

C. forskohlii is a perennial plant that grows to about 45 - 60 cm tall. It has four angled stems that are branched and nodes are often hairy. Leaves are 7.5 to 12.5 cm in length and 3 to 5 cm in width, usually pubescent, narrowed into petioles. Inflorescence is raceme, 15 - 30 cm in length; flowers are stout, 2 to 2.5 cm in size, usually perfect and calyx hairy inside. Upper lip of calyx is broadly ovate. The blue or lilac corolla is bilabiate. Lower lobes are elongated and concave so that they enclose the essential organs. The ovary is four parted and stigma is two lobed and the flower is cross-pollinated by wind or insects (Bailey, 1942). The root is typically golden brown, thick, fibrous and radially spreading. Roots are tuberous, fasciculated, 20 cm long and 0.5 to 2.5 cm in diameter, conical fusiform, straight, 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 is also fascinatingly diverse, being tuberous, semi tuberous or fibrous (Shah, 1989).

CULTIVATION PRACTICES

C. forskohlii thrives well in red, sandy loam soils with a pH ranging from 5.5 to 7. Humid climate with relative humidity between 83% - 95% and a temperature of 10 to 25°C is ideal for the crop. It requires an annual rainfall of 100 to 160 cm, necessarily between June-September (Shah and Kalakoti, 1998). It is propagated by seeds as well as vegetatively by terminal stem cuttings. Seed propagation is difficult and slow whereas propagation by terminal stem cutting is easy and economical. 10 to 12 cm long terminal cuttings with 3 to 4 pairs of leaves are planted in nursery beds to induce rooting. When the cuttings are one month old and have produced sufficient roots, they are transplanted to the main field. The best period for planting is during June/July and September/October and rooted cuttings should be planted at the interval of 60 cm. Regular care about watering, weeding and plant protection should be taken (Rajamani and Vadivel, 2009). 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 P₂O₅ and 50 kg K₂O 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). The leaf eating caterpillars, mealy bugs and root knot nematodes are the important pests that attack this crop. The wilt caused by *Fusarium chlamydosporum* is a very serious soil-borne disease but inoculation with *Trichoderma viride* and *Glomus mosseae* will give the best result in controlling the disease (Boby and Bagyaraj, 2003). The root rot caused by *Macrophomina phaseolina* affects the tuber yield up to 100% and application of bioformulation viz., *Trichoderma harzianum* and zinc sulphate exerted maximum reduction in root rot incidence (Kamalakaran et al., 2006). The crop is ready for harvest 4 1/2 to 5 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 of up to 2000 to 2200 kg/ha of dry tubers can be easily obtained (Rajamani and Vadivel, 2009).

C. forskohlii is mainly cultivated under contract farming system in India. A study conducted by Agila et al. (2006) 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 tech-

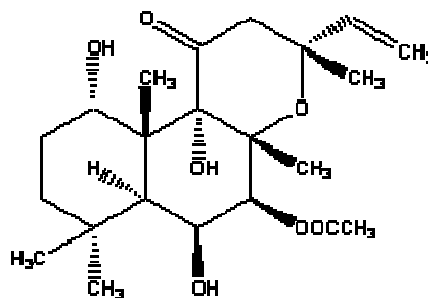
nology are the major effective factors for better performance of the coleus contract farming.

MEDICINAL USES

In India, the major medicinal species of *Coleus* is the tuberous *C. forskohlii*. *C. amboinicus*, *C. blumei*, *C. malabaricus* and *C. scutellaroides* are other species and are mainly used to treat dysentery and digestive disorders (De Souza et al., 1983). *C. forskohlii* is widely used in different countries for various ailments. In Egypt and Africa, the leaf is used as an expectorant, emmenagogue and diuretic. In Brazil, it is used as a stomach aid and in treating intestinal disorders (Valdes et al., 1987). It is used as a condiment in India and the tubers are prepared as pickle and eaten. In traditional Ayurvedic systems of medicine, *C. forskohlii* has been used for treating heart diseases, abdominal colic, respiratory disorder, insomnia, convulsions, asthma, bronchitis, intestinal disorders, burning sensation, constipation, epilepsy and angina (Ammon and Muller, 1985). 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). Forskolin is also used in the preparation of medicines preventing hair greying and restoring grey hair to its normal colour. Though grouped as a medicinal plant, it also contains essential oil in tubers, which has very attractive and delicate odour with spicy note (Misra et al., 1994). Essential oil has potential uses in food flavouring industry and can be used as an antimicrobial agent (Chowdhary and Sharma, 1998).

PHYTOCHEMISTRY

The tuberous root extracts of *C. forskohlii* contain minor diterpenoids viz., deactylforskolin, 9 - deoxyforskolin, 1, 9 - deoxyforskolin, 1, 9 - dideoxy - 7 - deactylforskolin in addition to forskolin (7 β - acetoxy - 8, 13-epoxy-1 α , 6 β , 9 α - trihydroxylabd-14-en-11-one) (Ammon and Kemper, 1982 and De Souza and Shah, 1988).



Forskolin

Forskolin was discovered in the year 1974 and was initially referred to as coleonol. After the identification of other coleonols and diterpenoids the name was later changed to forskolin (Saksena et al., 1985). Shah et al. (1980) reported that forskolin occurred exclusively in *C. forskohlii* and could not be detected in six other *Coleus* species viz., *C. amboinicus*, *C. blumei*, *C. canisus*, *C. malabaricus*, *C. parviflorus* and *C. spicatus* and six taxonomically related *Plectranthus* species viz., *P. coesta*, *P. incanus*, *P. melissoides*, *P. mollis*, *P. rugosus* and *P. stocksii*. Studies carried out using one hundred samples belonging to species of *Coleus*, *Orthosiphon* and *Plectranthus* of the sub family Ocimoideae at Japan also revealed the absence of forskolin in all the samples.

Second generation forskolin derivatives viz., Δ^5 -6-deoxy-7-deacetyl-7-methyl amino carbon forskolin (HIL 568), a potential antiglaucoma agent and 6-(3-dimethylamino propionyl) forskolin hydrochloride (NKH 477), a potential cardiogenic agent were developed (Hosono et al., 1990). Newer compounds are being identified from the root extracts of *C. forskohlii*. Xu et al. (2005) obtained six compounds from the roots of *C. forskohlii* and identified structures as 14-deoxycoleon U, demethylcryptojaponol, alpha-amyrin, betulinic acid, alpha-cedrol and beta-sitosterol and the compounds viz., alpha-amyrin and betulinic acid were isolated from *C. forskohlii* for the first time. Two new diterpenoids forskolin I (1alpha, 6 beta-diacetoxy-7 beta, 9alpha-dihydroxy-8,13-epoxylabd-14-en-11-one) and J, (1alpha,9alpha-dihydroxy-6beta,7beta-diacetoxy-8,13-epoxylabd-14-en-11-one) were isolated from *C. forskohlii* plants collected in Yunnan Province (Shen and Xu, 2005).

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). This was the first report about the occurrence of glycosides derived from labdane diterpene in the nature and these compounds showed relaxative effects on isolated guinea pig tracheal spirals *in vitro*. Later, three new minor labdane diterpene glycosides, forskoditerpenoside C, D and E and a novel labdane diterpene forskoditerpene A from the ethanol extract of the whole plant of *C. forskohlii* were isolated (Shan et al., 2008). Forskoditerpenoside C, D and E showed relaxative effects on isolated guinea pig tracheal spirals *in vitro* and an unusual 8,13-epoxy-labd-14-en-11-one glycoside pattern. Forskoditerpene A is the first known labdane derivative with a spiro element. Forskolin is in great demand in Japan and European countries for its medicinal use and related research purposes.

Mechanism of action

Forskolin being the major chemical constituent of the tuber, herbal preparations of it act on various multiple pharmacologic mechanisms. The blood pressure lower-

ing and antispasmodic effects of extracts of *C. forskohlii* roots were reported by Dubey et al. (1974) based on the extensive screening of Indian plants for biological activity at the Central Drug Research Institute, Lucknow. De Souza (1977) 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) 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; in forskolin it was β while in coleonol it was α . The pharmacological studies of forskolin and coleonol indicated that they had identical properties (Seamon and Daly, 1981).

The principle mechanism by which forskolin exerts its hypotensive activity is by stimulation of adenylate cyclase and thereby increasing cellular concentrations of the second messenger cyclic AMP (cAMP) (Seamon et al., 1981). Forskolin directly activates almost all hormone-sensitive adenylate cyclases in intact cells, tissues and even solubilised preparation of adenylate cyclase (Metzger and Lindner, 1981). 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). 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). Stimulation of adenylate cyclase is thought to be the mechanism by which forskolin relaxes a variety of smooth muscles. This action of forskolin proved the potential use of the molecule, not only as an invaluable research tool for understanding cyclic – AMP dependent physiological processes, but also as a potential therapeutic agent for diseases like cardiac insufficiency, hypertension, glaucoma, thrombosis, asthma and metastatic condition (Seamon, 1984).

Forskolin, by increasing cAMP level in turn, inhibits basophil and mast cell degranulation and histamine release, (Marone et al., 1987) lowers blood pressure (Dubey et al., 1981) and intraocular pressure, (Caprioli et al., 1984) inhibits platelet aggregation, (Agarwal and Parks, 1983; Wong, 1993) promotes vasodilation, (Dubey et al., 1981; Wysham et al., 1986) bronchodilation, (Lichey et al., 1984) and thyroid hormone secretion (Hays et al., 1985; Roger et al., 1987) and stimulates lipolysis in fat cells (Haye et al., 1985; Roger et al., 1987).

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).

Glaucoma

The effect of forskolin on aqueous humour dynamics and intraocular pressure was first described by Capriole and Sears (1983). 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).

Asthma

Forskolin was studied as bronchodilator for its potential use in the treatment of asthma (Bruka, 1986). It blocked bronchospasm, the chief characteristic of asthma and bronchitis in guinea pigs caused by histamine and leukotriene C-4 (Kreutner et al., 1985). In human basophils and mast cells, forskolin blocked the release of histamine and leukotriene C-4 (Marone et al., 1987). A study involving human revealed that inhaled forskolin powder formulations were capable of causing bronchodilation in asthma patients (Bauer et al., 1993).

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).

Antithrombotic effect

Forskolin inhibits platelet aggregation through adenylate cyclase stimulation, augmenting the effects of prostaglandins (Siegl et al., 1982; Adnot et al., 1982). 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). The use of crude *C. forskohlii* extract as a rational phytotherapeutic antithrombotic has been proposed (De Souza., 1993).

Anti-obesity

Henderson et al. (2005) 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 antiobesity 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.

Other uses

In addition to its cAMP stimulating activity, forskolin inhibits the binding of platelet-activating factor (PAF), independently of cAMP formation (Wong, 1993). 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). Forskolin also produces cyclic AMP independent effects through modulation of nicotinic acetylcholine receptor channel, desensitization, modulation of voltage dependent potassium channels, and reversal of multidrug resistance (Morris et al., 1991).

The safety of *C. forskohlii* and forskolin has not been fully evaluated. It should be avoided in people with ulcers, because it may increase stomach acid levels (Seamon et al., 1981).

EXTRACTION AND SEPARATION OF FORSKOLIN

Forskolin is extracted from tuber. The tubers are harvested at 75 to 85% moisture level on wet basis and stored at less than 12% moisture after drying. Sun drying required longer period than mechanical drying and recorded the lowest recovery of forskolin. Tubers mechanically dried at 40°C with tuber slice thickness of 0.5 cm and packed in polyethylene lined gunny bag retained the highest amount of forskolin (Rajangam, 2005). Different chromatographic methods are employed for quantification of forskolin and gas-liquid chromatography (GLC) method is the first developed method (Inamdar et al., 1980). Later, thin layer and high performance liquid chromatographic (HPLC) methods are employed. HPLC method is found to be more rapid and less sensitive than GLC and used to monitor variation in forskolin content in different germplasm (Inamdar et al., 1984). A monoclonal antibody specific for forskolin has been developed for affinity isolation of forskolin and it has been used for extremely sensitive quantification of forskolin in plant tissues at different stages of development (Yanagihara et al., 1996). Nuclear magnetic resonance data and a gas chromatography-mass spectral method are also used for forskolin quantification (Demetzos et al., 2002). Reversed-phase liquid chromatography with a photodiode array detector at 210 nm is successful in the qualitative and quantitative evaluation of forskolin in plant material and in market products claiming to contain forskolin (Schanebera and Khan, 2003). A simple, safe, rapid and economical reverse phase high performance liquid chromatography (RP-HPLC) method using activated

charcoal as an adsorbent in column is developed for the isolation of high-purity forskolin (Saleem et al., 2006). Wu et al. (2007) reported that HPLC-ELSD fingerprint method can be used in quality control of *C. forskohlii*.

IN VITRO 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. Sharma et al. (1991) reported that nodal segments as explants on MS medium supplemented with Kn (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). Reddy et al. (2001) 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 μ M IAA and 0.46 μ 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 shootlets is observed after 7 weeks of initial culture (Anbazhagan et al., 2005).

IN VITRO FORSKOLIN PRODUCTION

Study on tissue culture methods for forskolin production was carried out because of the relatively modest content of forskolin in the plant has limited its development as a drug (Mukherjee et al., 2000). Forskolin was identified in shoot differentiating culture, micropropagated plants and root organ suspension by TLC and HPLC. Forskolin produced by shoot differentiating culture was similar as that of the micropropagated plants whereas root organ suspension showed only traces of forskolin (Sen et al., 1992).

Krombholz et al. (1992) reported that root cultures of *C. forskohlii* initiated from primary callus or IBA-treated suspension cultures and maintained on Gamborg's B5 medium containing 1 mg/l IBA produced forskolin and its derivatives in amounts ranging from 500 to 1300 mg/kg dry weight, corresponding to about 4 to 5 mg/l.

Suspension cultures derived from gall calli which were obtained following infection with *Agrobacterium tumefaciens* (C58) were established in *C. forskohlii*. Studies on cell line selection following single cell cloning

or cell aggregate cloning were carried out to select cell lines capable of fast growth and for producing high level of forskolin. A fast growing cell line (GSO-5/7) was found to accumulate 0.021% forskolin in 42 days. The effect of cultural conditions on cell growth was studied to identify factors influencing biomass yield. Cell growth in suspension was found to be influenced significantly by carbon source, initial cell density and light or dark condition. Optimal cell growth (20 fold increase in biomass in a 42 day period) was obtained when the cells were grown in dark condition in B5O media containing 3% sucrose as sole carbon source with an initial cell density of 1.5×10^5 cells per ml. Forskolin accumulation was maximum (0.021%) in the stationary phase of cell growth. These suspension cultures showed continuous and stable production of forskolin (Mukherjee et al., 2007)

Molecular cloning and functional expression of geranylgeranyl pyrophosphate synthase from *C. forskohlii* have been demonstrated. Engprasert et al. (2004) proposed that forskolin was synthesised from Isopentenyl diphosphate (IPP), a common biosynthetic precursor via a non-mevalonate pathway. GGPP synthase is thought to be involved in the biosynthesis of forskolin, which is primarily synthesised in the leaves and subsequently accumulates in the stems and roots.

Conclusion

In the present review, an attempt has been made to congregate the morphology, distribution, medicinal uses, phytochemistry, analytical methods and various aspects of *C. forskohlii*. The available evidence indicates that *C. forskohlii* is the only known natural source of the diterpenoid forskolin. The pharmacological and biochemical investigations established that forskolin possesses multifaceted biological activities. But most of the studies used concentrated extract of forskolin in a non-oral delivery form for treating various disorders in animal models only and the effect of oral forskolin in humans has not been well established. Moreover still, there is paucity for the mechanism of other bioactive principles present in the herb except forskolin. Further researches in view of applicability of forskolin for treating human ailments without side effects and activity of other bioactive principles other than forskolin are needed.

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