

BIOLOGICAL ACTIVE EFFECTS OF FORSKOLIN EXTRACT

BY

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Abstract. Forskolin is the main ingredient in the Ayurvedic herb *Coleus Forskolii*. *Coleus* is a member of mint family and grows mainly in the subtropical areas in India, Burma and Thailand. Forskolin has been used in the treatment of allergies, respiratory problems, cardiovascular disorders, glaucoma, psoriasis, hypothyroidism, weight loss etc. Forskolin increased cyclic AMP and appears to have additional actions that are due to its ability to alter a number of membrane transport proteins. In these review are included a comprehensive account of morphology, distribution, medicinal and cosmetic uses and pharmacological aspects for forskolin.

Key words: *Coleus Forskolii*, Forskolin, morphology and distribution, medicinal and cosmetic applications.

1. Introduction

The genus *Coleus* was first described by Loureiro in 1790 and the generic name was derived from the Greek word ‘COLEOS’ meaning sheath. *Coleus* species belong to the family Labiatae and is found in tropical and subtropical Asia, Africa, Australia and Pacific. About nine species are listed in India. The ten main varieties of *Coleus* are listed in dictionaries and India in particular “The Wealth of India, A Dictionary of Indian Raw Materials and Industrial Products”.

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 genus *Coleus* consists of 150 species and the following species viz., *C. amboinicus*, *C. forskohlii*, *C. spicatus* and *C. malabaricus* occur naturally. The species name *forskohlii* was given to commemorate the Finnish botanist, Forskel.

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' [1], [2] 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 [3].

Different chromatographic methods are employed for quantification of forskolin and gas-liquid chromatography (GLC) method is the first developed method [4]. 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 [4]. 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 [5]. Nuclear magnetic resonance data and a gas chromatography-mass spectral method are also used for forskolin quantification [6]. 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 [1], [7]. A simple, safe, rapid and economical reverse phase high performance liquid chromatography (RP-HPLC) method using activated.

2. Therapeutic Effect of Forskolin

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 [8]. *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 [9].

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 [10]. 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 [11].

Forskolin is also used in the preparation of medicines preventing hair graying and restoring grey hair to its normal colour. Though grouped as a medicinal plant, it also contains essential oil in tubers, which has very attractive

and delicate odour with spicy note [12]. Essential oil has potential uses in food flavoring industry and can be used as an antimicrobial agent [1], [13].

The therapeutic properties of forskolin, the main diterpene constituent of this plant contributed to the emergence of *C. forskohlii* as an important 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 [14]. 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 [1], [15].

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 [16] based on the extensive screening of Indian plants for biological activity at the Central Drug Research Institute, Lucknow [17] found that the alcohol extracted from the tuber is helpful in lowering blood pressure and positive inotropic activities in animal models. Singh and Tandon [18] 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 group (-OAc) 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 [1], [19].

2.1. Cardiovascular Effects of Coleus

Coleus forskohlii has traditionally been used to treat hypertension, congestive heart failure, and angina. Coleus's basic cardiovascular action is to lower blood pressure, while simultaneously increasing the contractility of the heart.

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) [20]. Forskolin directly activates almost all hormone sensitive adenylate cyclases in intact cells, tissues and even solubilised preparation of adenylate cyclase [21]. 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 [19].

Of the 9 types of adenylate cyclase in humans, forskolin can activate all except type IX, which is found in spermatozoa [22]. 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 [23].

Forskolin, by increasing cAMP level in turn, inhibits basophile and mast cell degranulation and histamine release [24] lowers blood pressure [25] and intraocular pressure [26] inhibits platelet aggregation [27], [28] promotes vasodilatation [25], [29] bronchodilation [30] and thyroid hormone secretion [31], [32] and stimulates lipolysis in fat cells [1], [31], [33]. Coleus also increases cerebral blood flow, indicating that it may be beneficial in cerebral vascular insufficiency, and in enhancing post-stroke recovery.

2.2. Coleus and Glaucoma

Glaucoma is a condition in which the pressure in the eye is too high, due to an imbalance between the formation of aqueous humor in the eye and its absorption in or drainage out of the eye. Eventually, as the pressure builds up, the blood vessels nourishing the optic nerve are constricted, resulting in irreversible damage to the nerve and impaired vision culminating in blindness, if left untreated.

While there are no clinically proven alternative therapies for glaucoma, there are several treatments that may be beneficial and coleus is one of them.

The effect of forskolin on aqueous humor dynamics and intraocular pressure was first described by [33]. 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 [34] 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 [1], [35].

2.3. Coleus with Asthma and Allergies

Forskolin was studied as bronchodilator for its potential use in the treatment of asthma [36]. It blocked bronchospasm, the chief characteristic of asthma and bronchitis in guinea pigs caused by histamine and leukotriene C-4 [37]. In human basophiles and mast cells, forskolin blocked the release of histamine and leukotriene C-4 [38]. A study involving human revealed that inhaled forskolin powder formulations were capable of causing bronchodilation in asthma patients [39]. Forskolin seems to be a promising drug if used in an appropriate dosage for treatment of patients with congestive heart failure, glaucoma and asthma [1], [11], [14].

2.4. Antithrombotic Effect

Forskolin inhibits platelet aggregation through adenylate cyclase stimulation, augmenting the effects of prostaglandins [40], [41]. Its antithrombotic properties may be enhanced by cerebral vasodilatation and it was observed in rabbits. This vasodilatation was not potentiated by adenosine [42]. The use of crude *C. forskohlii* extract as a rational phytotherapeutic antithrombotic has been proposed [1], [43].

2.5. Coleus and Weight Loss

Henderson *et al.* [44] 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 [1], [45] and the administration of *C. forskohlii* extracts reduced body weight, food intake and fat accumulation in those rats.

In vitro (studies done in the lab) studies show that coleus stimulates fat metabolism. Researchers have found that many obese people have lower than normal Cyclic AMP production.

Because of these considerations, coleus may, theoretically, be a weight loss agent, especially for those with reduced Cyclic AMP production. In a recent study, six overweight women took 25 mg of coleus (250 mg capsules of 10% standardized forskolin extract) twice daily for eight weeks. At the end of the eight-week trial, the participants lost a mean of ten pounds, and reduced their percentage of body fat by nearly 8%. Blood pressure levels also trended lower during the trial.

2.6. Coleus and Depression

Depression is believed to be associated with an imbalance of neurotransmitters in the brain, serotonin and dopamine primarily. Where there is a shortage of serotonin, the supplements 5-HTP or tryptophan or the SSRI drugs like Prozac or Zoloft may be beneficial. If the catecholamine neurotransmitters (epinephrine, norepinephrine) are deficient the amino acids L-Phenylalanine or L-Tyrosine, or monoamine oxidase inhibitors like GeroVital (GH3) or Deprenyl are may be helpful. Recent research has also been evaluating drugs that increase Cyclic AMP as a means of elevating the catecholamines. Since forskolin elevates Cyclic AMP, it may improve neurotransmitter function and thereby relieve depression. Clinical trials using coleus to treat depression have not been done.

2.7. Coleus and Hypothyroidism

Forskolin has demonstrated the ability to increase thyroid hormone production and stimulate thyroid hormone release.

2.8. Coleus and Cancer Metastases

Research has shown coleus to be a potent inhibitor of tumor colonization in mice. It is theoretically possible that coleus could be used in humans to prevent or inhibit tumor metastases.

2.9. Coleus and Immune Enhancement

Forskolin appears to exhibit potent immune system enhancement by activating macrophages and lymphocytes.

2.10. Coleus and Psoriasis

In psoriasis, cells divide about 1,000 times faster than normal. Coleus helps to alleviate psoriasis by normalizing the cAMP/cGMP ratio.

2.11. Other Uses

In addition to its cAMP stimulating activity, forskolin inhibits the binding of platelet-activating factor (PAF), independently of cAMP formation [46]. Forskolin also appears to have an effect on several membrane transport proteins and inhibits glucose transport in erythrocytes, adipocytes, platelets and other cells [47].

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 [48]. 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 [1], [20].

2.12. Drug Interactions with Coleus

There is some evidence that forskolin may enhance the effects of beta-agonists such as albuterol. Forskolin may also act synergistically with epinephrine, ephedrine and pseudoephedrine. It is possible that the use of forskolin may decrease the needed dosages of beta-agonists. Anyone taking these drugs should consult their physician if they want to also use forskolin.

Because forskolin inhibits platelet aggregation and clotting, it may enhance the effects of anti-clotting medications such as warfarin, clopidogre, aspirin, enoxaparin, and dalteparin. Anyone taking any anti-clotting medications or supplements should consult their physician before adding forskolin to their regimen.

2.13. Cosmetic Applications

The main cosmetic application for forskolin must be as a treatment that allows with white skin to tan and at the same time, to protect themselves from UV rays just as do those with matte skin, which is now in the laboratory stage, was developed by a team of U.S. researchers. People with white skin, which are deficient in melanin, the pigment that gives skin a tan, have an increased risk of being diagnosed with skin cancer. Treatment, which consist of a forskolin based cream, an active ingredient extracted from the plant *Coleus Forskolii* is still in the laboratory stage. With this treatment, the researchers were able to restore system function of the pigment melanin deficient mice with white leather.

Skin pigmentation was obtained without being exposed mice to ultraviolet rays. These mice were then exposed to ultraviolet light, and scientists have found that their skin was able to protect themselves from harmful effects of radiation. Treatment is effective in reducing the number of cancer cases. The researchers arrived at these results by studying the role of a hormone that stimulates melanocytes and a receptor, Mc1r, which belongs to the signaling pathways that control skin pigmentation.

We give below various examples of formulation of cosmetics that contain forskolin:

- Sun gel for face with Extract of *Coleus*;
- Sunscreen tanning lotion to enhance the natural sun protection;
- Gel bronzer for the skin;
- Gel promoting skin pigmentation;
- Hair tonic with *Coleus* extract;
- Hair lotion cons gray hair(this lotion, applied to the hair and scalp daily helps delay the onset of gray hair);
- Treating gel preventing the onset of gray hair.

3. Conclusions

Coleus forskolii, one of the more than 150 species of genus *Coleus*, found in tropical and subtropical zones in Asia, Africa, Australia and Pacific Islands.

Forskolin is extracted from tuber, using organic solvents, and purified by the means of gas or HPLC chromatography.

Among the various therapeutic effects of forskolin extract in this article the following have been detailed: cardiovascular, glaucoma, asthma and allergies, anti-thrombotic, anti-depression, weight loss, hypothyroidism, cancer, psoriasis.

Beside all those effects mentioned above, there are another series of cosmetic applications for sunscreen tanning lotions, hair tonic, hair lotions cons gray hair, gel bronzer.

Our next researches will be focused into finding new applications of forskolin extract into various cosmetic products and its stability under various storage conditions.

Received: November 10, 2010

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EFECTE BIOLOGIC ACTIVE ALE EXTRACTULUI DE FORSKOLINA

(Rezumat)

Forskolina este principalul ingredient din rădăcinile plantei *Coleus Forskolii*. *Coleus* face parte din familia mentei și crește în special în zonele subtropicale în India, Burma, Thailanda. Forskolina a fost studiată intensiv în ceea ce privește aplicațiile din domeniul medical pentru a putea fi folosită în tratamentul alergiilor, problemelor respiratorii, afecțiunilor cardiovasculare, hipo-tiroidismului, psoriazisului, glaucomului, pierderii în greutate etc. Forskolina crește numărul de cicluri AMP și pare să aibă acțiune suplimentară în ceea ce privește abilitatea de a modifica numărul de proteine implicate în transportul prin membrane. În acest articol este inclus un studiu detaliat asupra morfologiei, distribuției plantei, aplicații medicale și cosmetice și aspecte farmacologice ale forskolinei.