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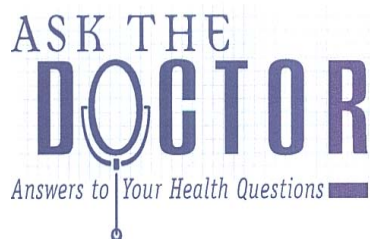


Coleus Forskohlii

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The Many Benefits of Coleus forskohlii:



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- ◆ **Hypothyroidism**
- ◆ **Depression**

Coleus forskohlii is a small member of the mint family which grows as a perennial on the sun-exposed, dry hill slopes of India, Nepal, Sri Lanka, and Thailand. It grows at an altitude of 1,000 to 6,000 feet in the subtropical, warm temperate climatic zone on the mountains.

The radially-spread rootstock is the portion of the plant used in the Ayurvedic system of medicine. It has been used primarily in cardiovascular disease, eczema, abdominal colic, respiratory disorders, painful urination, insomnia, and convulsions.

Modern scientific investigations are substantiating many of these traditional uses.

The discovery of forskolin

In 1974, the Indian Central Drug Research Institute conducted a very large and thorough screening of medicinal plants. The screening revealed the presence of a component of *C. forskohlii* which lowered blood pressure and relaxed intestinal spasms. Originally the component was named coleanol.

Additional investigation determined the exact chemical structure, and the name was then changed to forskolin. No other species of *Coleus* contains forskolin.

Between 1981 and 1994 forskolin was used in well over 5,000 research studies designed to better understand cellular processes governed by cAMP (discussed below). While most of these studies have

used this isolated constituent, there is evidence that other components within the plant extract enhance the absorption and biological activity of forskolin.

Pharmacology of forskolin



The basic mechanism of action of forskolin is the activation of an enzyme, adenylate cyclase, which increases cyclic adenosine monophosphate (cAMP) in cells. Cyclic AMP is perhaps the most important cell regulating compound. Once formed, it activates many other enzymes involved in diverse cellular functions.

Under normal situations, cAMP is formed when a stimulatory hormone (e.g., epinephrine) binds to a receptor site on the cell membrane and stimulates the activation of adenylate cyclase. This enzyme is incorporated into all cellular membranes and only the specificity of the receptor determines which hormone will activate the enzyme in a particular cell. Forskolin appears to bypass this need for direct hormonal activation adenylate cyclase via transmembrane activation. As a result of this activation of adenylate cyclase, intracellular cAMP levels rise.

The physiological and biochemical

effects of a raised intracellular cAMP level include: inhibition of platelet activation and degranulation; inhibition of histamine release; increased force of contraction of heart muscle; relaxation of the arteries and other smooth muscles; increased insulin secretion; increased thyroid function; and increased breakdown of fat cells (lipolysis).

Recent studies have found forskolin to possess additional mechanisms of action independent of its ability to directly stimulate adenylate cyclase and cAMP-dependent responses. Specifically, forskolin has been shown to inhibit a number of membrane transport proteins and channel proteins through a mechanism that does not involve the production of cAMP. The result is again a transmembrane signaling that results in activation of other cellular enzymes. Research is underway in an attempt to

determine the exact receptors to which the forskolin is binding.

Another action of forskolin is on antagonizing the action of platelet-activating factor (PAF) by interfering with PAF binding to receptor sites on cells. PAF plays a central role in many inflammatory and allergic processes.

Therapeutic uses

The therapeutic possibilities of *C. forskohlii* based on the pharmacology of forskolin are immense. There are many conditions where a decreased intracellular cAMP level is thought to be a major factor in the development of the disease process. At present, *C. forskohlii* appears to be extremely well indicated in these types of conditions which include: eczema (atopic dermatitis), asthma, psoriasis, angina, and high blood pressure. Although *C. forskohlii* can be used alone, it may prove to be most useful when combined with other botanicals and/or other measures in the treatment of these disorders.

Asthma and other allergic conditions

Allergic conditions such as asthma and eczema are characterized by a decrease in cAMP in the bronchial smooth muscle and skin, respectively. As a result of this derangement, mast cells degranulate and smooth muscle cells contract. In addition, these allergic conditions are also characterized by excessive levels of platelet activating factor.

Current drug therapy for allergic conditions like asthma and eczema is largely designed to increase cAMP levels by using substances which either bind to receptors to stimulate adenylate cyclase (e.g., corticosteroids) or inhibit the enzyme phosphodiesterase which break down cAMP once it is formed (e.g., me-

thyxanthines). These actions are different than forskolin's ability to increase the initial production of cAMP via a transmembrane activation of adenylate cyclase. The cAMP elevating action of forskolin supports the use of *C. forskohlii* extracts used alone or in combination with standard drug therapy in the treatment of virtually all allergic conditions.

Coleus forskohlii extracts may be particularly useful in asthma as increasing cellular levels of cAMP result in relaxation of bronchial muscles and relief of symptoms in asthma. Forskolin has been shown to have remarkable effects in relaxing constricted bronchial muscles in asthmatics.

The bronchials are composed of what is known as smooth muscle. This type of muscle is also found in the gastrointestinal tract, uterus, bladder, and arteries. Forskolin has been shown to have tremendous antispasmodic action on these various smooth muscles. This antispasmodic action of forskolin supports the long time use of *C. forskohlii* in the treatment of not only asthma, but also intestinal colic, uterine cramps (menstrual cramps), painful urination, angina, and hypertension.

Forskolin's ability to relax smooth muscle in bronchial asthma is most probably due to an increase in cAMP, although forskolin has other anti-allergic activities such as inhibiting the release of histamine and the synthesis of allergic compounds.

Psoriasis

Psoriasis is an extremely common skin disorder that seems to be caused by a relative decrease in cAMP when compared to another cell regulating compound, cyclic guanine monophosphate (cGMP). The result is a tremendous increase in cell division. In

fact, cells divide in psoriasis at a rate 1,000 times greater than the normal rate. Preliminary studies have indicated that forskolin may be of great benefit to individuals with psoriasis via its ability to normalize the balance that exists between cAMP and cyclic GMP.

Cardiovascular effects

Perhaps the most useful clinical applications of *C. forskohlii* extracts will turn out to be in cardiovascular diseases such as hypertension, congestive heart failure, and angina. The cardiovascular effects of *C. forskohlii* and its components have been studied in great detail. Its basic cardiovascular actions involve lowering of blood pressure along with improved contractility of the heart. Again this is related to increasing cAMP levels throughout the cardiovascular system which results in relaxation of the arteries and increased force of contraction. The net effect is tremendous improvement in cardiovascular function.

Several clinical and animal studies have suggested forskolin may significantly lower blood pressure as well as improve heart function in patients. In one human study involving seven patients with dilated cardiomyopathy, forskolin was shown to improve left ventricular function primarily via reduction of preload and without rising metabolic costs. This study confirmed earlier animal studies showing forskolin increases the contractile force of heart muscle.

Forskolin has also been shown to be a direct cerebral vasodilator indicating that it may prove to be useful in cerebral vascular insufficiency and post-stroke recovery.

An additional mechanism of action particularly beneficial in a wide range of cardiovascular conditions is inhibition of platelet aggregation. In this case

some good evidence indicates the a standardized *C. forskohlii* extract is superior to pure forskolin.

Glaucoma

In clinical studies, forskolin has been shown to greatly reduce

Other possible applications

C. forskohlii extracts concentrated and standardized for forskolin content may prove to be useful in a number of other conditions including weight-loss programs, hypothyroidism, malabsorption and digestive disorders, depression, prevention of cancer metastases, and immune system enhancement.

Weight-loss programs

Lipolysis, the breakdown of stored fat, is regulated by cAMP. Forskolin has been shown to stimulate lipolysis as well as inhibit the synthesis of fat in fat cells. Forskolin has also been shown to counteract the decreased response of fat cells to lipolytic hormone-like epinephrine associated with aging.

Hypothyroidism

Forskolin has been shown to increase thyroid hormone production as well as stimulate thyroid hormone release.

Malabsorption and digestive disorders

Forskolin stimulates digestive secretions including the release of hydrochloric acid, pepsin, amylase, and pancreatic enzymes. Forskolin has been shown to promote nutrient absorption in the small intestine. *C. forskohlii* extracts may prove to be quite useful in treating dry mouth as forskolin increases salivation.

Depression

Forskolin has been shown to exert antidepressant activity in animal studies.

Immune system

Forskolin exhibits potent immune system enhancement (primarily through activation of white blood cells) in several models.

Dosage

The forskolin content of *Coleus* root is typically 0.2 to 0.3 percent. Therefore, the forskolin content of crude *Coleus* products may not be sufficient to produce much of an effect. It may be best to use standardized extracts which have concentrated the forskolin content. The recommended dosage should be based upon the level of forskolin. The current recommendation for a *Coleus forskohlii* extract standardized to contain 18 percent forskolin is 50 mg (9 mg of forskolin) two to three times daily.

Toxicity

The animal studies on forskolin indicate an extremely low order of toxicity for forskolin. Based on the pharmacology of forskolin, it may be wise to restrict the use of *C. forskohlii* preparations in cases of low blood pressure and peptic ulcers. Furthermore, *C. forskohlii* preparations should be used with caution in patients on prescription medications, especially anti-asthmatics and anti-hypertensives due to its ability to possibly potentiate the drug's effect.