



## *Coleus forskohlii*

### Introduction

*Coleus forskohlii* is a botanical that has been used since ancient times in Hindu and Ayurvedic traditional medicine. The root portion of the plant has been traditionally used for medicinal purposes and contains the active constituent, forskolin. Forskolin was named after the Finnish botanist, Forskal. Historically, it has been used to treat hypertension, congestive heart failure, eczema, colic, respiratory disorders, painful urination, insomnia, and convulsions. Clinical studies of the plant and the forskolin constituent support these traditional uses, but also indicate it may have therapeutic benefit in asthma, angina, psoriasis, and prevention of cancer metastases.

### Description

*Coleus forskohlii* is a perennial member of the mint (Lamiaceae) family and grows in the subtropical temperate climates of India, Nepal, Sri Lanka, and Thailand. Plant height is approximately 1-2 feet and its striking leaves are teardrop shaped, shimmering green framing a bright purple center; leaf color varies depending on the amount of shade. A cluster of stalked pale purple or blue flowers branches off a single stem. The rootstock is typically golden brown, thick, fibrous, and radially spreading. The roots are harvested in the fall, when forskolin is at its most concentrated and the color is the brightest.<sup>1</sup>

### Active Constituents

The diterpene forskolin, derived from the root of the plant, is the primary constituent of clinical interest in *Coleus forskohlii*.<sup>2</sup> It was discovered by Western scientists in 1974 and was initially referred to as coleonol. Since that time, as other coleonols and diterpenoids have been identified, the name was changed to forskolin.<sup>3</sup> Forskolin is responsible for virtually all pharmacological activities attributed to *Coleus forskohlii*; extracts of this constituent have been used in nearly all existing studies. There is evidence, however, that other plant constituents, such as volatile oils and other diterpenoids and coleonols, may contribute to the pharmacological activity and absorption of forskolin.<sup>4</sup> Detailed analysis reveals approximately 20 constituents in various parts of the plant, but forskolin and other coleonols are present only in the root portion.<sup>5</sup>

### Mechanisms of Action

Forskolin's primary mode of action is to increase cyclic adenosine monophosphate (cAMP) and cAMP-mediated functions, via activation of the enzyme adenylate cyclase.<sup>6</sup> Forskolin has been shown to increase cAMP formation in all eukaryotic cells except sperm, without hormonal activation of adenylate cyclase.<sup>7</sup> Forskolin's potentiation of cAMP in turn inhibits basophil and mast cell degranulation and histamine release,<sup>8</sup> lowers blood pressure<sup>9</sup> and intraocular pressure,<sup>10</sup> inhibits platelet aggregation,<sup>11,12</sup> promotes vasodilation,<sup>9,13</sup> bronchodilation,<sup>14</sup> and thyroid hormone secretion,<sup>15,16</sup> and stimulates lipolysis in fat cells.<sup>17</sup> Forskolin also has a positive inotropic action on cardiac tissue via increased cAMP levels.<sup>18</sup>

In addition to its cAMP-stimulating activity, forskolin inhibits the binding of platelet-activating factor (PAF), independently of cAMP formation. This may be a result of forskolin's direct effect on PAF or via interference with PAF binding to receptor sites.<sup>12</sup> Forskolin also appears to have an effect on several membrane transport proteins, and inhibits glucose transport in erythrocytes, adipocytes, platelets, and other cells.<sup>19</sup>

### **Clinical Indications**

Intracellular cAMP levels are decreased in numerous diseases, including asthma, cardiovascular disease, eczema, psoriasis, hypertension, angina, and obesity; forskolin's ability to elevate cAMP has been shown to be of benefit in these circumstances.

### **Cardiovascular Disease**

Both animal and clinical studies demonstrate forskolin significantly lowers blood pressure via relaxation of vascular smooth muscle.<sup>9,18,20,21</sup> In a small study of seven patients with dilated cardiomyopathy, intravenous forskolin administered at 3  $\mu\text{g}/\text{kg}/\text{minute}$  significantly reduced diastolic blood pressure (17%) without increasing myocardial oxygen consumption; left ventricular function also improved.<sup>20</sup> In a similar study (patient sample size not available), 4  $\mu\text{g}/\text{kg}/\text{minute}$  of intravenous forskolin given to dilated cardiomyopathy patients resulted in decreased vascular resistance and a 19-percent improvement in left ventricle contractility. Heart rate increased an average of 16 percent in study patients. Subjects also exhibited a 20-percent reduction in arterial pressure accompanied by symptomatic flush.<sup>21</sup> Forskolin's ability to inhibit platelet aggregation is of additional benefit in cardiovascular disease.<sup>11,22</sup>

Forskolin also demonstrates a direct effect on cerebrovascular vasodilation via cAMP activation. In rabbits, intravenous infusion of 10  $\mu\text{g}/\text{kg}/\text{min}$  forskolin increased blood flow to the brain from  $39 \pm 5$  to  $56 \pm 9$  mL/min. This change was accompanied by a small decrease in mean arterial pressure, although cerebral oxygen consumption remained stable. These results indicate forskolin may be useful in cases of cerebral vascular insufficiency and post-stroke.<sup>13</sup>

### **Asthma and Allergies**

Asthma and other allergic conditions are characterized by decreased cAMP levels in bronchial smooth muscle, as well as high levels of PAF. In response to allergenic stimuli, mast cells degranulate, histamine is released, and bronchial smooth muscle contracts. Forskolin's activation of cAMP inhibits human basophil and mast cell degranulation,<sup>8</sup> resulting in subsequent bronchodilation.<sup>14</sup>

Research has demonstrated aerosolized dry forskolin powder results in significant relaxation of bronchial muscles and relief of asthma symptoms. In one randomized, double-blind, placebo-controlled trial, 16 asthma patients were given a single inhaled (aerosolized) 10-mg dose of dry forskolin powder, an asthma medication (0.4 mg fenoterol), or placebo. Both fenoterol and forskolin administration resulted in significant, equivalent bronchodilation, but patients taking fenoterol experienced marked finger tremor response and a decrease in plasma potassium levels. These side effects were not observed in patients receiving forskolin.<sup>23</sup>

In six asthmatics (ages 18-64 years), nebulized forskolin administration (1 mg and 5 mg per metered dose) resulted in an increase in forced expiratory volume. Two patients experienced immediate relief from bronchoconstriction and shortness of breath; the remaining four patients reported relief after 10-15 minutes. Blood pressure and heart rate remained stable in all patients and no tremors, palpitations, or other adverse effects were reported.<sup>14</sup>

### **Psoriasis**

Like asthma, psoriasis is characterized by decreased levels of cAMP in the skin in relation to another regulating substance, cyclic guanosine monophosphate (cGMP). This imbalance results in a much higher rate of cell division – 1,000 times greater than normal, resulting in psoriatic outbreaks. Although study details are not available, Ammon et al reported an improvement in symptoms of psoriasis in four patients supplemented with forskolin. The ability of forskolin to regulate cAMP levels in skin cells has been shown to have therapeutic benefit for sufferers of psoriasis.<sup>4</sup>

### Glaucoma

Glaucoma is characterized by elevated intraocular pressure (IOP). Several animal and human studies have demonstrated the ability of forskolin to lower IOP, possibly via cAMP activation and a reduction in aqueous flow.<sup>10,24-26</sup>

Caprioli et al demonstrated a significant decrease in IOP in rabbits, monkeys, and humans administered a topical forskolin suspension (1% forskolin). This effect was present at one hour post application and remained significant for at least five hours.<sup>26</sup> In one clinical trial of 20 young, healthy Japanese volunteers, two 50  $\mu$ L topical instillations of one-percent forskolin were applied to one eye while the other eye served as control, receiving only the topical vehicle. At one-hour post instillation, the IOP fell  $2.4 \pm 1.3$  mmHg and aqueous flow rate was reduced by 13 percent in the treatment eye compared to the control. Both results were statistically significant.<sup>25</sup>

In a randomized, double-blind, placebo-controlled, cross-over trial with two separate arms, 10 healthy, non-smoking men were given a forskolin (1%) suspension in one eye and placebo in the other eye; proxymetacaine (0.5%) was the local anesthetic. The forskolin suspension resulted in decreases in IOP, but the differences between the forskolin treatment and placebo treatment at eight hours post application were statistically insignificant. Six men participated in a second arm of the study and a different local anesthetic (0.4% oxybuprocaine) was used. In this study arm a highly significant 25-percent reduction of IOP was observed at six hours post application. The different results in the two arms may be attributable to the different topical anesthetics used prior to forskolin application.<sup>26</sup> These results suggest forskolin may be of benefit in reducing IOP in glaucoma patients.

### Cancer Metastases

Many metastasizing tumor cell lines induce platelet aggregation both *in vitro* and *in vivo*. Upon aggregation, platelets release substances that promote tumor growth.<sup>27</sup> Researchers have demonstrated forskolin's ability to block platelet aggregation via its stimulation of platelet adenylate cyclase and increase of intracellular cAMP.<sup>22</sup> Agarwal and Parks gave 82  $\mu$ g forskolin to mice 30-60 minutes prior to injection with a highly metastatic melanoma cell line (B16-

F10). Forskolin reduced tumor colonization in the lungs by 70 percent.<sup>28</sup>

### Obesity and Weight Loss

*In vitro* and animal studies demonstrate lipolysis in fat cells is stimulated by forskolin<sup>17,29,30</sup> via activation of adenylate cyclase and increased levels of cAMP. In a study involving 34 women, researchers discovered adipocytes from morbidly obese women have decreased adenylate cyclase activity, compared to adipocytes from normal weight women.<sup>31</sup> In a small study, six overweight women were given 250 mg *Coleus forskohlii*, standardized to contain 10-percent forskolin, twice daily for eight weeks. Average weight loss at the end of the trial was 10 pounds, with an eight-percent reduction in body fat. Blood pressure tended to be lower in all women during the trial. No adverse effects were reported, indicating *Coleus forskohlii* might be safe and effective for losing weight and body fat.<sup>32</sup> More research with a larger study population is indicated.

### Other Clinical Indications

Research has shown forskolin stimulates thyroid hormone release and increases thyroid hormone production.<sup>15,16</sup> Forskolin has been shown to stimulate digestive secretions, including hydrochloric acid, pepsin, amylase, and pancreatic enzymes,<sup>4,7</sup> suggesting clinical benefit in digestive disorders and malabsorption. Animal research indicates forskolin exerts an antidepressant action via activation of cAMP.<sup>33</sup> *In vitro* research indicates forskolin has potent immunostimulating properties.<sup>34,35</sup>

### Drug/Botanical Interactions

Because forskolin has an inhibitory effect on platelet aggregation, it should be avoided or used with caution in conjunction with anticoagulant medications.<sup>22</sup> Caution should be used when giving forskolin with antihypertensive agents as it may have a potentiating effect on these drugs.<sup>9</sup>

### Side Effects and Toxicity

*Coleus forskohlii* and forskolin extracts have an excellent safety profile and are generally without toxicity or side effects at the recommended dosage.

## Warnings and Contraindications

Caution should be used in a patient with ulcers as forskolin can increase stomach acid levels.<sup>7</sup> Caution should also be used in a patient with low blood pressure due to forskolin's hypotensive effects.<sup>9</sup> Because of forskolin's effect on platelet aggregation, *Coleus forskohlii* should be used with caution or avoided in patients with bleeding disorders or on blood-thinning medication.<sup>22</sup> *Coleus forskohlii* extracts have not been studied in pregnant or lactating women.

## Dosage and Administration

Many studies used a concentrated extract of forskolin in a non-oral delivery form (injectable, aerosolized, topical ophthalmic) – for cardiovascular, respiratory, or ocular conditions. Whether oral forskolin provides clinical benefit in these conditions has not been established. Oral *Coleus forskohlii* extracts are typically standardized to 10-percent forskolin, with recommended dosages ranging from 100-250 mg twice daily.

## References

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