Coleus forskohlii

Coleus Forskohlii is a herb in Ayurveda (/supplements/Ayurveda/), its component Forskolin is an activator of Adenyl Cyclase: it 'activates' cells and this activation differs depending on the cell. Can boost Testosterone (/topics/Testosterone/) and induce fat loss (/search.php?q=fat+loss) (more potent in men), under-researched given the possibilities.

This page features 70 unique references to scientific papers.

Confused about what actually ***Works***?

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Summary (All Essential Benefits/Effects/Facts & Information)

Coleus Forskohlii is an ancient Indian (Ayurvetic) herb that is commonly used currently as a fat burning (/search.php?q=fat+burning) compound through its main compound 'Forskolin'. Forskolin is commonly used as a research tool *in vitro* to activate an enzyme that increases a molecule called cAMP. When cAMP increases, a wide range of signalling properties can occur because of it. Forskolin's ability to increase cAMP *in vitro* is potent and reliable.

The main supplementation use of Forskolin is to increase cAMP in fat cells, which increases the rate of fat loss (/search.php?q=fat+loss) and can make other fat burners *better* at fat burning.

However, cAMP can induce a wide variety of effects when increased. It has been shown to increase Testosterone (/topics/Testosterone/) levels in men, have some anti-cancer effects, some anti-inflammatory effects, and interacts with muscle tissue as well (although the result of this is not too clear).

In general, increasing cAMP can in part mimic caloric restriction and exercise as cAMP is a signal of energy deprivation or energy usage.

Things to Know

Also Known As

Forskolin, Coleonol, 7beta-acetoxy-1alpha,6beta,9alpha-trihydroxy-8,13-epoxy-labd-14-en-11-one

Is a Form of

- Fat-Burner (/supplements/Fat-Burner/)
- Ayurveda (/supplements/Ayurveda/)
- Testosterone Booster (/supplements/Testosterone+Booster/)

Goes Well With

- Alpha(2)Adrenoreceptor *ant*agonists like Yohimbine (/supplements/Yohimbine/)/Rauwolscine (/supplements/Rauwolscine/)
- Beta adrenergic agonists like Isoprenaline/Ephedrine (/supplements/Ephedrine/)
- Methylxanthines like aminophylline/Caffeine (/supplements/Caffeine/)

Does Not Go Well With

- Alpha(2)adrenoreceptor agonism

Caution Notice

Examine.com Medical Disclaimer ()

How to Take (recommended dosage, active amounts, other details)

Coleus forskohlii tends to be dosed at 500mg of a supplement that contains 10% forskolin by weight, taken in at least two divided doses throughout the day (250mg twice daily). The aerial parts tend to be used due to a higher forskolin content, but this is not a relevant point if it is standardized to 10%.

It is currently not known if this is the optimal dosage or manner of which to spread the dose.

Human Effect Matrix

The **Human Effect Matrix** looks at human studies (excluding animal/petri-dish studies) to tell you what effect Coleus forskohlii has in your body, and how strong these effects are.

GRADE	LEVEL OF EVIDENCE
A	Robust research conducted with repeated double blind clinical trials
B	Multiple studies where at least two are double-blind and placebo controlled
C	Single double blind study or multiple cohort studies
D	Uncontrolled or observational studies only

LEVEL OF EVIDENCE ()	EFFECT	CHANGE ()	MAGNITUDE OF EFFECT SIZE ()	SCIENTIFIC CONSENSUS	COMMENTS
C	Blood Pressure			100%	

	(/topics/Blood+Pressure/)			See 2 studies (/show_rubric_effect.php?id=128&effect=Blood%20Pressure&selection=all)	No significant influence on blood pressure was noted with coleus supplementation
C	Weight (/topics/Weight/)		★☆☆ Minor	50% See all 4 studies (/show_rubric_effect.php?id=128&effect=Weight&selection=all)	Mixed effects on overall weight, may be more effective in men rather than women. Overall, it requires more evidence to see if it has a role in weight loss regimens.
C	Asthma (/topics/Asthma/)		★★☆ Notable	100% See 2 studies (/show_rubric_effect.php?id=128&effect=Asthma&selection=all)	Although more evidence is required, it appears to be more effective at suppressing asthmatic symptoms than other nutraceuticals. Mechanisms may be related to beta-adrenergic... show
C	Intraocular Pressure (/topics/Intraocular+Pressure/)		★☆☆ Minor	100% See 2 studies (/show_rubric_effect.php?id=128&effect=Intraocular%20Pressure&selection=all)	Somewhat effective as ocular eyedrops in reducing ocular pressure.
C	Fatigue (/topics/Fatigue/)		★☆☆ Minor	100% See study (/show_rubric_effect.php?id=128&effect=Fatigue&selection=all)	Less fatigue reported as a side-effect, no comparator or ability to assess potency.
C	Testosterone (/topics/Testosterone/)		★☆☆ Minor	100% See study (/show_rubric_effect.php?id=128&effect=Testosterone&selection=all)	Increase of testosterone observed in men not overly potent and is highly variable.
C	Bone Mineral Density		★★☆	100%	

	(/topics/Bone+Mineral+Density/)		Notable	See study (/show_rubric_effect.php?id=128&effect=Bone%20Mineral%20Density&selection=all)	Definitely requires more evidence, but a DXA confirmed increase in bone mass in men over 12 weeks makes this notable (rather than an increase in bone mass in osteoporotic... show
C	Lean Mass (/topics/Lean+Mass/)		★☆☆ Minor	100% See study (/show_rubric_effect.php?id=128&effect=Lean%20Mass&selection=all)	Somewhat effective (2lbs over 12 weeks relative to placebo) although somewhat confounded with the increase in bone mass, as lean mass is inclusive of bone and skeletal muscle.
C	Fat Mass (/topics/Fat+Mass/)		★☆☆ Minor	100% See study (/show_rubric_effect.php?id=128&effect=Fat%20Mass&selection=all)	Somewhat effective in reducing fat mass in obese and overweight persons.
D	HDL-C (/topics/HDL-C/)		★★☆ Notable	100% See study (/show_rubric_effect.php?id=128&effect=HDL-C&selection=all)	Needs to be replicated in larger trials, but the degree of increase was quite remarkable.

Disagree? Join the Coleus forskohlii Discussion (/discussion/Coleus+forskohlii/)

Complete Summary

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1. Source and Composition

1.1. Source

Coleus Forskohlii of the family *Lamiaceae* (alternate name of *Plectranthus barbatus*) is an Ayurvetic (/contribute/supplements/Ayurvetic/) medicine traditionally used for various cardiovascular, gastrointestinal, and central nervous system ailments.[1] It also has some implications in lung health and urinary health.[2]

Other names of coleus include 'falso boldo' (in brazil[3])

1.2. Composition

The aerial parts of *coleus forskohlii* (leafs and stem) include:

- The forskolin series of related compounds (A,G,H,I,J)and isoforskolin[4][5][6][7] The main **forskolin** compound used in research has the technical name *7beta-acetoxy-1alpha,6beta,9alpha-trihydroxy-8,13-epoxy-labd-14-en-11-one*.[8]
- The Forskoditerpenoside series (A,C,D,E) of diterpene structures.[9][10]
- (16S)-Coleon E[3]
- 4beta,7beta,11-enantioeudesmantriol[10]
- Rosmarinic Acid (/supplements/Rosmarinic+Acid/) (leaves)[11]
- Abietane diterpenoids[12]
- Chamaecydin[4]
- Scutellarein as 4′-methyl ether 7-O-glucuronide[3]
- Luteolin as 7-O-Glucuronide[12]
- Apigenin (/supplements/Apigenin/) as 7-O-glucuronide[12]
- Acacetin as 7-O-glucuronide[12]
- Alpha-cedrene[4]
- Oleanolic Acid[4] and Betulinic acid[4]
- Beta-sitosterol[4]

Whereas the root portion contains:

- 14-deoxycoleon U[13]
- Demethylcryptojapnol[13]
- Alpha-Amyrin and Alpha-Cedrol[13]
- Betulinic acid[13]
- Beta-sitosterol[13]

It is typically used for its active component, Forskolin, which is a direct activator of a cellular intermediate called Adenylate Cyclase.[14] Also called coleonol, Forskolin is found in varying concentrations in different plants of *Coleus Forskohlii*.[2] It is a yellowish brown powder when supplemented, and has a pleasing aroma yet bitter taste; when supplementing the whole plant the color is more brown in appearance.[2] Forskolin has poor solubility in water but is otherwise quite stable.[15]

1.3. Derivatives of Forskolin

Forskolin itself has poor water solubility, and activates 8 out of 9 isoforms of Adenylate Cyclase. This is seen as undesirable by some, as increasing cAMP in other organs aside from the target organ can give rise to unforeseen side-effects.[16]

Derivates of Forskolin have been developed, FD-1 (6-{N-{2-isothiocyanatoethyl}aminocarbonyl}forskolin) has affinity for type II receptors and also III, V to lesser degrees. 5,6-dehydroxy-7-deacetyl-7-nicotinoylforskolin (FD-4) appears to have high affinity for type III receptors and no difference between II and V. Finally, 6-{3-(Dimethylamino)propionyl}14,15-dihydroforskolin appears to have great affinity for type V over type II, with lesser effects on type III.[16] This information is relevant as type II are ubiquitous (everywhere), type III are more located to olfactory tissues, atria and brown fat, and type V is the major isoform of the adult cardiac tissue.[17][16] Potencies of some of these isoforms relative to parent forskolin range from 100-300%.[16]

2. Pharmacology

Coleus Forskohlii is well absorbed in the cat gastrointestinal tract after oral administration[18] and can be absorbed in all areas of the intestines and colon (in rats) although the duodenum seems to have highest uptake.[19]

Forskolin appears to be subject to P-Glycoprotein efflux in the intestines, and coingestion of a P-glycoprotein inhibitor may increase oral bioavailability.[19]

3. General Mechanism of Action

3.1. Enzymatic Interaction: Adenylate Cyclase

Forskolin is an adenylate cyclase activator, which increases levels of **cyclic adenosine monophosphate** (cAMP) in cells.[20][14] It is a highly reliable and effective cAMP increasing agent, and is routinely used as a research tool to investigate the effects of cAMP increases in a cell.[8] Out of the 9 isoforms of the AC enzyme[16]

This increase in cAMP does *not* increase lipolysis *per se* at low concentrations of 0.1-1uM, but when it surpasses 10uM it can induce lipolysis on its own.[20] Low doses are effective in increasing lipolysis when paired with beta(2)adrenergic agonists though, suggesting the fat burning effects of Forskolin are dependent on either high dosages or other agents (such as adrenaline secretion from exercise).[20]

The increase is seen 1 minute after incubation in adipocytes, and its ability to increase cAMP is inhibited by alpha(2)adrenoceptor agonism, and also by insulin secretion.[21]

Adenylate Cyclase is more sensitive to intervention after periods of starvation in the cardiac and muscle cells, which also accompanies a decrease in AC levels.[22]

3.2. Increasing cAMP

This mechanism of increasing cAMP is similar to exercise in regards to increasing activity of some enzymes, downstream of mitochondrial biogenesis (also, a non-significant increase in mitochondrial density at 4uM forskolin).[23] This cAMP increasing ability by Forskolin also appeared to non-significantly activate AMPK.[23]

4. Neurology

4.1. Mechanisms

Coleus leaves appear to have acetylcholineaster inhibiting properties with an IC_{50} value of 1.02+/-0.02mg/mL *in vitro*[12][3] which appears to survive simulated gastric digestion[12] and has been noted to be relevant following oral ingestion of 600mg/kg in rats.[11] These effects are thought to be secondary to Rosmarinic Acid (/supplements/Rosmarinic+Acid/) which has an IC_{50} value of 0.44mg/mL, and the inhibition appears to be reversible.[11][3] Rosmarinic acid has been detected in the brain (20.4-

24.1μM 30-60 minutes after intraperitoneal injection of 1g/kg) following ingestion of coleus leaf tea and acetylcholinesterase activity has been noted to be decreased by 5.5-10% (60 minute and 30 minutes, respectively).[11] Acetylcholineasterase inhibition has also been noted with isolated rosmarinic acid to the level of 12.8-13.5% following ingestion of 550μmol/kg.[11]

> Coleus forskohlii leaves (not commonly supplemented, as many supplements contain the root) appear to have acetylcholinesterase inhibiting properties due to the rosmarinic acid content. These effects are confirmed *in vivo*

5. Interactions with Obesity

5.1. Human studies

In regards to human *in vivo* studies, they appear to be promising but limited in numbers and power. One study in overweight women noted that two doses of 250mg 10% extract reduced weight gain.[24] There was not significant weight loss in the experimental group, but there was a significant difference between the experimental (slight loss) and control (weight gain).[24] In overweight men, the same dose appears to cause favorable changes in body composition over a period of 12 weeks.[25] Testosterone and bone mass were also increased in the Coleus Forskohlii group. One study that did not investigate weight changes primarily noted that over a period of 2 months with 500-700mg Coleus Forskohlii there was a 2.38-2.6% reduction in BMI.[26]

There may be notable differences between obese and normal weight humans, as obese persons seem to have lower activity adenylate cyclase enzymes in fat cells, which is partially corrected upon weight loss via caloric restriction.[27] Also, men may have more benefit than women as testosterone can act as a fat burner/muscle preserving agent, although only one study has been conducted on men so far.[25]

5.2. Metabolic Rate

One study on overweight men consuming 250mg of Coleus Forskohlii twice daily found no significant effect on increasing the Metabolic Rate (/topics/Metabolic+Rate/).[25]

6. Interactions with Skeletal Muscle

6.1. Muscle Protein Synthesis

Forskolin is able to increase activity of Adenylate Cyclase in skeletal muscle.[28] Through increasing cAMP, it has been speculated that Forskolin can increase muscle protein synthesis by activating PI3K and Akt, independent of the insulin receptor[29] and that this reaction is subject to desensitization.[30]

6.2. Muscle contractility

Forskolin, *in vitro* at concentrations of 1uM, has been shown to increase electical-stimulated skeletal muscle contractility in the mouse diaphragm.[31][32] The theorized mechanims of this is increasing cAMP levels, inducing PKA activity which acts on the ryanodine receptor and increases Ca^{2+} efflux from the sarcoplasmic reticulum. [33]

Although biological plausibility exists, no studies have been conducted on Coleus Forskohlii and muscle contraction *in vivo*.

6.3. Nutrients and Muscle cells

Forskolin has been implicated *in vivo* in reducing insulin's effects on the mTOR/Akt pathway in skeletal muscle.[34] Specifically, Forskolin appeared to reduce insulin's ability to phosphorylate Akt (with no affect on total Akt) and similar results were seen when looking at 4EBP1, with mTOR and S6K1 unaffected by all treatments.[34]

Forskolin is also able to inhibit myocyte GLUT4 translocation in vitro, and GLUT1 to a lesser degree.[35] This may also be downstream of cAMP, as it is seen in adipocytes as cAMP is known to adversely influence GLUT4 translocation via its promoter,[36][37] and also in muscle cells.[38]

In regards to fat metabolism, the activation of cAMP/PKA in myocytes seems to improve lipid metabolism,[39] and is one of the junction points of exercise and health in muscle cells.[40][41][42] Possibly through a myokine called Myonectin.[43]

7. Interactions with Heart Health

7.1. Blood Pressure

The active compound of Coleus Forskohlii, Forskolin, appears to either relax blood vessels and depress blood pressure or to have no overall effect on blood pressure.

It does not appear to reduce blood pressure via cholinergic or histamine means,[18] and provides a sustained reduction in blood pressure at 0.1-1mg/kg bodyweight in anathesized cats; with more reduction seen in those with higher baseline blood pressures.[18] Higher dosages do not increase potency of the blood pressure decrease, but instead prolong the time it can act; a parallel to the effects of forskolin on intraocular pressure.[18]

This vasorelaxant ability of forskohlii may be synergystic with Prostaglandin E1.[44]

7.2. Cardiac tissue

Forskolin is able to activate Adenylate Cyclase in the myocardium, and exerts a positive ionotropic effect which may be beneficial to failing hearts.[45] This has been observed *in vivo* with cat and rabbit hearts.[18]

8. Interactions with Organs

8.1. Eyes and Intraocular pressure

One study noted decreases in Intra-Ocular Pressure (IOP) with forskohlii in man[46] via its effects as an adenylate cyclate activator.[47][48] That being said, past studies have used a topical method of delivery (eye drops). Recently, this effect has been seen after oral ingestion of a Forskohlii/Rutin/Thiamin/Riboflavin combination by about 20% after 40 days of treatment in persons with Primary Open Angle Glaucoma.[49]

8.2. Liver

Coleus Forskohlii extract at 0.5% of feed intake in rats results in induction of various enzyme systems in the liver, alongside an increase in liver weight. Dose dependent increases in transcription for Cyp2b10, Cyp2c29, Cyp3a11, and Gstm2 were noted.[50] These changes were seen after 1 week, and ceased upon cessation of Coleus intake. This intake was estimated to be 740mg/kg bodyweight of Coleus daily; 24mg in total for the rats.[50] The CYP2C induction is of clinical relevance, as it is the enzyme that metabolizes warfarin.

Isolated forskolin has weaker induction of CYP3A and Glutathione enzymes, and does not increase liver weight at 0.05% of the diet.[50] This induction may be mediated by agonism of the Pregnane X receptor, which is independent of its activities on Adenylate Cyclase.[51]

9. Interactions with Hormones

9.1. Testosterone

One intervention in overweight men noted increases in testosterone with 250mg Coleus Forskohlii (10% Forskolin by weight) over the course of 12 weeks.[25] Although there were significant differences at baseline (5.06+/-1.21ng versus 4.12+/-0.82ng Total Test, 15.90+/-13.39pg v. 13.28+/-7.26pg free test; higher values in Coleus group) increases were still at 6 weeks and 12 weeks in Coleus while no changes occurred in control. Total test increased by 16.77+/-33.77% and free test by 3.47+/-8.10 after 12 weeks, with high inter-individual variance.[25]

The hypothesized mechanism of action is via increasing intra-testicular cAMP levels, which mimick the mechanisms of action of luteinizing hormone in the testicles.[52] LH normally increases cAMP itself, but circumventing LH to increase cAMP can increased steroidogenesis *per se*.[53][54] Even some other studies investigating herbs like Cordyceps (/supplements/Cordyceps/) in the testes will use forskolin as a standard by which to compare the efficacy of the newer drugs.[55]

Coleus extract may also induce CYP3A4 in the liver, which theoretically should lead to increased metabolism of testosterone.[50] However, testosterone was not measured in this rat study; isolated forskolin had a much lesser effect.

9.2. Insulin

Forskolin has been shown, *in vitro*, to be able to release insulin (as well as glucagon and somatostatin) when incubated in pancreatic cells.[56]

10. Nutrient-Nutrient Interactions

10.1. Beta-Adrenergic Agonists

Its is able to potentiate the effects of the beta-adrenergic agonist isoproterenol, and seems to be highly effective until isoproterenol reaches concentrations of 1uM (in which afterwards, descending returns are seen),[20] forskolin showed dose dependent benefits in increasing cAMP alongside isoproterenol.

In situations where beta-adrenergic agonists do not stimulate (hyporesponsiveness), low doses of forskolin are able to rescue the effectiveness of beta-adrenergic agonists.[57] Additionally, 1uM forskolin (although not lesser concentrations) are able to rescue beta-adrenergic desensitization.[58]

This synergy has been noted *in vivo* using isoproterenol and forskolin, via IV.[59]

Beta-Adrenergic agonists incluce Synephrine (/supplements/Synephrine/), Ephedrine (/supplements/Ephedrine/), Capsaicin (/supplements/Capsaicin/) and *possibly* raspberry ketones (/contribute/supplements/raspberry+ketones/); as well as endogenous adrenaline secretion.

10.2. Methylxanthines

Forskolin is synergistic with methylxanthines, as methylxanthines have the ability to reduce adenosine's suppressive influence on elevated cAMP levels in adipocytes via acting as adenosine inhibitors.[60][20] This combination of Forskolin and the Methylxanthine Aminophylline is even more synergistic with the addition of a beta-adrenergic agonist, such as Ephedrine (/supplements/Ephedrine/).

Some methylxanthines, such as theophylline and Caffeine (/supplements/Caffeine/), also possess phosphodiesterase inhibitory properties. PDE inhibition results in increased cAMP by alleviating degradation, and forskolin does not influence PDEs.[20] The combination of methylxanthines and forskolin can increase production of and alleviate degradation of cAMP to promote synergism *in vitro*.

Forskolin has also been shown to increase sarcoplasmic loading of Calcium and modulate Calcium spikes from the sarcoplasmic reticulum (via phospholambin)[61] which augments caffeine's ability to induce calcium release.[62]

Methylxanthines include theophylline, theobromine, and Caffeine (/supplements/Caffeine/). These can be found in high amounts in tea, chocolate, and coffee; respectively.

10.3. Alpha-Adrenergic Antagonists

When coincubated (in the cell at the same time), and alpha-adrenergic agonism by insulin or agonists can inhibit the increases in cAMP seen by forskolin.[63] Co-incubation of an alpha-adrenergic antagonist with the agonist and forskolin can rescue some of the effects by negating the inhibition.[63]

Interestingly, sensitizing cells (in this study, colonic carcinoma cells) by incubating with an alpha-adrenergic agonist [63] After exposure to an agonist for 30+ minutes, cells have 20-fold increases in forskolin-stimulated cAMP for a short time (20-40 minutes).[63][64]

11. Safety and Toxicity

Coleus Forskohlii supplementation can cause an increase in stomach acid levels, and may be a bad idea for those currently suffering from stomach ulcers.[65]

In cats, the LD^{50} appears to be 68mg/kg bodyweight forskolin.[18]

Scientific Support & Reference Citations

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(Common misspellings for Coleus forskohlii include forskolhii, forshkolii, forskholii, forskoli, forsholii, forsholi, forshkohli)

(Common phrases used by users for this page include what is coleus forskohlii, coleus forskolii affects what hormones, coleus forskohlii liver, coleus forskohlii and luteinizing hormone, coleus and cat heart, active compounds in coleus)

(Users who contributed to this page include Sol (/user/Sol/), KurtisFrank (/user/KurtisFrank/))

Quick Summary:

Coleus Forskohlii is a herb in Ayurveda (/supplements/Ayurveda/), its component Forskolin is an activator of Adenyl Cyclase: it 'activates' cells and this activation differs depending on the cell. Can boost Testosterone (/topics/Testosterone/) and induce fat loss (/search.php?q=fat+loss) (more potent in men), under-researched given the possibilities.

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