

RISK PROFILE

COLEUS FORSKOHLII

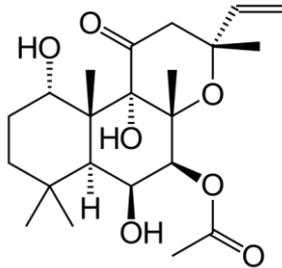
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1. Identification of substance

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| Chemical name (IUPAC): | |
| INCI | Coleus barbatus root extract, Coleus forskohlii flower extract, Coleus forskohlii root extract, Coleus forskohlii root oil, Plectranthus barbatus root extract |
| Synonyms | Coleus forskohlii / Coleus barbatus / Plectranthus forskalaei / Plectranthus forskohlii Forskolin / colforsin / coleonol |
| CAS No. | 223748-52-5 (Coleus forskohlii root extract) 66575-29-9 (forskolin/colforsin) |
| EINECS No. | 266-410-9 (forskolin/colforsin) |
| Molecular formula | Forskolin: C ₂₂ H ₃₄ O ₇ |
| Chemical structure | Forskolin:  |

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| Molecular weight | Forskolin: 410,5 |
| Contents (if relevant) | Forskolin, a diterpene compound derived from the roots of the plant, is considered to be the main active constituent in <i>Coleus forskohlii</i> . However, the plant also contains several other pharmacologically active substances; e.g. terpenoids, tannins, flavonoids, phlobatannins, saponins and cardiac glycosides (Samuelson 1992, Khatun 2011). |
| Physiochemical properties | Forskolin: off-white powder (Sigma-Aldrich Co.). |

2. Uses and origin

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| Uses | <p>➤ Cosmetic products</p> <p>According to the CosIng database <i>Coleus forskohlii</i> extracts are used in cosmetic products with the following functions:</p> <ul style="list-style-type: none"> -skin conditioning -emollient -humectant -oral care -masking <p>More than 50 products were identified in the databases Codecheck and EWG's Skin Deep. These comprise i.a. the following product categories:</p> <ul style="list-style-type: none"> -Body (firming) lotion -Facial cleanser -Moisturizer -Sun lotion -Shower gel <p>The source Good Guide mentions the following 24 products many of which are not contained in the Codecheck database. ¹</p> <ul style="list-style-type: none"> • Sunless Tanning (13) • Concealer (7) • Moisturizer (3) • Eye Cream & Treatment (1) <p>There are also many other products being announced on the web.</p> <p>With few exceptions the extract and the oil are not featured in the different announcement. One the few exceptions say: "Lipolytic Coleus Forskohlii Root Extract". Many of the products mentioned in the Codecheck and EWG databases are skin firming products sorting under the categories anti-cellulite and sculpturing – but these products contain also the usual other active ingredients in more prominent positions in the list of ingredients (xanthines, ivy, escin etc.).</p> |
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¹ <http://www.goodguide.com/ingredients/266575-coleus-forskohlii-root-extract>

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| | <p>Very little is known about the in-use concentrations. In nearly all the instances the ingredient is about in the middle of the list of ingredients.</p> <p>A raw material meant to be used as a cosmetic products ingredient contains Dipropylene Glycol, Commophora mukul Resin Extract and Coleus forskohlii Root Extract. In a model formulation the ingredient' concentration is 1.0 %. (COSSMA). This means that the Coleus forskohlii Root Extract is added to the product in a concentration somewhat less than 1%. The extent to which the molecule forskolin is present in the extract, apparently, varies greatly. It can be up till 40% it seems.</p> <p style="text-align: center;">➤ Medicinal products</p> <p>Coleus forskohlii has been described in Ayurvedic materia medica and in ancient Hindu medicinal texts as a remedy for several complaints; e.g. heart diseases such as hypertension and CNS disorders such as insomnia and convulsions. It has also been used to treat conditions such as congestive heart failure, eczema, colic, respiratory disorders and painful urination. Studies have indicated that it may also have therapeutic benefits in asthma, angina and psoriasis (Samuelsson 1992, Altern Med Review 2006, Natural Products Database 2011).</p> <p>The main active constituent in Coleus forskohlii is forskolin, a diterpene obtained from the roots. It has primarily been used for its antiasthmatic, spasmolytic, and antihypertensive effects. While the majority of studies have used the isolated forskolin extract, it has been postulated that the whole plant may be more effective, due to the presence of multiple compounds which may act synergistically (Natural Products Database 2011).</p> <p>Forskolin (colforsin) is an adenylate cyclase stimulator activating membrane-bound adenylate cyclase and increasing intracellular cyclic adenosine monophosphate (cAMP) concentrations. It also activates a number of key enzymatic pathways and binds to different transporters and receptors. All different types of adenylate cyclase in humans are activated, except the type found in spermatozoa. Forskolin lowers blood pressure and intraocular pressure, promotes vasodilation and bronchodilation, stimulates thyroid function, increases insulin secretion, inhibits histamine release from mast cells, and increases the utilization of fats as an energy source (lipolysis). The substance also has a positive inotropic action on cardiac tissue via increased cAMP levels, and is also an antihypertensive. In addition to the effects mediated by cyclic nucleotides, forskolin may act through direct binding to PAF receptors. This binding may inhibit platelet aggregation in addition to blocking inflammatory reactions mediated by platelet-derived products. Neutrophil activation, vascular permeability, and smooth muscle contraction are reduced, while coronary blood flow may be increased (Samuelsson 1992, Altern Med Review 2006, Natural Products Database 2011, Drugs 2011).</p> <p>In vitro and animal studies have shown that lipolysis in fat cells have been stimulated by forskolin. In a small study on mildly overweight women it was found that Coleus forskohlii did not promote weight loss, rather help mitigate weight gain (Altern Med Review 2006,</p> |
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| | <p>Henderson 2005).</p> <p>Extracts of <i>Coleus forskohlii</i> have been used in folk medicine to interrupt pregnancy. A study on pregnant rats showed that treatment with the highest dose of <i>Coleus forskohlii</i> extract (880 mg/kg per day) caused delayed fetal development and an anti-implantation effect. These findings justify the use of <i>Coleus forskohlii</i> extracts for abortive purposes (Almeida 2000).</p> <p style="text-align: center;">➤ Food</p> <p>Herbal remedies containing <i>Coleus forskohlii</i> extract have been used for their putative “fat-burning” properties. A product with a standardized extract from the roots of <i>Coleus forskohlii</i> (ForsLean®), containing 10, 20 and 40 % forskolin, has been sold to be used as sports nutrition and in weight management (Sabinsa corporation).</p> <p>Dosage, oral: 250 mg 1-3 times per day, standardized to contain 1% forskolin per dose, or 50 mg 1-2 times per day, standardized to contain 18% forskolin per dose. Dried root: 6-12 g/day. Fluid extract: 6-12 mL/day (Natural Products Database 2011). Another source says the typical dosage is 100-300 mg/day of an extract containing 10 % - 20 % forskolin (Drugs 2011).</p> |
| <p>Origin Natural (exo /endo) Synthetic</p> | <p>Ancient Ayurvedic plant and member of the mint and lavender family, which grows in the mountains of the subtropical temperate climates in Asia and east Africa (Altern Med Review 2006, Drugs 2011).</p> |
| <p>Contraindications / Interactions</p> | <p><i>Coleus forskohlii</i> has been reported to lower blood pressure and should therefore be used with caution in hypotensive individuals and in individuals treated with antihypertensive medications (or agents which predispose to orthostasis), vasodilators (nitrates, calcium channel blockers) and herbs with hypotensive properties, due to risk of additive vasodilation. To be used with caution in individuals who would not tolerate transient hypotensive episodes (cerebrovascular or cardiovascular disease).</p> <p>Avoid use in peptic ulcer disease (based on pharmacologic activity and/or in vitro studies). Avoid use in patients with autosomal dominant polycystic kidney disease.</p> <p><i>Coleus forskohlii</i> may alter platelet aggregation and coagulation, and could thereby enhance the adverse/toxic effect of antiplatelet agents, anticoagulants and thrombolytic agents. Based on pharmacologic activity, this herb may be contraindicated in individuals with active bleeding (eg, peptic ulcer, intracranial bleeding). Use with caution in individuals with a history of bleeding, haemostatic disorders, or drug-related haemostatic problems. Use with caution in individuals taking anticoagulant medications, including warfarin, aspirin, aspirin-containing products, NSAIDs, antiplatelet agents (eg, ticlopidine, clopidogrel, dipyridamole), or other herbs with anticoagulant/antiplatelet properties. Discontinue use prior to dental or surgical procedures (generally at least 14 days before).</p> <p>Use with caution in individuals with diabetes or in those who may be predisposed to hypoglycemia. Effects of drugs with hypoglycemic activity may be potentiated (including insulin and oral hypoglycemics). Blood sugar should be closely monitored, and the dosage of hypoglycemic medications may require adjustment. Use with caution</p> |

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| | <p>in patients with thyroid disorders</p> <p>Possible theoretical interactions with the concurrent use of <i>Coleus forskohlii</i> and a number of drugs; e.g. antihistamines, decongestants, anticoagulant medications (including warfarin), aspirin or aspirin-containing products, NSAIDs, antiplatelet agents, (eg, ticlopidine, clopidogrel, dipyridamole), antihypertensives, antidepressants, bronchodilators, chronotropic drugs, drugs dependent on pH and gastric action, glaucoma agents, inotropic agents, antidiabetic agents, insulin, thyroid agents, vasodilators (nitrates, calcium channel blockers), antihistamines, antiobesity agents.</p> <p>(Natural Products Database 2011, Altern Med Review 2006, Drugs 2011).</p> |
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3. Regulation

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| Norway | No regulation ² |
| EU | Forskolin is not listed in any EU Directive/Regulation Annexes, and there are no know restrictions to the use of this substance. |
| Rest of the world | Internet searches have not revealed any information about specific regulations for the use of <i>Coleus forskohlii</i> in the rest of the world. |

4. Relevant toxicity studies

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| Absorption Skin GI tractus | No data available |
| Distribution | No data available |
| Metabolism | <p>No data available on the metabolism of neither <i>Coleus forskohlii</i> extract/oil nor forskolin.</p> <p>Forskolin has been found to induce CYP3A gene expression in cultured hepatocytes by functioning as agonist of the pregnane X-receptor. Herbal therapy with <i>Coleus forskohlii</i> extract/oil should therefore be carefully monitored in patients on combination therapy, to avoid potential herb-drug interactions (Xunshan 2004).</p> |
| Excretion | No data available |
| Local toxic effects Irritation Sensitivity | No data available. |
| Systemic toxic effects Acute Repeated dose | <p>In general, there is very limited information available regarding toxicity of <i>Coleus forskohlii</i> and forskolin.</p> <p>Information on toxicity of <i>Coleus forskohlii</i> and forskolin is limited. Embryo-related toxicity has been reported and <i>Coleus forskohlii</i> has been used in folk medicine to interrupt pregnancy.</p> |

² The Norwegian medicinal products agency considered MN a medicinal remedy. Because of that up till 2008 topical products containing the substance were considered medicines – meaning a topical product containing it were automatically classified a medicine. This regime has since been lifted

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| Mutagenicity /genotoxicity | According to the EWG there are great data gaps regarding use of Coleus forskohlii extract/oil in cosmetics, and it has not been assessed for safety in cosmetics by the industry panel CIR. |
| Carcinogenicity | |
| Reprotoxicity / Teratogenicity | |
| Other effects | |

5. Exposure estimate and critical NOAEL / NOEL

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| NOAEL/NOEL critical | <p>No data available from independent sources.</p> <p>Sabinsa corporation in India is manufacturing a herb remedy containing a standardized extract from the roots of Coleus forskohlii, marketed as ForsLean®. According to data on their corporate web sites, a sub-chronic toxicity study of ForsLean® (daily for 28 days at varied doses) gave a no observed effect level (NOEL) of 100 mg/kg body weight for both male and female rats. In a similar sub-acute oral toxicity study the NOEL was found to be 1000 mg/kg body weight. There is no information on which strength of ForsLean® was administered. However, it's said to be "varied doses". Available ForsLean® products contain 10, 20 and 40% forskolin. (Sabinsa corporation).</p> |
| Exposure cosmetic products | <p>Rough estimates of the systemic exposure dose (SED) for leave-on face, body lotion and body wash products are given below:</p> <p>For leave-on face products the surface area is estimated to 565 cm² (face surface area) Amount of product per cm²: 1 mg (SCCS guidelines 2011, assumed leave-on, not rinse-off) Number of applications per day: 2 Concentration of Coleus forskohlii in products: 1 % (no information on concentration, 1 % is an assumption) Skin penetration rate: assumed 100 % (worst case) as no data are available (SCCS guidelines) Body weight: 60 kg (SCCS guidelines) SED face product: 565 x 1 x 2 x 0.01 x 1/60 = 0.18 mg/kg bw/day</p> <p>For body lotion products the surface area is estimated to 15670 cm² (body and head area, female) Amount of product per cm²: 1 mg (SCCS guidelines 2011) Number of applications per day: 2.28 (SCCS guidelines 2011) Concentration of Coleus forskohlii in products: 1 % (no information on concentration, 1 % is an assumption) Skin penetration rate: assumed 100 % (worst case) as no data are available (SCCS guidelines) Body weight: 60 kg (SCCS guidelines) SED body lotion: 15670 x 1 x 2.28 x 0.01 x 1/60 = 5.95 mg/kg bw/day</p> <p>For sun screen – and self tanning - products the surface area is estimated to 17500 cm² (total body area) Amount of product per cm²: 1 mg (SCCS guidelines 2011) Number of applications per day: 2 Concentration of Coleus forskohlii in products: 1 % (no information on concentration, 1 % is an assumption)</p> |

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| | <p>Skin penetration rate: assumed 100 % (worst case) as no data are available (SCCS guidelines) Body weight: 60 kg (SCCS guidelines) SED sun screen: $17500 \times 1 \times 2 \times 0.01 \times 1/60 = 5.8 \text{ mg/kg bw/day}$</p> <p>For body wash products the calculated daily exposure is 2.79 mg/kg bw/day (SCCS guidelines 2011) Skin penetration rate: assumed 100 % (worst case) as no data are available (SCCS guidelines) Concentration of <i>Coleus forskohlii</i> in products: 1 % (no information on concentration, 1 % is an assumption) SED body wash: $2.79 \text{ mg/kg bw/day} \times 1 \times 0.01 = 0.03 \text{ mg/kg bw/day}$</p> |
| Margin of Safety (MoS) | <p>NOEL: 100 mg/kg bw</p> <p>Face product: SED: 0.18 mg/kg bw/day MoS = $100/0.18 = 555$</p> <p>Body lotion: SED: = 5.95 mg/kg bw/day MoS = $100/5.95 = 17$</p> <p>Sun screen: SED: 5.8 mg/kg bw/day MoS = $100/5.8 = 17$</p> <p>Body wash: SED: 0.03 mg/kg bw/day MoS = $100/0.03 = 3333$</p> |

6. Other sources of exposure than cosmetic products

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| Food stuffs | Available in over-the-counter herbal remedies. |
| Pharmaceuticals | No data |
| Other sources | No data |
| Adverse side effects - from uses other than cosmetics | In general, intake of herbs may cause transient adverse effects such as nausea, vomiting, and GI distress due to a variety of chemical constituents. |

7. Assessment

Coleus forskohlii and its major active constituent, forskolin, act through multiple pharmacological mechanisms and therefore have a lot of different effects. Primarily these effects are linked to increased intracellular levels of cAMP.

Extracts and/or oils from the herb *Coleus forskohlii* are constituents in some cosmetics and herbal remedies. Such extracts and oils contain various substances, whereas the main constituent is forskolin. The substances may have their own adverse/negative effects, in addition to possibly contribute to the pharmacological activity and absorption of forskolin, and thereby enhancing the adverse effects of forskolin.

Some of the calculated MoS values indicate that there might not be a sufficient safety margin using *Coleus forskohlii* in cosmetic products, although these values are based on insufficient data material and assumptions.

As herbal preparations of *Coleus forskohlii* in general and forskolin in particular have many different pharmacological effects, such preparations should be used with caution. The current use of *Coleus forskohlii* in cosmetics does not possess the necessary safety precautions.

8. Conclusion

There seems to be a significant data gap on possible toxic effects of *Coleus forskohlii* and forskolin. This data gap should warrant a restrictive use of this herb and/or substance, to ensure a sufficient protection of the consumers. A regulation reflecting this is needed, until further data possibly can document a low hazard risk for *Coleus forskohlii* and forskolin used in cosmetic products. We will therefore suggest prohibiting the use of *Coleus forskohlii* in cosmetic products, until safe use can be documented.

9. References

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10. Annexes

None