BOTANICAL ADULTERANTS BOTANICAL ADULTERANTS BOTANICAL ADULTERANTS

on Adulteration of Skullcap

By Stefan Gafner, PhD*and Mark Blumenthal American Botanical Council, PO Box 144345, Austin, TX 78714 *Corresponding author: <u>email</u>

Keywords: Scutellaria lateriflora, skullcap herb, adulterant, adulteration

Goal: The goal of this bulletin is to provide timely information and/or updates on issues of adulteration of *Scutellaria lateriflora* to the international herbal products industry and extended natural products community in general. It is intended to complement the previously published works regarding skullcap adulteration, e.g., the *American Herbal Pharmacopoeia* Skullcap Monograph published by Upton et al.¹ and the <u>article by Foster in *HerbalGram*</u>,² by presenting new data on the occurrence of adulteration, the market situation, and consequences for the consumer and the industry.

1 General Information

1.1 Common name: Skullcap³

1.2 Other common names:

English: Blue skullcap, helmet flower, hoodwort, European or greater skullcap, Quaker bonnet, mad-dog skullcap, mad weed, scullcap, Virginia skullcap⁴

French: Scutellaire, scutellaire latériflore, scutellaire de Virginie, toque, toque casquée⁵

German: Helmkraut, seitenblütiges Helmkraut⁵

Italian: Scutellaria

Spanish: Escutelaria, escutelaria de Virginia

1.3 Accepted Latin binomial: Scutellaria lateriflora^{6,7}

1.4 Synonyms: Cassida lateriflora; Scutellaria polybotrya^{6,7}

1.5 Botanical Family: Lamiaceae (formerly Labiatae)

1.6 Plant part and form: The flowering aerial parts of *S. lateriflora* are used fresh, or dried as an infusion, as a tincture, or in the form of a fluid extract.¹ Suggested daily dosages vary, depending on the author, and correspond to 0.25-12 g of dried aboveground flowering parts.^{1,8,9}



1.7 General use(s): Traditionally, skullcap is used to help relieve nervousness and anxiety, as a sleep aid (mainly for stress-related cases of insomnia), or as an antispasmodic.^{1,7,8}

2 Market

2.1 Importance in the trade: Skullcap is not a widely traded botanical commodity. In 2001, approximately 16 tons (35,000 pounds) of material were reportedly harvested and sold worldwide.¹⁰ No statistics on more recent volumes of harvested skullcap material could be identified in the published literature. The limited popularity of the herb is also shown by recent sales data from the United States (Table1), where it ranked between #99 and #107 of all single herbal dietary supplements in the Natural retail channel, and between #149 and #157 in the Mainstream Multi-Outlet retail channel. (T. Smith e-mail to S. Gafner, September 2, 2015 and September 3, 2015)

2.2 Supply sources: Most supplies on the North American market appear to be obtained from cultivated sources both in the United States (e.g., Minnesota, Missouri, North Carolina, Oregon, and Washington) and internationally (e.g., Chile, Costa Rica, and Mexico).¹¹ According to a report for the Australian government, Australian growers formerly supplied skullcap, but production halted after 2003 when global prices dropped and local growers were not able to compete with the prices from abroad.¹² The majority of the skullcap used in products sold in Australia is now imported (H. Wohlmuth e-mail to S. Gafner, January 19, 2015). There is some commercial material available that is harvested in the wild in North America, but the majority (85% according to a report from 2001) is obtained from cultivation.¹⁰

2.3 Raw material forms: In the United States, many companies that manufacture products containing properly authenticated skullcap grow it themselves.¹¹ Bulk skullcap raw material is mainly sold as cut and sifted, in form of a teabag cut, or as powdered aboveground parts, which may be more susceptible to adulteration, since the distinct features for macroscopic identification are no longer recognizable.

2.4 Market dynamics: In 2001, an estimated 16 tons of skullcap were harvested and sold on world markets at a price of US \$9-13/kg.10 Since the cessation of production in Australia, prices for imported skullcap from North America have been gradually increasing and reached Australian (AUD) \$42/kg (US \$31/kg based on the exchange rate from June 1, 2006) for organic crops and AUD 25-30/kg (US \$19-22/kg) for conventional crops in 2006.12 Based on a 2008 newsletter of the Australian raw material supplier Network Nutrition, growers in the United States have experienced issues with cultivation due to difficulties with seed germination, crop failure, and various other issues. This has led to a shortage in raw material and the appearance of material where skullcap was substituted with other species of Scutellaria.13 In recent years, the demand for skullcap has been has been subject to fluctuations but overall trended flat or was slightly increasing. Currently, growers under contract can obtain between US \$18-19/kg for conventional and US \$24-29/kg for certified organic skullcap (E. Fletcher e-mail to S. Gafner, January 20, 2015; L. Ballard oral communication to S. Gafner, January 28, 2015). Pricing for the consumer is in the range of US \$43-47/kg for conventionally-grown herb and US \$70-110/kg for organically grown skullcap, according to an informal survey, by a co-author of this Bulletin (SG), of smaller companies that had listed pricing on the Internet.

3. Adulteration

3.1 Known adulterants: Canada germander (*Teucrium canadense*, Lamiaceae); germander (*T. chamaedrys*); *Scutellaria* spp., e.g., Alpine skullcap (*S. alpina*), Chinese skullcap (*S. baicalensis*), hoary skullcap (*S. incana*), heartleaf skullcap (*S. ovata*), and marsh skullcap (*S. galericulata*).^{1,8}

3.2 Sources of information confirming adulteration: The most comprehensive review on adulteration of skullcap has been published by Foster in *HerbalGram* for the ABC-AHP-NCNPR Botanical Adulterants Program.² Other sources for information on skullcap adulteration include the American Herbal Pharmacopoeia monograph on *Scutellaria lateriflora* by Upton et al.,¹ and the PhD thesis by Brock.⁸ Some of the adulteration seems to be due to the sale of mislabeled seed material, e.g., the inadvertent cultivation

Channel	2012		2013		2014	
	Rank	Sales [US\$]	Rank	Sales [US\$]	Rank	Sales [US\$]
Natural ^a	107	556,856	106	577,065	99	625,734
Mainstream Multi-Outlet ^b	n/a	19,355	157	22,735	149	27,997

Table 1: Sales data for skullcap dietary supplements from 2012-2014.

^aAccording to SPINS (SPINS does not track Whole Foods Market sales, which is a major natural products retailer in the US) ^bAccording to SPINS/IRI (the Mainstream Multi-Outlet channel was formerly known as food, drug and mass market channel [FDM], exclusive of possible sales at Walmart)

n/a: not available

Source: T. Smith (American Botanical Council) e-mail September 2, 2015 and September 3, 2015

of S. incana in North America, or of S. ovata in the United Kingdom.^{1,8} Leroy Ballard, president at Nature's Cathedral, Inc., an American grower and supplier of native American medicinal plants, commented that there are still between 1350 and 1800 kg (3000 and 4000 lbs) of S. incana sold as "Scutellaria spp." in the United States, but most of this material is exported overseas. (L. Ballard oral communication to S. Gafner, January 28, 2015). According to Brock, it is not clear how much of the skullcap material used by herbalists in the UK is actually S. ovata.8 Further evidence of ongoing adulteration of skullcap products available in the US market is demonstrated by the results from a study in 2011 by researchers at the United States Department of Agriculture, where 5 out of 13 commercial dietary supplements from US manufacturers purchased on the Internet were adulterated, reportedly with Canada germander and Chinese skullcap.¹⁴ [Note: The original publication does not state the source of the purchased products, but one of the authors has confirmed that they were from American (US) manufacturers. (P. Chen e-mail to S. Gafner, September 4, 2015)] Adulteration of commercially sold skullcap raw material with germander (species not identified) was also reported in 2012 by Walker and Applequist.¹⁵ Germander was formerly sold routinely as a bulk botanical in the United States but it is no longer offered by most herbal suppliers in the North American market (L. Ballard oral communication to S. Gafner, January 28, 2015).

3.3 Accidental or intentional adulteration: As indicated above, some of the adulterated material on the market may be due to rare accidental misidentification when material is harvested in the wild, or the cultivation of crops where the seeds have been mislabeled, which is likely the case for some of the adulteration with other species from the genus Scutellaria (except adulteration with Chinese skullcap, S. baicalensis, which does not grow in the same geographical area as S. lateriflora). The reasons behind the adulteration of skullcap with germander species is a matter of debate. Some experts suggest that it is accidental, but it is now believed that at least part of the adulteration is deliberate since the *Teucrium* species have a heavier dry weight than skullcap and therefore, a much higher yield is obtained when harvesting germander (E. Fletcher e-mail to S. Gafner, January 20, 2015; A. Chandra, e-mail to S. Gafner, January 23, 2015).^{12,16} Nomenclatural confusion may also play a role, as pink skullcap is a common name applied to Canada gemander.²

3.4 Frequency of occurrence: There is no comprehensive published study on the frequency of skullcap adulteration. The only study looking at the adulteration of skullcap dietary supplements included a limited amount of samples (n = 13) from manufacturers in the United States purchased over the Internet.¹⁴ In this study, 38% of the samples were found to be adulterated. On the other hand, a study looking at whole or minimally processed skullcap raw materials (n = 10) purchased from vendors within the United States, did not find any adulterated material, although the authors

of the study specify that they "have seen a recent sample of commercial skullcap, not included within this study, that was over 50% *Teucrium*".¹⁵ Similarly, a study investigating the authenticity of 11 commercial dietary supplements (10 extracts and one product made with crude powdered material) sold in the United States, using species-specific DNA primers, concluded that all nine samples from which DNA was obtained contained *S. lateriflora.* Two samples, including the product made with powdered raw herb, did not contain DNA of sufficient quality to determine the identity of the material (D. Harbaugh Reynaud e-mail to S. Gafner, January 14, 2016). No chemical assays were performed on these samples to confirm the results.

3.5 Possible safety/therapeutic issues: Substitution of S. lateriflora was a prominent issue in 2002 due to an Australian herbal product's being implicated in the death of a patient due to liver failure.¹⁷ According to the label, the herbal product contained kava (Piper methysticum, Piperaceae), passionflower (Passiflora incarnata, Passifloraceae) and skullcap. The authors of the case report suggested that the liver failure was possibly due to the ingestion of kava, a botanical that has been linked to rare occurrences of liver toxicity.18 However, the causative agent for the death of the Australian patient was never confirmed. The Australian Therapeutics Goods Administration (TGA) analyzed the product and determined that it did not contain skullcap. Some of the known skullcap adulterants, Teucrium species are known to cause liver injury in humans.¹⁹ The hepatotoxicity in *Teucrium* has been ascribed to the diterpenoid fraction.²⁰ The liver toxicity of germander is influenced by a number of factors, including diet, the type of germander preparation, and possibly genetic factors.^{21,22} In contrast to many of the germander neo-clerodane diterpenes, those with a tetrahydrofuran moiety did not show hepatotoxic effects. The neo-clerodane diterpenes isolated from skullcap by Bruno et al.²³ are different since they are substituted with either a dihydrofuran-fused tetrahydrofuran moiety or a fused tetrahydrofuran-y-lactone ring. The detection of these specific diterpenes may offer a way to uncover adulteration, although subsequent studies failed to detect diterpenes in skullcap.^{24,25}

The root of Chinese skullcap (S. baicalensis) is widely used in Traditional Chinese Medicine. There are some reports of allergic reactions, diarrhea, and stomach discomfort after ingestion or injection of Chinese skullcap.²⁶ There are also a small number of case reports that have linked Chinese skullcap to liver injury,27,28 but this implication is based on previous reports where causality between Chinese skullcap ingestion and liver injury reportedly has not been established,²⁹ or on case reports implicating a proprietary mixture of flavonoids from Chinese skullcap, catechins from betelnut palm (Areca catechu, Arecaceae), and zinc bisglycinate sold as a medical food under the brand name Limbrel[®] (Primus Pharmaceuticals, Phoenix, AZ).²⁸ Aboveground parts of barbed skullcap (S. barbata), a skullcap species native to China, are similarly used and theoretically could be substituted for S. lateriflora, though this has

not been formally reported. Since *S. lateriflora* does not grow naturally in China, and based on current knowledge, is not generally cultivated there, there is a greater likelihood that attempts by companies to procure *S. lateriflora* from Chinese suppliers could result in use of Chinese species.

The substitution of skullcap with material from other species of Scutellaria does not pose an apparent safety risk, although the data on use in humans with the adulterating species is more limited. *Scutellaria galericulata*, which is also used in herbal medicine, is believed to have similar actions and indications as S. lateriflora.16 The ethnobotanical use of S. galericulata and S. incana in North America is described by Moerman.³⁰ Scutellaria galericulata herb has been used by the Delaware tribe of Native Americans as a gastrointestinal aid and a laxative. The Ojibwe tribe used the aboveground parts for heart trouble. Scutellaria incana decoctions were used by the Cherokee as abortifacient, to treat diarrhea, against breast pain and as a gynecological aid, but ethnobotanical research suggests that Native American tribes used the root of the plant rather than the aboveground parts.³⁰ In addition, the chemical composition of these species, with the exception of the flavonoids, has not been established in detail.

3.6 Analytical methods to detect adulteration: Confirmation of species identity and purity may be achieved by organoleptic methods, if conducted by qualified personnel (e.g., a botanist) for plant material in its whole form. For establishing the identity of cut or powdered raw material, a combination of a physical assessment test (e.g., macroscopic or microscopic) with chemical identification methods or a suitable genetic approach is considered appropriate. Chromatographic methods, such as high-performance thin-layer chromatography (HPTLC) and high-performance liquid chromatography (HPLC), can be used for chemical characterization of raw material and extracts. A comprehensive evaluation of publicly available methods for the authentication of skullcap and detection of adulterants in skullcap, the Skullcap Laboratory Guidance Document, is available through the ABC-AHP-NCNPR Botanical Adulterations Program website.31

3.7 Perspectives: Industry expert Steven Foster believes that "there is no accidental misidentification of *Teucrium canadense* as *Scutellaria lateriflora*. That is a myth. One can easily harvest a pick-up truck load of *T. canadense* in a morning, whereas one would be hard-pressed to harvest a few pounds of any *Scutellaria* spp. from any wild habitat anywhere in the United States in a day. The adulteration of *Scutellaria lateriflora* with *Teucrium canadense* is pure and simple 'under the radar' economic adulteration." (S. Foster, e-mail to S. Gafner, January 28, 2015)

4 Conclusions

Based on a survey in the United Kingdom,³² skullcap is a highly regarded medicinal herb with herbal medicine practitioners. It has remained relatively popular in the United States as a botanical to treat anxiety and stressrelated conditions.¹ The substitution of skullcap with germander species is particularly deplorable because of the known toxicity of species of plants in the genus *Teucrium*. Such adulteration is easily detected by a variety of analytical methods, a detailed report of which is available in the <u>Skullcap Laboratory Guidance Document</u>,³¹ and as such, the potentially dangerous presence of *Teucrium* material labelled as skullcap in botanical raw materials or finished products cannot be excused.

5 References

- Upton R, Graff A, Soria T, Swisher D. American Herbal Pharmacopoeia and Therapeutic Compendium: Skullcap Aerial Parts: Scutellaria lateriflora L.: Standards of Analysis, Quality Control and Therapeutics. Scotts Valley, CA: American Herbal Pharmacopoeia; 2009.
- Foster S. Adulteration of skullcap with American germander. *HerbalGram.* 2012:(93);34-41. Available at: http://cms. herbalgram.org/herbalgram/issue93/FEAT_skullgerm.html. Accessed April 21, 2016.
- McGuffin M, Kartesz JT, Leung AY, Tucker AO. American Herbal Products Association's Herbs of Commerce. 2nd ed. Silver Spring, MD: American Herbal Products Association; 2000.
- Gruenwald J, Brendler T, Jaenicke C, et al. (eds). PDR for Herbal Medicines, 2nd ed. Montvale, NY: Medical Economics Co; 2000:678.
- 5. The Plant List. Version 1.1 (September 2013). Available at: http://www.theplantlist.org. Accessed April 21, 2016.
- List PH, Hörhammer L. Scutellaria. In: *Hager's Handbuch* der Pharmazeutischen Praxis, Volume 6. Berlin: Springer Verlag; 1979:339-341.
- 7. Tropicos.org. Missouri Botanical Garden. Available at: http:// www.tropicos.org. Accessed April 21, 2016.
- Brock CA. American skullcap (*Scutellaria lateriflora* L.): a study on its effects on mood in healthy volunteers. PhD thesis. London: University of Westminster; 2012. Available at: http://westminsterresearch.wmin.ac.uk/12194/1/Christine_BROCK.pdf. Accessed April 21, 2016.
- Health Canada: Natural Health Products Ingredients Database. Skullcap. Available at: http://webprod.hc-sc.gc.ca/ nhpid-bdipsn/monoReq.do?id=159. Accessed April 21, 2016.
- Greenfield J, Davis JM. Medicinal Herb Production Guide: Skullcap (*Scutellaria lateriflora* L.). Chapel Hill, NC: North Carolina Consortium on Natural Medicines; 2004.
- 11. Upton R. Skullcap *Scutellaria lateriflora* L.: An American nervine. *J Herb Med.* 2012;2(3):76-96.
- 12. Yap G. Prospects for medicinal herbs: Assessment of market potential for selected medicinal herb products (Valerian, Arnica, Skullcap, Echinacea, Goldenseal). Barton, Australia: RIRDC. 2006.
- Gorman R. Buyer Beware: Scutellaria lateriflora. In: Nutralink. Network Nutrition Pty Ltd, Australia. 2008. Available at: http://www.google.com/url?sa=t&rct=j&q=&esrc=s&sou rce=web&cd=1&ved=0CCAQFjAA&url=http%3A%2F%2 Fnetworknutrition.com.au%2Fcontent.cfm%3FLive%3D0 %26ContentType%3DContent%26ContentID%3D84%2 6TEI%3D150%26TLI%3D0&ei=SEvJVMOXLu3GsQS0 p4G4CQ&usg=AFQjCNFc5twJHGECqPA0znGIXbB62bi P3Q&sig2=d4U1iWtoAjBOTAZvJU3MxA. Accessed April 21, 2016.
- 14. Sun J, Chen P. A flow-injection mass spectrometry fingerprinting method for authentication and quality assessment of *Scutellaria lateriflora*-based dietary supplements. *Anal Bioanal Chem.* 2011;401(5):1577-1584.
- 15. Walker KM, Applequist WL. Adulteration of selected unpro-

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cessed botanicals in the U.S. retail herbal trade. *Econ Bot.* 2012;66(4):321-327.

- Wills RBH, Stuart DL. Generation of high quality Australian skullcap products. Barton, Australia: RIRDC. 2004. Available from: https://rirdc.infoservices.com.au/downloads/04-020.pdf. Accessed April 21, 2016.
- Gow PJ, Connelly NJ, Hill RL, Crowley P, Angus PW. Fatal fulminant hepatic failure induced by a natural therapy containing kava. *Med J Aust.* 2003;178(9):442-443.
- Teschke R, Sarris J, Schweitzer I. Kava hepatotoxicity in traditional and modern use: the presumed Pacific kava paradox hypothesis revisited. *Brit J Clin Pharmacol.* 2012;73(2):170-174.
- Laliberte L, Villeneuve JP, 1996. Hepatitis after the use of germander, a herbal remedy. *Can Med Assoc J.* 1996;154(11):1689-1692.
- Opinion of the Scientific Committee on Food on teucrin A, major component of hydroalcoholic extracts of *Teucrium chamaedrys* (wild germander). European Commission, Health & Consumer Protection Directorate General. Brussels, Belgium. 2003. Available at: http://ec.europa.eu/food/fs/ sc/scf/out173_en.pdf. Accessed April 21, 2016.
- 21. Nencini C, Galluzzi P, Pippi F, Menchiari A, Micheli L. Hepatotoxicity of *Teucrium chamaedrys* L. decoction: Role of difference in the harvesting area and preparation method. *Ind J Pharmacol.* 2014;46(2):181-184.
- 22. Zhou S, Koh HL, Gao Y, Gong ZY, Lee EJ. Herbal bioactivation: The good, the bad and the ugly. *Life Sci.* 2004;74(8):935-968.
- Bruno M, Cruciata M, Bondi ML, et al. Neo-clerodane diterpenoids from *Scutellaria lateriflora*. *Phytochemistry*.

1998;48(4):687-691.

- Lin LZ, Harnly JM, Upton R. Comparison of the phenolic component profiles of skullcap (*Scutellaria lateriflora*) and germander (*Teucrium canadense* and *T. chamaedrys*), a potentially hepatotoxic adulterant. *Phytochem Anal.* 2009;20(4):298-306.\
- 25. Li J, Wang YH, Smillie TJ, Khan IA. Identification of phenolic compounds from *Scutellaria lateriflora* by liquid chromatography with ultraviolet photodiode array and electrospray ionization tandem mass spectrometry. *J Pharm Biomed Anal.* 2012;63:120-127.
- Gardner Z, McGuffin M (eds). American Herbal Products Association's Botanical Safety Handbook. 2nd ed. Boca Raton, FL: CRC Press; 2013.
- Teschke R, Wolff A, Frenzel C, Schulze J. Herbal hepatotoxicity–an update on traditional Chinese medicine preparations. *Aliment Pharmacol Ther.* 2014;40:32-50.
- Chalasani N, Vuppalanchi R, Navarro VJ, et al. Acute liver injury due to Flavocoxid (limbrel), a medical food for osteoarthritis. A case series. *Ann Intern Med.* 2013;156: 857-860.
- Dhanasekaran R, Owens V, Sanchez W. Chinese skullcap in move free arthritis supplement causes drug induced liver injury and pulmonary infiltrates. *Case Reports Hepatol.* 2013;2013:965092.
- 30. Moerman DE. *Native American Ethnobotany*. Portland, OR: Timber Press; 1988.
- Gafner S. Skullcap Adulteration Laboratory Guidance Document. Austin, TX: ABC-AHP-NCNPR Botanical Adulterants Program. 2015. Available at: http://cms.herbalgram.org/ BAP/LGD/SkullcapLabGuidanceDocument.html. Accessed January 15, 2016.

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Version # , Author,	Date Revised	Section Revised	List of Changes
Version 1, S. Gafner new	n/a	n/a	none

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