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HerbClip™

FILE: ▪Skullcap (*Scutellaria lateriflora*)
▪Anxiolytic
▪Sedative

HC 070432 - 247

Date: December 31, 2003

RE: Anxiolytic Effect of a Skullcap Extract

Wolfson P, Hoffmann DL. An investigation into the efficacy of *Scutellaria lateriflora* in healthy volunteers. *Alternative Therapies* 2003;9:74–78.

In 1987, it was estimated that 13.3% (24 million) of the United States population had an anxiety disorder. Benzodiazepines are the most widely prescribed class of anxiolytic (i.e., antianxiety) agents for this disorder; however, their use is associated with adverse side effects (e.g., ataxia, mild amnesia, habituation, and oversedation). Thus, a need exists for new medicines that reduce anxiety without impairing alertness or memory, diminishing cognitive abilities, or resulting in habituation. Herbal sedatives have been used for centuries and continue to be used in many cultures. In modern European herbal literature, phytomedicines that affect the central nervous system are known as nervines. Nervines are classified on the basis of their effects, as stimulating, relaxing, or tonic. In this article, the authors investigate the efficacy of the tonic nervine skullcap (*Scutellaria lateriflora*).

Skullcap is a perennial herb indigenous to North America and Europe that is dispensed primarily as a tea or a tincture to diminish symptoms of premenstrual dysphoric disorder. In the early 1900s, eclectic physicians prescribed skullcap for nervous excitability, inability to sleep without pain, restlessness, and irritability. In Europe, skullcap "retains a solid reputation" in clinical phytotherapy, and the "*British Herbal Pharmacopoeia* describes it as having anticonvulsive and sedative actions, and indicates its use in nervous tension states and epilepsy." Despite the extensive use of skullcap, little is known about the chemistry and constituents of this herb. It is known, however, that the essential oil of this plant is composed mainly of sesquiterpenes.

A double-blind, placebo-controlled, crossover trial was conducted in 19 healthy men and women aged 20–70 years to assess the effectiveness of skullcap on three outcome variables: energy, cognition, and anxiety. Four treatment conditions were tested: two placebo capsules;

one 350-mg capsule of organically grown, freeze-dried skullcap (Eclectic Institute, Sandy, OR); one 100-mg capsule of organically grown, freeze-dried skullcap extract (Phytos, San Anselmo, CA); and two 100-mg capsules of organically grown, freeze-dried skullcap extract (Phytos). Each of the four experimental conditions was separated by at least two days, and the effects of treatment were evaluated at baseline and 30, 60, 90, and 120 minutes after administration. The subjects rated their "experience of the three factors" on an ordered scale; the ratings for energy ranged from "sedating" to "stimulating," for cognition from "diminished" to "increased," and for anxiety from "relaxed" to "tense."

All three skullcap treatments had "noteworthy" results on the three outcome variables relative to the placebo, although the effects on anxiety were the "most pronounced." The effects on energy and cognition were considered "mild." The duration of action was less than two hours, except for the two-capsule treatment, which continued to have a "mild anxiolytic effect" at two hours in some subjects. No side effects from the three skullcap preparations were reported in this study; however, reports in the literature suggest the hepatotoxicity of *Scutellaria* species. The science section of the February 9, 1999, issue of the *New York Times* lists skullcap as a tranquilizer that can cause liver damage. In addition, Foster and Tyler state in a 1998 publication that "A report in the medical literature summarized the observed hepatotoxic effects of the herb [skullcap] in four women who had been consuming proprietary products supposedly claiming it for the relief of stress."[1] However, no reports in the literature have specifically implicated *S. lateriflora* as being hepatotoxic.

The three skullcap preparations tested had a "meaningful anxiolytic effect compared with an herbal placebo." No overt toxicity or side effects were reported. The authors suggest that "studies using validated instruments in clinically impaired populations are warranted in order to assess the clinical anxiolytic effects of *S. lateriflora*." They further suggest that the effects of other herbal anxiolytics (e.g., kava-kava [*Piper methysticum*] and valerian [*Valeriana officinalis*]) and of prescription antianxiety medications be compared with those of *S. lateriflora* to "define more specifically the clinical potential of *S. lateriflora* as a treatment for anxiety." While this study is the first of its kind – comparing the effects of freeze-dried skullcap to a freeze-dried skullcap extract, there are aspects of the article which contribute to an appearance of bias. In Figures 2 to 3 to 4, the scale becomes progressively smaller, exaggerating the differences between the freeze-dried herb and the 200 mg of the extract. Also, since the blinded subjects took 2 capsules of placebo and of 2 capsules of the extract, they would very likely expect to have a stronger effect than from 1 capsule of freeze-dried herb or 1 capsule of the extract. In this regard, it was not placebo-controlled, but placebo-biased and 2 capsule extract-biased by comparison to the herb. This is especially unacceptable in a study in which the results are based entirely upon subjective impressions. These significant pitfalls undermine the legitimacy of the comparisons of the products made by the authors.

—Brenda Milot, ELS

After HerbClip 070432.247 was printed, one of the American Botanical Council's peer reviewers had these comments to make regarding the article:

There is some confusion about the results of the authors' research through a lack of appropriate characterization of the extract and of the Figures in the article. Assuming that the lines designating treatments A, B, C, and D in the Figures 2-4 represent the 1) placebo, 2) Eclectic freeze-dried (FD) herb, 3) Phytos 100 mg FD extract, and 4) Phytos 200 mg FD extract, respectively, then the 100 mg extract ends up having less of an effect than placebo after 2 hours in all 3 categories studied, whereas the 350 mg FD herb is much more potent than 100 mg extract and almost equivalent to 200 mg extract as an anxiolytic. Clearly, the measured anti-anxiety effects of two 100 mg capsule of extract > one 350 capsule of FD herb > one 100 capsule of extract.

The authors also state that the higher potency / lower weight of the 200 mg extract compared to 350 mg of commercial freeze-dried herb is not unusual between products, and that such variations can be due to a number of factors including "mechanism of extraction." This obviously does not apply to an unextracted herb in this case, and they do not explain that the extract likely represents a larger amount of the beginning herb. The article doesn't say what the strength of the solid extract is, but 5:1 could be expected, so the 100 mg extract likely represents at least 500 mg of herb which thereby lost potency through extraction (350 mg herb was shown more potent than 100 mg of extract). This is only a guess since the authors do not specify the relative strength of their extract.

There are other aspects of this article which contribute to its appearance of bias and lack of credibility. Going from Figure 2 to 3 to 4, the scale is progressively smaller which visually exaggerates the differences between the FD herb and 200 mg of the extract. In addition, since the blinded subjects took 2 capsules of placebo and of 2 capsules of the extract, they would very likely expect to have a stronger effect than from one capsule of FD herb or one capsule of the extract. In this regard, it was not placebo-controlled, but placebo-biased and 2 capsule extract-biased by comparison to the herb.

[1]Foster S, Tyler VE. *Tyler's Honest Herbal*, 4th ed, Binghamton, NY: Hawthorn Press; 1998; 360.

The American Botanical Council has chosen not to include the original article due to the prohibitive reprint fee required by the publisher.