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File: ■ Rhodiola (*Rhodiola rosea*, Crassulaceae)

■ Anxiety

■ Stress

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RE: Rhodiola Extract Reduces Mild Anxiety and Stress in an Open-label Study

Cropley M, Banks AP, Boyle J. The effects of *Rhodiola rosea* L. extract on anxiety, stress, cognition and other mood symptoms. *Phytother Res*. December 2015;29(12):1934-1939.

Stress and anxiety are common in college students. Rhodiola (*Rhodiola rosea*, Crassulaceae) root extract is used to regulate anxiety, stress, fatigue, and depression. The purpose of this randomized, open-label study was to evaluate the effects of rhodiola on self-reported mild anxiety and stress in college students.

The study was conducted at the University of Surrey; Guildford, Surrey, United Kingdom. Subjects were healthy, nonsmoking students (n = 81, aged 18-35 years) who scored > 30 on the Spielberger State-Trait Anxiety Inventory (STAI). Exclusion criteria were as follows: (1) pregnancy or breastfeeding; (2) consumption of > 5/day caffeine-containing beverages; (3) color blindness; (4) clinically significant hepatic or renal abnormality on preliminary lab tests; (5) body mass index > 33; (6) history of alcohol, narcotic, benzodiazepine, or other substance abuse or dependence within the preceding 12 months; (7) positive alcohol breath test at any visit; (8) use of any other medication that could interfere with study outcome and/or study treatment within the 2 weeks or 5 half-lives preceding the first treatment phase; (9) current or recent (within 3 months) participation in another clinical trial studying any drug or device; and (10) any other condition that could compromise the subject's participation in the study.

Subjects were randomly assigned to the untreated control group (41 subjects) or to the rhodiola treatment group (40 subjects, 1 of whom did not complete the study due to use of another medication). The rhodiola group received 200-mg tablets of Vitano® (also known as Vitango®; Dr. Willmar Schwabe GmbH & Co. KG; Karlsruhe, Germany) twice daily, before breakfast and before lunch, for 14 days. Vitano is made from the proprietary rhodiola root extract Rosalin (WS® 1375; Dr. Willmar Schwabe GmbH & Co. KG), a 1.5-5:1 dry extract. [Note: Information available online indicates that WS 1375 is a 60% per weight ethanolic extract, with 1 tablet corresponding to 300-1000 mg of rhodiola root and rhizome as needed to maintain chemical standardization.] The primary outcome measures were anxiety (measured with the STAI) and stress (measured with the

Perceived Stress Scale). Secondary outcome measures were mood (measured with the Profile of Mood States Inventory, which includes 6 subscales measuring various aspects of mood), sleepiness (measured with the Milford Epworth Sleepiness Scale), sleep quality (measured with the Leeds Sleep Evaluation Questionnaire), reaction time (a measure of cognition; evaluated with the simple reaction time test and the choice reaction time test), attention (measured with the sustained attention to response test), and speed of thinking (measured with the symbol digit processing test). Subjects were evaluated at baseline, 4 hours after the initial dosing, on day 7, and on day 14.

Treatment compliance was 100%. Baseline measurements were similar between groups. There were 4 adverse events (AEs) in the rhodiola group and 2 in the control group, none of which were considered treatment-related. At 14 days, the rhodiola group had significant decreases in anxiety and stress, controlling for baseline values, compared with control (both $P < 0.01$). There was no significant effect at earlier time points, though at 7 days, there was a possible nonsignificant trend towards reduced anxiety and stress in the rhodiola group ($P = 0.08$ and $P = 0.06$, respectively). On the Profile of Mood States Inventory, at 14 days, the rhodiola group had significantly reduced scores on the anger ($P < 0.05$), confusion ($P < 0.01$), and total negative mood ($P < 0.01$) scales compared with control; reduced scores on the depression subscale ($P < 0.01$) were not time dependent. There were no significant differences between groups on mood subscales measuring fatigue, tension, or vigor, nor on any measure of sleep or cognitive performance (i.e., reaction, attention, and thinking speed).

The authors conclude that rhodiola (Vitano) extract is effective in treating mild anxiety and stress. They also conclude that rhodiola has a general positive effect on mood, since it improved some mood parameters, and that it has no effect on cognition. The study has many limitations, including no placebo group and self-reported outcome measures. The authors consider it unlikely that results were due to a placebo effect because the benefits appeared over time and were not seen equally in all mood subscales. However, an important limitation is that the authors do not discuss the school schedules of the student subjects. Stress and anxiety could decrease over a 2-week period as students adjust to new schedules, complete exams, or look forward to a school recess, and it is unclear whether subjects from the rhodiola and untreated control groups had comparable schedules and stressors during the study period. A placebo group would have helped to resolve these limitations. This research was supported by a grant from Dr. Willmar Schwabe GmbH & Co. KG.

—Heather S. Oliff, PhD

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