

**A Combination of Magnesium, B Vitamins, Rhodiola, and Green Tea (L-theanine) Alleviates Chronic Stress in Healthy Volunteers: A Randomized, Placebo-Controlled Study**

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**Objectives:** The effect of a combination of magnesium, vitamin B6, B9, B12, and Teadiola® (rhodiola and green tea/L-theanine extracts) on stress was evaluated in chronically stressed but otherwise healthy subjects. The effects on stress-related quality-of-life (QoL) parameters, like sleep and perception of pain were also explored.

**Methods:** This single-blinded study (NCT04391452) included adults with stress for  $\geq 1$  month and with  $\geq 14$  points on Depression Anxiety Stress Scale (DASS)-42 stress questionnaire. Subjects were randomized (1:1) to receive either the dietary supplement combination (n = 49) or placebo (n = 51), once daily, for 28 days, with a follow-up assessment at day 56. Primary endpoint was the change in DASS-42 stress score from baseline (BL) to day 28 in dietary supplement vs placebo groups. Secondary endpoints included changes from BL in DASS-42 scores at days 14 and 56; sleep quality (Pittsburgh Sleep Quality Index [PSQI]) at days 14, 28, and 56; pain perception

(temperature threshold) in response to cold/warm thermal stimulations at day 28.

**Results:** At BL, DASS-42 score (mean [SD]) was 26.3 (6.7) with dietary supplement and 26.8 (8.0) with placebo. At day 28, the scores decreased to 17.6 (7.3) and 20.1 (9.4), respectively, with a significant between-group difference of 3 points (effect size [ES],  $-0.29$ ; 95% CI  $[-0.57, -0.01]$ ;  $p = 0.04$ ). Similar reductions were observed earlier, at day 14 (ES,  $-0.40$ ; 95% CI  $[-0.68, -0.11]$ ;  $p = 0.006$ ), that remained stable up to day 56 (ES,  $-0.34$ ; 95% CI  $[-0.62, -0.06]$ ;  $p = 0.02$ ). At day 28, a significant reduction in sensitivity to cold pain was reported with dietary supplement vs placebo ( $p = 0.01$ ) and a trend for lesser sensitivity to hot pain was observed ( $p = 0.06$ ). No significant effect was observed on overall sleep quality, but a trend towards improvement in daytime dysfunction due to sleepiness (PSQI-7 component score) was noticed with dietary supplement vs placebo at day 28 ( $p = 0.06$ ) which became significant at day 56 ( $p < 0.001$ ).

**Conclusions:** The combination is effective for management of stress in healthy individuals. Its beneficial effects on stress-related QoL aspects, notably pain perception, deserve further investigation.

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