Effect of the phytoadaptogen Rhodiola rosea L. on benzodiazepine withdrawal in rats

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Rhodiola rosea L. (Crassulaceae) is traditionally used in Eastern Europe and Asia for decades to alleviate everyday anxiety, psychological stress, insomnia and depression, and to stimulate the nervous system enhancing physical and mental performance. In the present study the anxiolytic-like effects of Rhodiola (R) were assessed using the elevated plus-maze and forced swimming test in male Wistar withdrawn rats. It is well documented that withdrawal from normal dosage benzodiazepine produced in animals typical anxiety response and can result in a number of symptomatic patterns coming on within 1-4 days of discontinuation. After 21 days of treatment with diazepam (2 mg/kg IP) rats were tested 24-, 48-, 72- and 96 h after the last injection in the elevated plus-maze test of anxiety and the locomotor activity in optovarimex was checked. An increase in the percentage number of entries onto the open arms in the elevated plus-maze and in horizontal and/or vertical locomotor activity in optovarimex is interpreted as an anxiolytic response. Stress-related behavioral alterations were evaluated also by the forced swimming test (Porsolt test) on the 96th h after the last diazepam treatment. Two swim sessions were conducted: the initial 6-min pretest; and a 6-min retest followed 24 h later. The total period of immobility during the 6-min testing period was recorded and data were assessed using the Student’s t-test. All data were analyzed by one-way ANOVA and post-hoc comparisons for statistical significance were made by the Dunett’s test.

Compared with control-treated rats, withdrawn animals showed significant decreases in the percent number of entries onto open arms of the plus-maze on the 72nd and 96th hour (F 1.11 = 6.33; p<0.03) and reduced vertical locomotor activity in optovarimex on the 96th h after the last diazepam injection (F1.11 = 13.19; p<0.0025), indicating an anxiogenic response. Rhodiola rosea (60 mg/kg, PO) applied during the 21 – diazepam treatment and 1 h before testing significantly reversed the anxiogenic effects after diazepam withdrawal on the 48th; 72nd and 96th hour in the elevated plus-maze (F1.11 = 12.4, p<0.004; F1.11 = 7.4, p<0.03; F1.11 = 6.5 p<0.03) respectively, and were ineffective in optovarimex. In the forced swimming test chronic administration of diazepam plus R (F 1.12 = 17.33; p<0.0003) significantly decreased the duration of immobility as compared with withdrawn rats.

Our present findings are consistent with earlier proposals about adaptogenic, antidepressant and anxiolytic effects of R. rosea in behavioral tests and variant animal models (1) and also with the preliminary clinical findings (2) that Rodiola improve significant the symptoms in patients with generalized anxiety disorder (GAD). We suggest that chronic treatment with Rhodiola rosea may prove to be a promising adjuvant medication for successful withdrawal strategy.