



EFFECTS OF RHODIOLA ROSEA L. STANDARDIZED EXTRACT ON NOCICEPTIVE REACTIONS AND LOCOMOTOR ACTIVITY

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ABSTRACT

PURPOSE: Rhodiola rosea L. is an adaptogen increasing resistance to the harmful effects of various stressors. Our aim was to study the effects of standardized extract of Rhodiola rosea L. on nociception and locomotor activity of rats. **METHODS:** Male Wistar rats (n = 8), divided in 3 groups were treated i.p. with: 1st group with saline (controls); 2nd and 3rd group with Rhodiola rosea L. standardized extract 50mg/kg or 100mg/kg. Two nociceptive tests were used. Criterion for hot-plate test was the reaction time in seconds on heated surface, for analgesimeter – the paw pressure reaction in cm. Locomotor activity was measured as horizontal and vertical movements in activity cage for 5 minutes. The statistic evaluation was done by ANOVA. **RESULTS:** In hot-plate test rats with both doses of extract increased significantly the latency of reaction. In analgesimeter Rhodiola rosea in the low dose increased the paw reaction on 120th and 180th min. In activity cage rats treated with the low dose significantly increased vertical activity compared to the controls, but did not change the horizontal activity. **CONCLUSIONS:** Our data suggest that the studied extract influence nociceptive reactions. Rhodiola rosea L. standardized extract in low dose stimulates predominant the vertical locomotor activity.

Key words: adaptogen, plant extract, analgesic effect, hot-plate test, rats.

INTRODUCTION

Medicinal plants have been used from centuries in disease therapy. The presence of more than one active substance in plant extracts support their use for more than one indication. Rhodiola rosea L. is an adaptogen increasing resistance to the harmful effects of various stressors (1). Approximately, 140 compounds have been isolated from the root and the rhizome of Rhodiola rosea L., and these have been classified into different chemical groups. The phenylpropanoid (e.g., rosavin) and phenylethanoid (e.g., salidroside) derivatives are thought to be the most critical constituents needed for the numerous health benefits of Rhodiola rosea L. extracts. It was reported that Rhodiola rosea L. extract administration can improve cognitive function, reduce mental fatigue, promote free radical mitigation, has anti-oxidative, neuroprotective effects and increase endurance performance (2). Nociception is the neural processes of encoding and processing noxious stimuli. Nociception triggers a variety of

autonomic responses and may also result in a subjective experience of pain.

Aim: Our aim was to study the effects of standardized extract of Rhodiola rosea L. on nociception and locomotor activity of rats.

MATERIAL AND METHODS

Male Wistar rats weighing 170-220g were divided into 3 groups (n=8). The rats were kept under standard laboratory conditions in an 8:00 – 20:00 light/dark cycle and provided with food and water ad libitum. The test extract was administered intraperitoneally. The following experimental groups were used: 1st group received saline (0.1ml/100g); 2nd and 3rd group received Rhodiola rosea L. standardized extract 50mg/kg and 100mg/kg respectively. The rats were injected with the extract daily for a month as well as during the test period. The used extract in our study was standardized to 3% rosavins and 1% salidroside. Two nociceptive tests were used – analgesimeter test (Randall-Selitto)^[3] and hot-plate test and locomotor

activity was measured as horizontal and vertical movements in an automatic activity cage.

Locomotor activity test

The original automatic activity cage (Ugo Basile, Italy) with UV detector for horizontal and vertical movements was used. The rats were tested 30 min after i.p. administration of the extract. Each rat had single test for 5 min. The horizontal and vertical movements were measured in relative units.

Analgesimeter test

The original analgesimeter set up (Ugo Basile, Italy) was used. The antinociceptive effect of *Rhodiola rosea* L. was assessed using a mechanical noxious stimulus as previously described by Randall & Sellitto (3). Nociceptive threshold, expressed in grams, was measured in centimeters by applying an increasing pressure to the right hind paw of unrestrained rats until the rat squeaked and/or a struggle was obtained. The accepted “zero time” in this study started 30 min after i.p. administration of the test substance. The rats were tested at 0, 60th, 120th and 180th min.

Hot-plate test

The original hot-plate set up (Ugo Basile, Italy) was used. A transparent glass cylinder was used to keep the rat on the heated surface of the plate. The temperature of the hot plate was set at

55±0.5°C. Latency time was defined as the time between the zero point and the time when animal licked its hind paw or jumped off to avoid thermal pain. The accepted “zero time” in this study started 30 min after i.p. administration of the test substance. To minimize tissue damage, a cut-off time of 30 sec was adopted. The latencies of both forepaws licking or jumping were measured for each animal at 0 and 60th min.

Statistical evaluation

The values obtained were expressed as mean ±S.E.M. The comparison between groups was made by Student's test analysis of variance (ANOVA) in the Excel and Instant computer programs. A value of $p < 0.05$ was considered as a significant difference.

RESULTS

1. Locomotor activity

In activity cage the control group showed mean horizontal activity of 227 units and mean vertical activity of 20 units. Rats treated with the low dose of *Rhodiola rosea* L. standardized extract significantly ($p < 0.05$) increased vertical activity compared to the controls, but did not change the horizontal activity. Rats treated with the high dose of the extract did not change significantly the locomotor activity compared to the control group. (**Figure 1**)

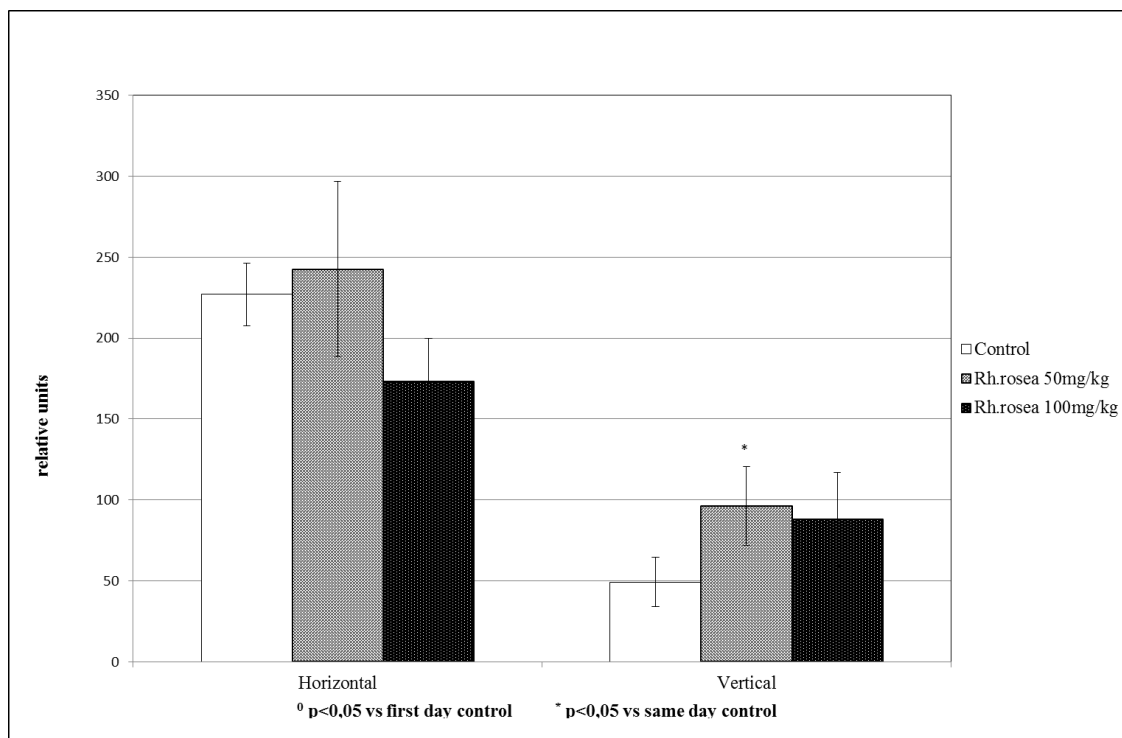


Figure 1. Effect of *Rhodiola rosea* L. standardized extract on locomotor activity test

2. Nociception

In analgesimeter test the control animals showed average pressure reaction between 11 and 15 cm. Rats treated with *Rhodiola rosea* L. in the low dose increased significantly ($p < 0.05$)

the paw reaction on 120th and 180th min of testing compared with the respective control group. The group treated with the high dose of *Rhodiola rosea* L. standardized extract did not change the latency of reaction. (**Figure 2**)

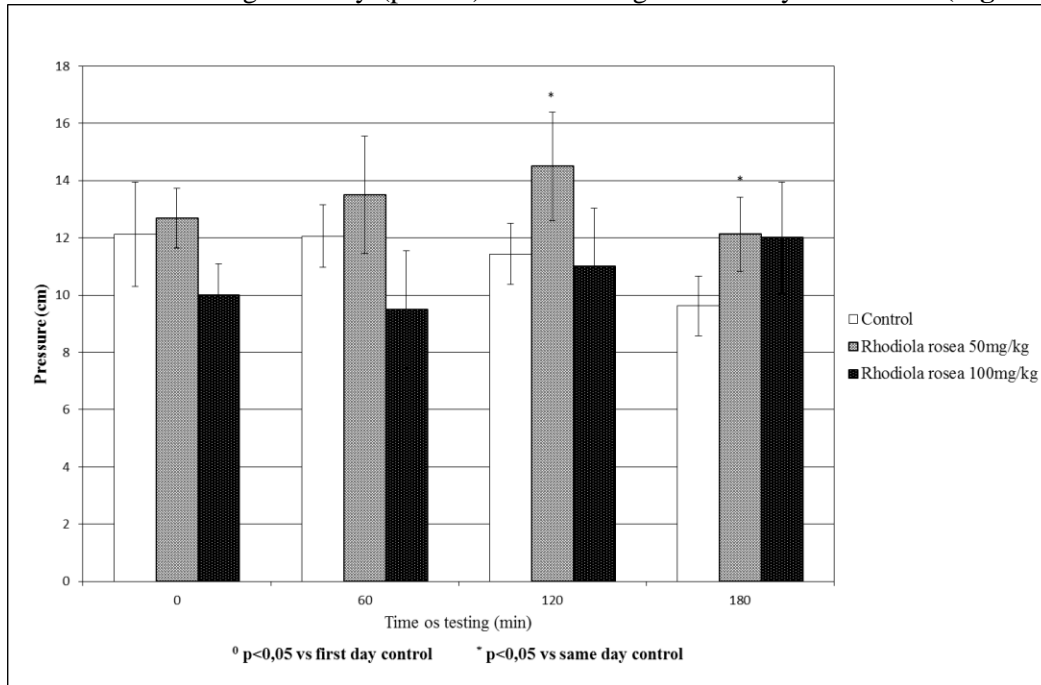


Figure 2. Effect of *Rhodiola rosea* L. standardized extract on analgesimeter test

In hot-plate test the average latency of the controls was between 21 and 26 sec. The animals treated with both doses of *Rhodiola rosea* L. standardized extract increased significantly

($p < 0.05$) the latency of reaction on heated surface compared with the respective control group. (**Figure 3**)

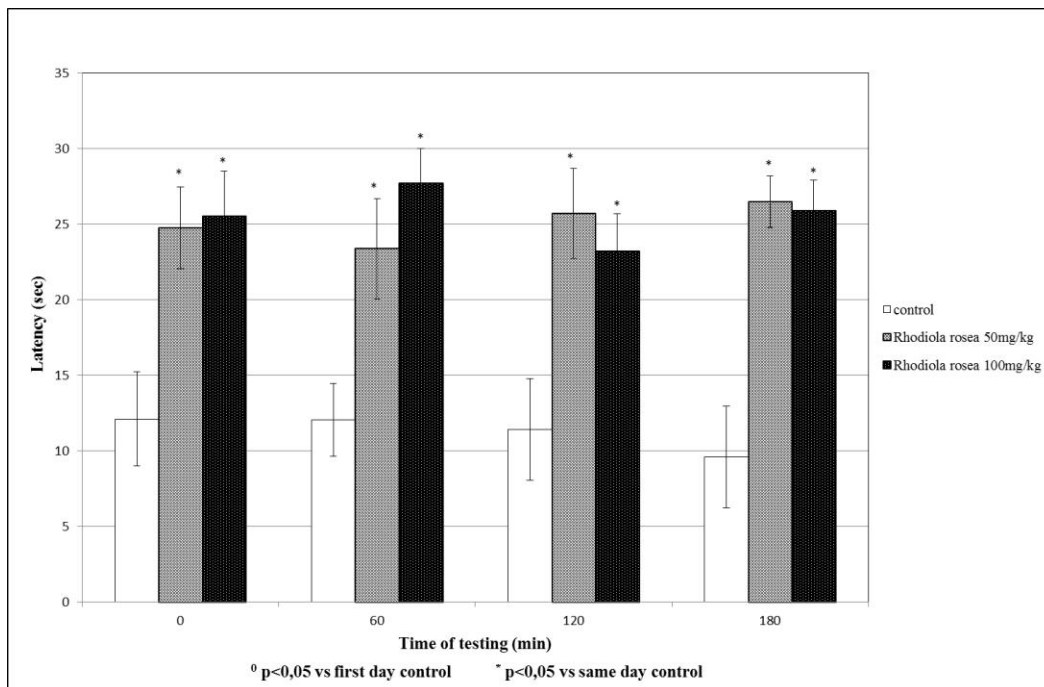


Figure 3. Effect of *Rhodiola rosea* L. standardized extract on hot plate test

DISCUSSION

The use of natural products to help the organism to adapt within the daily stress is a common practice that is increasing within the general population. However, there is a lack of scientific studies to evaluate the exact mechanisms in which adaptogens implement their action. In this study we found that *Rhodiola rosea* L. standardized extract in low dose stimulates predominant the vertical locomotor activity, which suggests the involvement of noradrenergic mechanisms in this effect. Our data also suggest that the studied extract influence nociceptive reactions. The extract exerts in both doses significant ($p < 0.05$) analgesic effect on thermal hyperalgesia assessed with the hot-plate test. On analgesimeter test *Rhodiola rosea* L. standardized extract in the low dose tends to decrease the mechanical pain because it increases the paw pressure reaction on 120th and 180th min of testing. We could speculate that chronic treatment with *Rhodiola rosea* L. in low dose increase the resistance both to mechanical and to thermal stimuli. These could be as a result of stabilization of cell membranes and/or inhibition of pro-inflammatory cytokines` production. Effects of *Rhodiola rosea* have been also associated to an ability to induce opioid peptide biosynthesis and through the activation of both central and peripheral opioid receptors (4). Recent studies in models such as carrageenan and formaldehyde-induced arthritis in rats have shown that *Rhodiola rosea* L. possesses anti-inflammatory activity, possibly by inhibiting phospholipase A₂ and cyclooxygenase-1 and 2.

(5) In conclusion to clarify the exact influence of the studied extract on nociception, more tests should be performed.

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