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# Nootropic Activity of *Rhodiola rosea* Root

Syeda Sanobar*, Dharmendra Ahuja

## Abstract

Nootropic are mediator that enhance the cognitive skills of brain function, Alzheimer's disease, primarily affects the elderly population and is estimated to account for 50–60% of dementia cases in persons over 65 years of age. The present study aimed to evaluate the Nootropic activity of *Rhodiola rosea.* Methanoilc extract of *R. rosea* was used to estimate elevated plus maze (EPM) model in mice, the effect of extract on learning and memory in number of entries open and closed arms using the EPM in mice at a dose of 300 and 500 mg/kg. *R. rosea* extract in EPM showed transfer latency entries, which is indicative of cognition improvement. The results suggested that the treatment of methanolic extract of R. rosea enhances memory in EPM experimental models.

**Keywords:** Elevated plus maze, Nootropic activity, *Rhodiola rosea*

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## Introduction

Memory constitutes one of the elementary functions of brain, brain uses the process of memory to record the experiences that can be utilized to adapt their responses to the environment.[1,2] In spite of numerous attempts and diagnostic tools the pathological evaluation of various diseases affecting the brain is the greatest challenge for modern day scientist and medical professional. Therefore, the background of brain diseases is still poorly defined. One such disease is age-related dementia commonly known as Alzeimer's disease. An estimated 50–60% of world population above the age of 60 years are suffering from this disorder.[3-5]

Nootropic medications are herbs that act on the brain (GkNootropic = acts on the mind) and their extracted phytoconstituents are known as smart medications.[6] "Nootropics" are substances that improve cognitive abilities. Learning and reminiscence ability can be regarded as both a psychological and a synaptic-neural connection shift. Cognitive deficiencies have long been recognized as serious and recurring neurological illnesses linked to a variety of mental and neurodegenerative conditions.[7]

In the family Crassulacea, there are over 200 species belonging to the Rhodiola genus, almost 20 of which are utilized as ethno-medicines in Asia,[8] including *Rhodiola rosea, Rhodiola alterna, Rhodiola brevipetiolata, Rhodiola crenulatia, Rhodiola kirilowia, Rhodiola quadrifida, Rhodiola sachalinens, R. alterna, R. ros*ea plants are found predominantly in the Himalayan stretch, including China, Tibet, and Mongolia, although they are also grown commercially in Europe and North America. Supplements of *R. rosea* are available in the form of pills and juice on the market.[9,10] The terms "golden root" or "roseroot" are commonly used to describe this plant. According to the literature, *R. rosea* has various pharmacological effects. It has been reported to have adaptogenic (anti-stress), hepatoprotective, immune-modulatory, as well as antiviral, anti-inflammatory, and antibacterial activities.[8-11] There are several different types of polyphenols and flavonoids, *as well as* proanthocyanidins and tyrosol and cinnamyl alcohol found *in R. rosea*. There are also glycosides and organic acids, essential oils, sugars, lipids, and alcohols, as well as proteins.[11] Rosavin, cinnamyl alcohol, salidroside, and tyrosol are among the polyphenols found in *R. rosea* plants, and they are the primary active constituents of the plants.[10,11] This investigation's goal was to investigate the effects of a methanolic extract of *R. rosea* on learning and memory in number of entries in mice using the elevated plus maze (EPM) as an a nootropic activity.

Department of Pharmacology, Faculty of Pharmaceutical Science, Jayoti Vidyapeeth Women's University Jaipur, Rajasthan, India

**Corresponding Author:** Syeda Sanobar, Faculty of Pharmaceutical Science, Jayoti Vidyapeeth Women's University Jaipur, Rajasthan, India. Phone: +91-8497907995. E-mail: sanoafnan@gmail.com

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## Materials and Methods

### Collection of Plant Material

Dried roots of *R. rosea* (Golden root) family Crassulaceae were procured from local vendor, Seremban, Negeri Sembilan, Malaysia. Roots are authenticated by Dr. Long chiau Ming, Associated Professor, Deputy Dean Faculty of Pharmacy, Quest international university Perak. (QUIP-RR/02/2019).

### Photochemical Evaluation

The phytoconstituents present in *R. rosea* extracts were determined using a variety of chemical tests performed on the extracts.[12]

### Experimental Animals

Swiss Albino mice weighing between 20 and 25 g were procured from Mahaveer Enterprises Hyderabad. Animals were housed in standard laboratory conditions at 22 ± 25°C with 12 h light-dark cycle with free access to chow and water *ad libitum*. The research protocol was approved by (IAEC/1447/PO/Re/S/11/34/A).

### EPM Method

Swiss albino mice of male and female (20 ± 5 g) were categorized into five groups, containing six animals in each group.

- Group I –Control
- Group II – EPM
- Group III – EPM + *R. rosea* 300 mg/kg, p.o.
- Group IV – EPM + *R. rosea* 500 mg/kg, p.o.
- Group V – EPM+ Piracetam 100mg/kg, p.o.

EPM consists of two opposite open arms (50 × 10 cm) crossed with two enclosed arms of the same dimensions with 40 cm high walls. The arms were connected with a central square (10 × 10 cm) to give the apparatus a plus sign appearance. All arms are joined centrally in a square. All the walls and base are colored with black paint and placed in soundproof room. During the assessment, rodents were placed with their head facing open arms. During the whole experimentation, trouble from external stimuli is avoided which may cause anxiety.

The calculations were made for meantime given in the open arms, number of entries open arm using formula-[100×open/(open+enclosed)] and (100×open/total entries), respectively.

One hour after administration of vehicle, extracts of *R. rosea* were assessed for memory enhances or behavior studies using EPM test. Extracts were used a dose of 300 and 500 respectively for 30 successive days. In a room with poor lighting condition, the maze was placed above 50 cm above the ground level. Each mice were separately retained at the end of exposed (open) arm directed away from the center. Transfer latency (TL) which is time taken by the experimental animal to enter the unexposed (closed) are from the exposed arm was then recorded. The mice were allowed to stay in the unexposed (closed) arm for up to 15 Sec and then retained to their cages. The same procedure was repeated on 3rd, 7th, 14th day 21st and 28th day post drug administration. TL was recorded on each afore mentioned day.[13-15]

### Statistical Analysis

The data were analyzed using a statistical package of social version 19.0 (SPSS) software. Descriptive statistics were used to present data in terms of mean ± SEM followed by Tukey's Multiple Comparison Test *post hoc* test. Analyzed data was using Graph Pad Prism software (version 8.4.2 V; SanDiego, CA). The *P*-value are reported as mean ± Score data expressed in terms of mean ± S.E.M, $n = 6$. followed by Tukey multiple comparison test, $^{a}P < 0.001$, $^{b}P < 0.01$, $^{c}P < 0.05$.

## Results and Discussion

Primilanary phytochemical study of *R. rosea* extract shows presence of various secondary metabolites such as Phytosteroids, alkaloids, glycoside, flavonoids, terpenoids, Vitamins, and tannins.

### Elevated Plus Maze (EPM) for *R. rosea*

EPM is an improvement of memory in cognitive deficit and this test was specific for selective attention, the mice treated with normal saline spent additional time in close arms on 0 day (4.57 ± 0.31), 14th, 21st and 28 days (5.14 ± 0.56, 5.74 ± 0.31 and 5.74 ± 0.31) animal are exposed to EPM significantly decreased close arms entries on 3 days, 7–28 day (7.14 ± 0.28, 1.31 ± 0.11 and 1.51 ± 0.14) entries in closed arm during 5 min of time period. treatment with methanolic extract of *R. rosea* a 300 and 500, in close arms on 0 day (4.41 ± 1.21), 14th, 21st and 28 days (6.58 ± 1.61, 3.42 ± 0.36 4.32 ± 0.16, 7.21 ± 0.12, 5.16 ± 1.31 and 6.31 ± 0.17) significantly increased close arms entries on 3 day, 7–28 day, boost during the proportion of number in close arm entries As shown in [Table 1 and Figure 1].

The mice treated with normal saline spent additional time in open arms on 0 day (1.11 ± 0.21), 14th, 21st and 28 days (0.58 ± 0.26, 0.74 ± 0.69, and 0.66 ± 0.38) animal are exposed to EPM significantly increased open arms entries on 3 days, 7–28 day (1.58 ± 0.32, 4.87 ± 1.85 and 4.72 ± 1.14) entries in open arm during 5 min of time period. treatment with methanolic extract of *R. rosea* a 300 and 500 in open arms on 0 day (1.24 ± 0.64, 1.38 ± 0.57), 14th, 21st and 28 day (0.45 ± 0.14, 0.32 ± 0.20, 0.67 ± 0.79, 0.75 ± 0.34, 0.62 ± 0.40 and 0.85 ± 0.54) significantly decreased open arms entries on 3 day, 7–28 day, boost in the proportion of number of open arm entries. Time spent in open arm whereas, in the closed arm number of entries and time spent was appreciably ($P < 0.01$) vehicle-treated extract as shown in [Table 2 and Figure 2].

Memory formation is a multi-step process involving numerous neural transmitters and neurotransmitters. ACh is a neurotransmitter found in the cholinergic neural system that plays a key part in human and animal memory.[16] EPM performance is a satisfying motivation test that can be used to evaluate spatial reference and spatial working memory.[17] Even during the last minutes of the first trial, the mice convert from initial maze exploration to learned avoidance of the open arms, and change into an acquired phobic-like state after a later, second exposure to

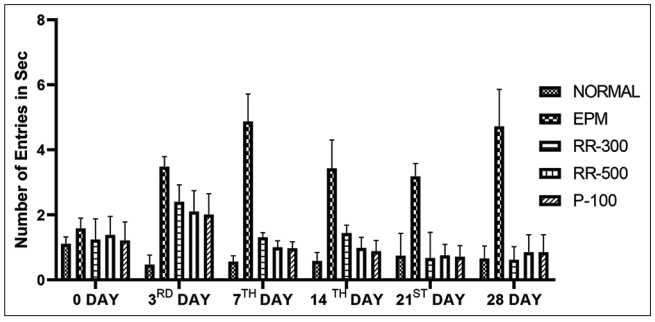


**Figure 1:** Effects of *Rhodiola rosea* in open arm entries on elevated plus maze

**Table 1:** Effect of *Rhodiola rosea* on number of entries in open arm

| Groups | Number of entries in open arm | | | | | |
|---|---|---|---|---|---|---|
| | 0 Day | 3rd Day | 7th Day | 14th Day | 21st Day | 28th Day |
| | OA | OA | OA | OA | OA | OA |
| Normal | 1.11±0.21 | 0.47±0.29 | 0.56±0.18 | 0.58±0.26 | 0.74±0.69 | 0.66±0.38 |
| EPM | 1.58±0.32 | 3.48±0.31[b] | 4.87±1.85[c] | 3.43±0.87[a] | 3.18±0.40[a] | 4.72±1.14[a] |
| RR- 300 mg/kg | 1.24±0.64 | 1.51±0.52[ns] | 0.45±0.14* | 1.44±0.24* | 0.67±0.79*** | 0.62±0.40*** |
| RR- 500 mg/kg | 1.38±0.57 | 2.40±0.64[ns] | 0.32±0.20* | 1.71±0.33*** | 0.75±0.34*** | 0.85±0.54*** |
| Piracetam -100 | 1.36±0.54 | 1.38±0.57 | 1.38±0.57** | 1.38±0.57** | 1.38±0.57*** | 1.38±0.57*** |

All the values are mean±SEM, $n$=6, followed by multiple comparison Tukey's test, ns: Not significant,*$P$<0.05, **$P$<0.01, ***$P$<0.001, versus EPM and versus normal group

**Table 2:** Effect of *Rhodiola rosea* on number of entries in closed arm

| Groups | Number of entries in closed arm | | | | | |
|---|---|---|---|---|---|---|
| | 0 Day | 3rd Day | 7th Day | 14th Day | 21st Day | 28th Day |
| | CA | CA | CA | CA | CA | CA |
| Normal | 4.57±0.31 | 4.12±0.88 | 4.32±0.44 | 5.14±0.56 | 5.74±0.31 | 4.71±0.53 |
| EPM | 7.14±0.28 | 3.14±0.55$^{ns}$ | 4.11±0.12$^{ns}$ | 1.18±0.45$^{c}$ | 1.31±0.11$^{b}$ | 1.51±0.14$^{b}$ |
| RR- 300 mg/kg | 3.29±1.21 | 3.42±1.50$^{ns}$ | 4.51±1.81$^{ns}$ | 5.28±1.61* | 5.38±0.16* | 5.96±1.31* |
| RR 500 mg/kg | 3.42±0.36 | 4.15±0.33$^{ns}$ | 5.31±1.32$^{ns}$ | 5.61±0.12** | 5.75±1.10* | 6.31±0.17** |
| Piracetam- 100 | 3.42±0.36 | 3.42±0.36 | 3.42±0.36 | 3.42±0.36 | 3.42±0.36 | 3.42±0.36 |

All the values are mean±SEM, $n$=6, followed by multiple comparisons Tukey's test, ns: Not significant, *$P$<0.05, **$P$<0.01, ***$P$<0.001, versus EPM and $^{a}P$<0.001, $^{b}P$<0.01, $^{c}P$<0.05 versus normal group

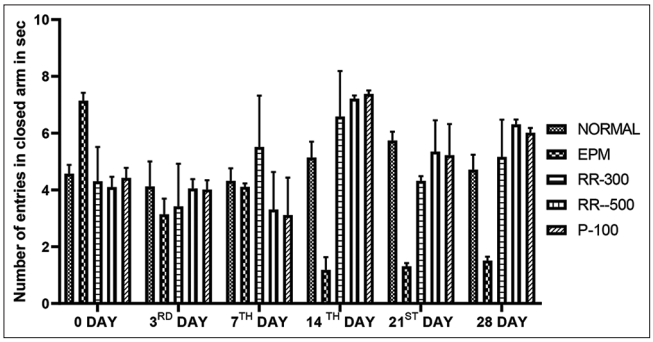


**Figure 2:** Effects of *Rhodiola rosea* extracts on closed arm enteries in elevated plus maze

the EPM.[18,19] Furthermore, because the arms have been explored and the avoidance of the exposed parts has been taught, the initial motivating approach/avoidance conflict scenario is lessened in a second exposure to the maze. With the second trial in closed arm, introducing a motivational conflict was able to keep the exploration at the initial level.[20] The study's findings clearly showed that the percent number of entries, number of entries in open arm and closed arm activity, and the number of entries in open arm and closed arm activity all indicated memory loss in the EPM-induced group, indicating that sleep deprivation causes disorders that are irreversible. Piracetam has an effect on NMDA glutamate receptors which are involved with learning and memory processes. Piracetam, which is a derivative of GABA, plays an important role in cognitive function. Many neural system accommodations take place in the chronic neurological deficit situation which may not be present in the acute deficit. In chronic deficits, it is critical to test the chronic efficacy of the drug to determine possible tolerance development or induction of a persisting effect.

## Conclusion

Increasingly, consumers prefer natural nootropics since they are more convenient and less expensive. Currently, there is a huge global push to explore medicinal plants for boosting cognitive function and owing to its less adverse effects. *R. rosea* has gained popularity as a medicinal herb and has been used in Chinese medicine for its adaptogenic properties. This research study was aimed at investigating the nootropic effect of *R. rosea* extracts. Besides, the extracts were evaluated for potential phytoconstituent effective against plays an important role in cognitive function, many neural system accommodation stake place in the chronic neurological deficit situation which may not be present in the acute deficit effects of the extracts may be ascribed to the presence of various phytoconstituent including alcohol derivatives, flavonoids, and phenolic compounds, polyphenol includes Rosavin, cinnamyl alcohol, salidroside and tyrosol major components, a variety of glycosides and the essential oils.

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