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## COMPARISON ANXIOLYTIC-LIKE EFFECTS OF VALERIANA SISYMBRIFOLIA IN THE MALE AND FEMALE RATS

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### Abstract

**Introduction:** Anxiety is a common disorder that a lot of people suffer from it and accompanies physiologic symptoms such as tachycardia, perspiration disorders, lack of sense and sometimes paralysis of limbs etc.

**Method:** This study was carried out to compare the anxiolytic effects of herbal tea of Valerianasisymbriifolia between male and female rats. In order to do this, 14 male rats weighing 150 to 200 grams were divided into two groups including control1, treatment1 (treated rats by herbal tea Valerian sisymbriifolia) and 14 female rats weighing 100 to 150 grams were divided into two groups including control2, treatment2(treated rats by herbal tea Valerian sisymbriifolia). Treatment groups rats (n = 7/group) had ad libitum access to the tea from Valerianasisymbriifolia 0.3% (w/v), for a period of 24 hours before test. Then, the behavior of rats was tested in order to sedative (locomotors activity) and anxiolytic (elevated plus maze) activity. All the data were given as Means  $\pm$ S.E.M. Data were analyzed by one-way ANOVA following by Tukey test.

**Finding:** The study revealed that anxiolytic effect of herbal tea of Valerianasisymbriifolia in male rats is stronger than female rats.

**Keywords:** Anxiety; Anxiolytic; Valerianasisymbriifolia; Rat; Elevated plus maze

### Introduction

Pathological anxiety is one of the most common emotional disorders and treatment of phobias or panic attacks is still not trivial. Pharmacological treatment plays an important role in the therapeutic concept Benzodiazepines have been the most widely used anxiolytics in general practice for many years (Holm, 1988) and are relatively safe drugs for a short term treatment of anxiety despite their drug dependence potential and side effects (Ballinger, 1990; Lader, 1999).

However, the realization that benzodiazepines present a narrow safety margin between the anxiolytic effect and those causing unwanted side effects has prompted many research to evaluate new compounds in the hope that other anxiolytic drugs will have less undesirable effects (Griffiths, Lamb, Ator, Roache, & Brady, 1985; Grundmann, Nakajima, Seo, & Butterweck, 2007). There are so many herbal teas to have anxiolytic effects. *Valerianasisymbrifolia* L. (Valerianaceae family) is a medicinal plant used in complementary and alternative medicine for its sedative and anxiolytic properties. Valerian's effects on the central nervous system have been well documented and attributed to many of its active compounds: valepotriates, baldrinals, valerenic acid, valeranal and valeranone, and other constituents in the essential oils (Bent, Padula, Moore, Patterson, & Mehling, 2006; Cavadas et al., 1995; Dietz, Mahady, Pauli, & Farnsworth, 2005; Houghton, 1999; Khom et al., 2007; Leathwood & Chauffard, 1985; Miyasaka, Atallah, & Soares, 2006). The anxiolytic properties of valerian have been demonstrated in animals (Hattesoehl et al., 2008; Murphy, Kubin, Shepherd, & Ettinger, 2010). This study evaluated the anxiolytic effects *Valerianasisymbrifolia* in male rats in compared to female rats.

## **Materials and Methods**

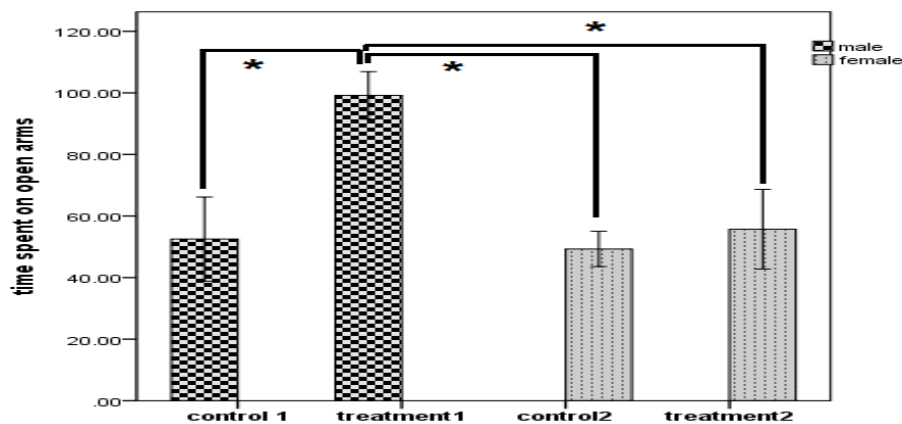
This was an experimental study in which 14 male wistar rats weighing 150 to 200 grams and 14 female rats weighing 100 to 150 grams were randomly selected and tested. All animals were housed under standard environmental conditions of temperature, relative humidity and light (at  $23 \pm 2$  °C, 40—60% humidity, 12 h light: 12 h dark cycle (lights on at 08:00 h)). The *Valerianasisymbrifolia* rhizome powder was used for this study male rats were divided into two groups including control1, treatment1 (treated rats by herbal tea valerian *sisymbrifolia*) and also female rats were divided into two groups including control2, treatment 2 (treated rats by herbal tea *Valerianasisymbrifolia*). Treatment groups rats (n = 7/group) had ad libitum access to the tea of *Valerianasisymbrifolia* 0.3% (w/v) for a period of 24 hours before test. Then, the behavior of rats was tested in order to sedative (locomotor activity) and anxiolytic (elevated plus maze) activity. Elevated plus maze (EPM) is made up of wood and includes two open arms (each 50×10 cm) and two closed arms (each 50× 10 × 40 cm) and a central plate (10 ×10 cm). Open and closed arms are across from each other and are located 50 cm above the floor of the room. This is an experimental non-conditional anxiety testing model and does not require any animal training and learning (Miladi-Gorji, Vafaei, Rashidy-Pour, Taherian, & Jarrahi, 2007; MILADI, RASHIDIPOUR, VAFAEI, & TAHERIAN, 2008). In the day of the test, the animals were transferred to the laboratory in the

afternoon between 17:00 p.m. and 21:00p.m, and then in order to test the anxiety level , the animal was located in an elevated plus-maze (in the plate and across from the open arm) and the important anxiety behavior indices including the number of entrances to open and closed arms and the time of staying in open and closed arms were tested and recorded for 5 minutes (Miladi-Gorji et al., 2007; MILADI et al., 2008; Pellow, Chopin, File, & Briley, 1985; Pellow & File, 1986; Tsuda, Suzuki, Misawa, & Nagase, 1996; Zhang & Schulteis, 2008). The total number of entrances into two arms are considered as a locomotor activity (Clément et al., 2007). The statistical analysis of data was performed by one-way analysis of variance (ANOVA) followed by Tukey post hoc analysis. In all cases differences were considered significant if  $p < 0.05$ .

### Findings of the study

ANOVA following by Tukey test showed that there is a significant difference in rats behavior on time spent in open arms of EPM between treatment 1 compared to other groups. But time spent on open arms in the treatment 2 group compared to control group was not significantly (Diagram 1). The number of entries into the open arms in treatment 2 increased significantly (Diagram 2). Time spent on closed arms for treated group by Herbaltea of Valerianasisymbrifolia (treatment 1) decreased significantly in compared to control 2 group (Diagram 3). Number of closed arms entries and total number of open and closed arms increased in male rats but not significantly (Diagram 4, 5).

### Diagrams



**Diagram 1: shows the period of staying in open arms for treatment 1 group is significantly more than the other groups using ANOVA following by Tukey test.**

\*: shows the significant difference ( $P < 0.05$ )

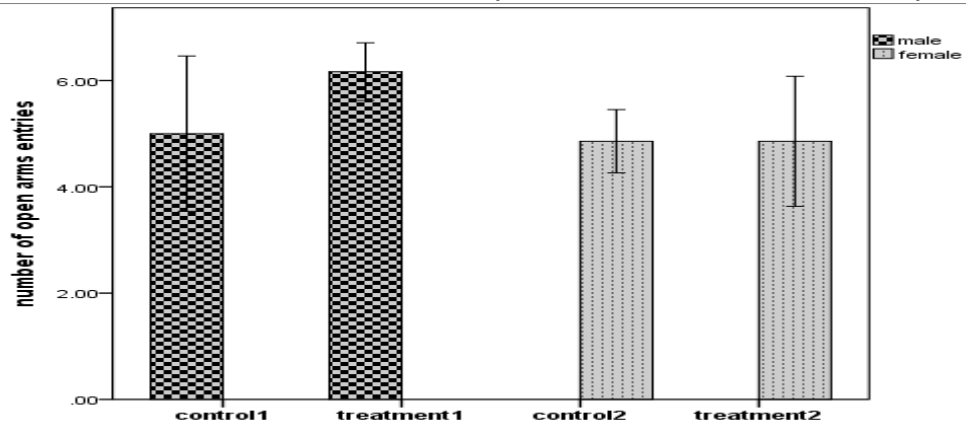


Diagram 2: shows the number of entrances into the open arms.

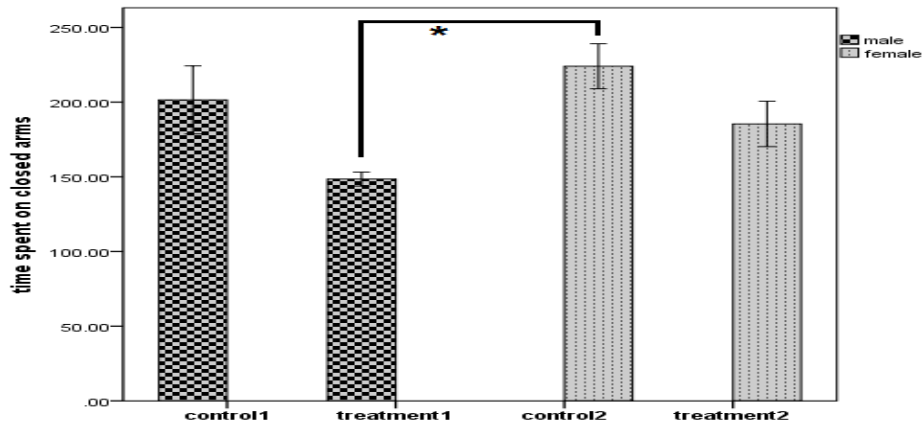


Diagram 3: shows that the period of staying in closed arms for treatment1 group is significantly less than the control2 group using ANOVA following by Tukey test.

\*: shows the significant difference (P<0.05)

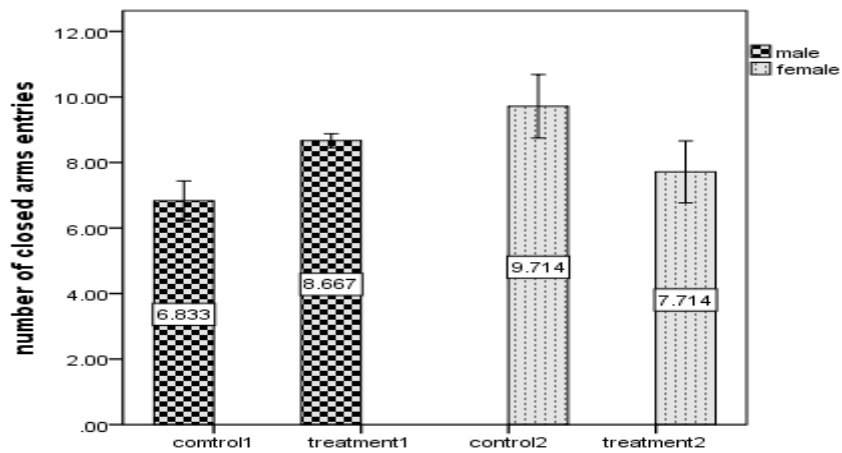
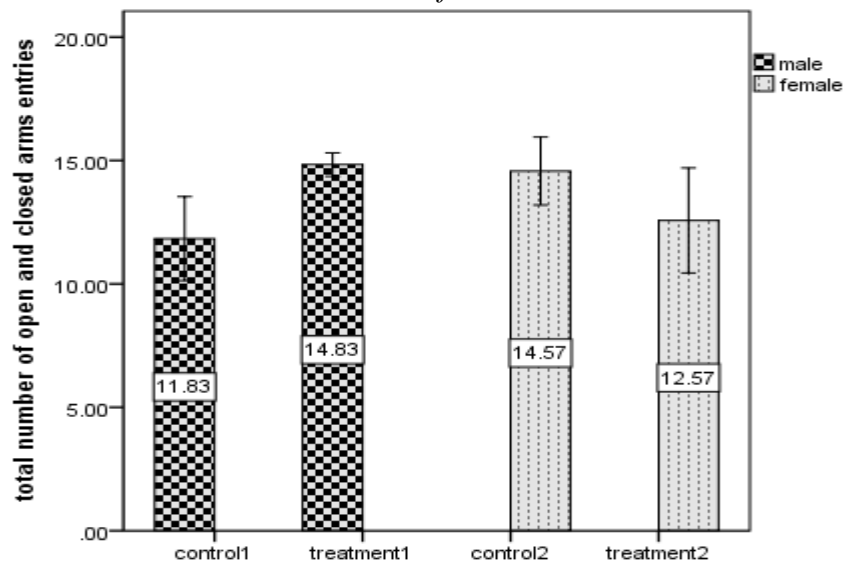


Diagram 4: shows that the number of entrances into closed arms.



**Diagram 5: shows the total number of entrances into open and closed arms.**

## Discussion

An increase of the time and the proportion of the entrances into the open arms without a changed locomotor activity is regarded as a powerful marker for an anxiolytic substance effect (Pellow et al., 1985). Close arm entries are selectively correlated with the locomotor activity (Rodgers & Johnson, 1995). The drugs that cause stimulation and increase the locomotor activity were reported to increase number of close arm entries (Varty et al., 2002). In the elevated plus maze, an anxiolytic or anxiogenic-like effect is evaluated by the relation of entries into open arm and the time spent on the open arms of the plus maze in comparison to the same parameters of the control group. An increase of the time spent and number of entries into the open arm without changed locomotor activity was regarded as a powerful marker for the anxiolytic effect (Pellow et al., 1985). The enhancement of total arm entries might suggest a nonspecific locomotor stimulant effect which is the co-load on “locomotor activity” and “anxiety”, whereas close arm entries load highly and selectively on locomotor activity (Espejo, 1997; Rodgers & Johnson, 1995). Increase time spent in open arm, percent entries in open arm, total entries and closed arm entries indicated anxiolytic effect. The present study showed the treated groups by of Herbal tea of Valerianasisymbrifolia in male rats induced anxiolytic behavior and did not increase locomotor activity and this indicate Herbal tea of Valerianasisymbrifolia has anxiolytic effects. But indices of anxiety behavior in the elevated plus maze in the female rats did not show anxiolytic effects. Previous studies showed the binding of valerian extract to GABAA receptors in rat cortical membrane preparation (Cavadas et al., 1995). It has been shown that valerian extract, aqueous or hydroalcoholic, contained GABA and other amino acids that could displace labeled

muscimol(Cavadas et al., 1995) , suggesting that specific constituents of valerian extract can directly bind to GABAA receptors. The GABA content of valerian extract could also be responsible for the stimulated release and reuptake of GABA. This could be an indirect mechanism of GABA agonistic activity of valerian extract (M. Santos et al., 1993; M. S. Santos, Ferreira, Cunha, Carvalho, & Macedo, 1994). Additionally, derivatives of valerenic acid inhibit the local catabolism of GABA by inhibition of the enzyme GABAse, which could also increase GABA concentration (Riedel, Hänsel, & Ehrke, 1982). These mechanisms might have been operational in our *in vitro* brainstem model, but in *in vivo* models, the role of exogenous GABA in producing central nervous system (CNS) sedative effects is questionable because of the very low permeability of GABA across the blood-brain barrier (Cavadas et al., 1995). The significance of the inhibition of GABA catabolism by valerenic acid derivatives in *in vivo* models is not yet known. But in this study valerian in the female rats had not anxiolytic effects. The previous studies have showed anxiolytic effects of valerian in female rats(Murphy et al., 2010). Perhaps this contradiction is because of the role of sex hormones or age of animal.However, more research is needed to investigate anxiolytic effects of valerian in the female rats.

## Results

The results of this study showed that Herbal tea of Valerianasisymbrifolia in male rats has anxiolytic effects,significantly,compared to controlgroup. But it was not significantly in the female rats.

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