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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 ofvaleriana sisymbrifolia 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 sisymbrifolia) and 14 female rats weighing 100 to 150 gramswere divided into two groups including control2, treatment2(treated rats by herbal tea valerian sisymbrifolia). Treatmentgroups rats (n = 7/group) had ad libitum access to the tea from valerianaSisymbrifolia0.3% (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. All the data were given as Means±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 valeriana sisymbrifoliain male rats is stronger thanfemale rats.

Keywords: Anxiety; Anxiolytic; valeriana sisymbrifolia; 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. Valeriana sisymbrifolia 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, valerenal 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 (Hattesohl et al., 2008; Murphy, Kubin, Shepherd, & Ettinger, 2010).This study evaluated the anxiolytic effectsvaleriana Sisymbrifoliain male rats in compared to female rats.

Materials and Methods

This was an experimental study in which 14 maleWistar rats weighing 150 to 200 grams and 14 female rats weighing 100 to 150 gramswere randomly selected and tested. All animals were housed under standard environmental conditions of temperature, relative humidity and light (at23±2 °C, 40—60% humidity, 12 h light: 12 h dark cycle (lights on at 08:00 h).The valeriana sysimbrifolia rhizome powder was used for this study.male ratswere 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, treatment2(treated rats by herbal tea valerian sisymbrifolia).Treatment groups rats (n = 7/group) had ad libitum access to the tea of valerianasisymbrifolia0.3% (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

afternoonbetween 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 wasperformed by one-way analysis of variance (ANOVA)followed by Tukey post hoc analysis. In all cases differences wereconsidered 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 treatment1compared to other groups. But time spent on open arms in the treatment2 group compared tocontrol group was not significantly(Diagram1). The number of entries into the open arms in treatment 2 increasedsignificantly (Diagram 2). Time spent on closed arms for treated group by Herbaltea ofvaleriana sisymbrifolia (tratment1)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 ratsbut not significantly (Diagram 4, 5).

Diagrams

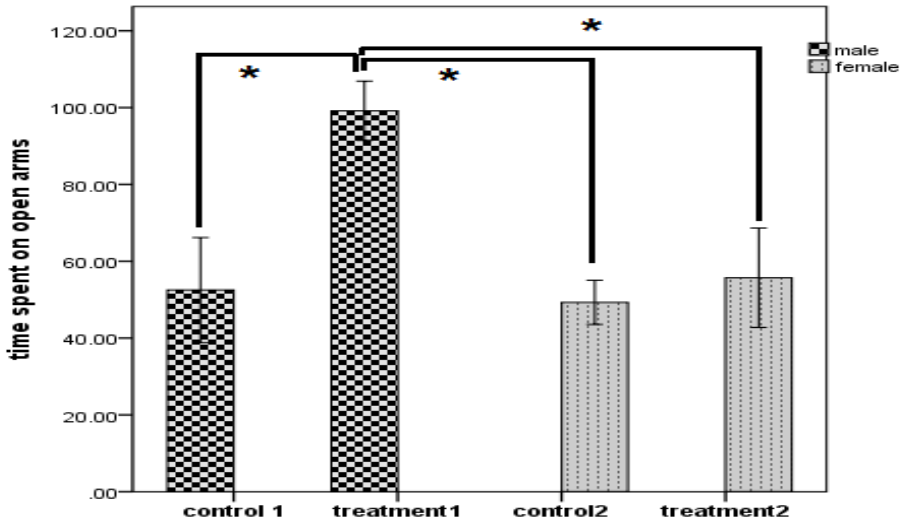

Diagram 1: Shows the period of staying in open arms for treatment1 group is significantly more than the other groups using ANOVA following by Tukey test

*: shows the significant difference (P<0.05)

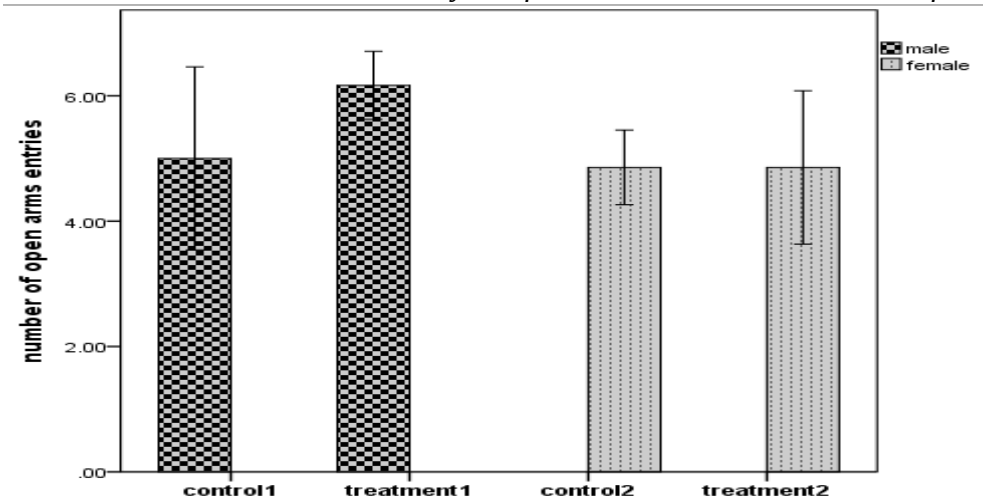

Diagram 2: Shows the number of entrances into the open arms

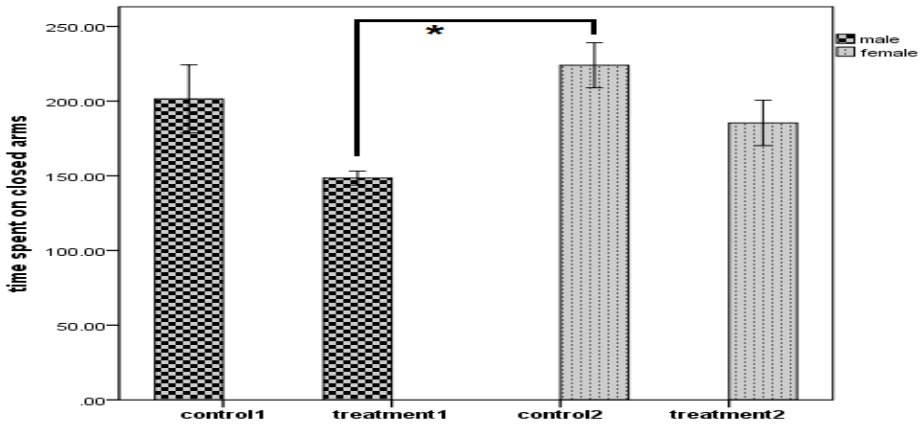

Diagram 3: Shows that the period of staying in closed arms for treatment1 group is significantly less than the control2 group using ANOVA following by Tukey test

*: shows the significant difference (P<0.05)

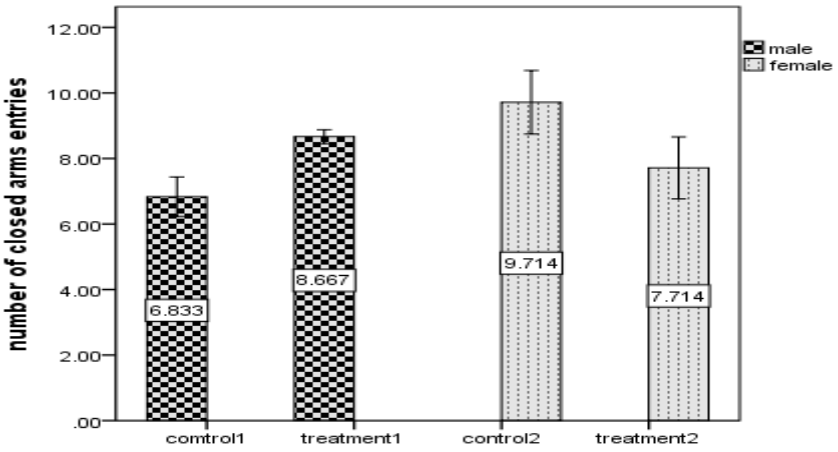

Diagram 4: Shows that the number of entrances into closed arms

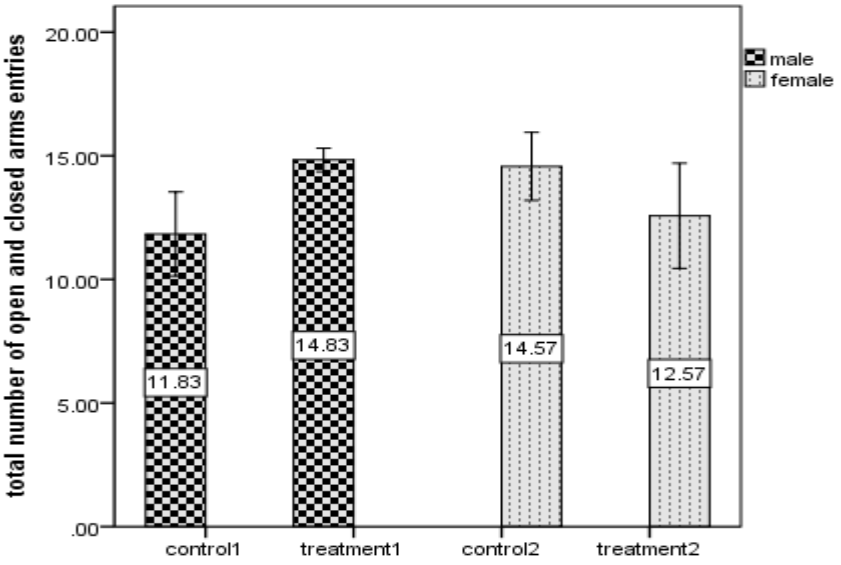

Diagram 5: Shows the total number of entrances into open and closed arms

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 valerian sisymbrifolia in male rats induced anxiolytic behavior anddid not increase locomotor activity and this indicate Herbal tea of valeriana sisymbrifolia has anxiolytic effects. Butindicesofanxietybehavior 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 therole 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 Valeriana sisymbrifolia in male rats has anxiolytic effects, significantly, compared to control group. But it was not significantly in the female rats.

References

1. Ballinger, B. R. (1990). New drugs. Hypnotics and anxiolytics. *BMJ: British Medical Journal, 300*(6722), 456.
2. Bent, S., Padula, A., Moore, D., Patterson, M., & Mehling, W. (2006). Valerian for sleep: a systematic review and meta-analysis. *The American journal of medicine, 119*(12), 1005-1012.
3. Cavadas, C., Araujo, I., Cotrim, M., Amaral, T., Cunha, A., Macedo, T., & Ribeiro, C. F. (1995). In vitro study on the interaction of Valeriana officinalis L. extracts and their amino acids on GABAA receptor in rat brain. *Arzneimittel-Forschung, 45*(7), 753-755.
4. Clément, Y., Joubert, C., Kopp, C., Lepicard, E. M., Venault, P., Misslin, R., . . . Chapouthier, G. (2007). Anxiety in mice: a principal component analysis study. *Neural plasticity, 2007*.
5. Dietz, B. M., Mahady, G. B., Pauli, G. F., & Farnsworth, N. R. (2005). Valerian extract and valerenic acid are partial agonists of the 5-HT 5a receptor in vitro. *Molecular Brain Research, 138*(2), 191-197.

6. Espejo, E. F. (1997). Structure of the mouse behaviour on the elevated plus-maze test of anxiety. *Behavioural brain research, 86*(1), 105-112.
7. Griffiths, R. R., Lamb, R. J., Ator, N. A., Roache, J. D., & Brady, J. V. (1985). Relative abuse liability of triazolam: experimental assessment in animals and humans. *Neuroscience & Biobehavioral Reviews, 9*(1), 133-151.
8. Grundmann, O., Nakajima, J.-I., Seo, S., & Butterweck, V. (2007). Anti-anxiety effects of Apocynum venetum L. in the elevated plus maze test. *Journal of ethnopharmacology, 110*(3), 406-411.
9. Hattesohl, M., Feistel, B., Sievers, H., Lehnfeld, R., Hegger, M., & Winterhoff, H. (2008). Extracts of Valeriana officinalis L. sl show anxiolytic and antidepressant effects but neither sedative nor myorelaxant properties. *Phytomedicine, 15*(1), 2-15.
10. Holm, M. (1988). Prescription of benzodiazepines in general practice in the county of Arhus, Denmark. *Danish medical bulletin, 35*(5), 495-499.
11. Houghton, P. J. (1999). The scientific basis for the reputed activity of Valerian. *Journal of Pharmacy and Pharmacology, 51*(5), 505-512.
12. Khom, S., Baburin, I., Timin, E., Hohaus, A., Trauner, G., Kopp, B., & Hering, S. (2007). Valerenic acid potentiates and inhibits GABA A receptors: molecular mechanism and subunit specificity. *Neuropharmacology, 53*(1), 178-187.
13. Lader, M. H. (1999). Limitations on the use of benzodiazepines in anxiety and insomnia: are they justified? *European Neuropsychopharmacology, 9*, S399-S405.
14. Leathwood, P., & Chauffard, F. (1985). Aqueous extract of valerian reduces latency to fall asleep in man. *Planta medica, 51*(02), 144-148.
15. Miladi-Gorji, H., Vafaei, A., Rashidy-Pour, A., Taherian, A., & Jarrahi, M. (2007). Emami abarghoii M, Sadegi H. Anxiolytic Effects of the aqueous extracts of Portulaca Oleracea in mice. *J. Medicinal Plants*, *19*(5), 23-28.
16. MILADI, G. H., RASHIDIPOUR, A., VAFAEI, A. A., & TAHERIAN, A. A. (2008). The role of morphine dependence on the level of anxiety in Rat.
17. Miyasaka, L. S., Atallah, Á. N., & Soares, B. (2006). Valerian for anxiety disorders. *The Cochrane Library*.
18. Murphy, K., Kubin, Z., Shepherd, J., & Ettinger, R. (2010). Valeriana officinalis root extracts have potent anxiolytic effects in laboratory rats. *Phytomedicine, 17*(8), 674-678.

19. Pellow, S., Chopin, P., File, S. E., & Briley, M. (1985). Validation of open: closed arm entries in an elevated plus-maze as a measure of anxiety in the rat. *Journal of neuroscience methods, 14*(3), 149-167.
20. Pellow, S., & File, S. E. (1986). Anxiolytic and anxiogenic drug effects on exploratory activity in an elevated plus-maze: a novel test of anxiety in the rat. *Pharmacology Biochemistry and Behavior, 24*(3), 525-529.
21. Riedel, E., Hänsel, R., & Ehrke, G. (1982). Inhibition of γ-aminobutyric acid catabolism by valerenic acid derivatives. *Planta medica, 46*(12), 219-220.
22. Rodgers, R., & Johnson, N. (1995). Factor analysis of spatiotemporal and ethological measures in the murine elevated plus-maze test of anxiety. *Pharmacology biochemistry and behavior, 52*(2), 297-303.
23. Santos, M., Ferreira, F., Cunha, A., Carvalho, A., Ribeiro, C., & Macedo, T. (1993). Synaptosomal GABA release as influenced by valerian root extract--involvement of the GABA carrier. *Archives internationales de pharmacodynamie et de thérapie, 327*(2), 220-231.
24. Santos, M. S., Ferreira, F., Cunha, A. P., Carvalho, A. P., & Macedo, T. (1994). An aqueous extract of valerian influences the transport of GABA in synaptosomes. *Planta medica, 60*(03), 278-279.
25. Tsuda, M., Suzuki, T., Misawa, M., & Nagase, H. (1996). Involvement of the opioid system in the anxiolytic effect of diazepam in mice. *European journal of pharmacology, 307*(1), 7-14.
26. Varty, G. B., Cohen-Williams, M. E., Morgan, C. A., Pylak, U., Duffy, R. A., Lachowicz, J. E., . . . Coffin, V. L. (2002). The gerbil elevated plus-maze II: anxiolytic-like effects of selective neurokinin NK1 receptor antagonists. *Neuropsychopharmacology, 27*(3), 371-379.
27. Zhang, Z., & Schulteis, G. (2008). Withdrawal from acute morphine dependence is accompanied by increased anxiety-like behavior in the elevated plus maze. *Pharmacology Biochemistry and Behavior, 89*(3), 392-403.