ARTICLE

INVESTIGATION ANXIOLYTIC EFFECTS OF HERBAL TEA OF VALERIANA SISYMBRIFOLIA VAHL. COMPARED TO LAVANDULA ANGUSTIFOLIA ON THE FEMALE RATS

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ABSTRACT

Introduction: *Anxiety is a natural human reaction that involves both mind and body. Anxiety is defined by a diffuse, unpleasant, vague sense of apprehension. It is often concomitant with autonomic symptoms, such as perspiration, palpitations, headache, and tightness in the chest.* ***Method:*** *This study was carried out to compare the anxiolytic effects of the herbal tea of Lavandula angustifolia versus Valeriana sisymbrifolia and these effects were assessed and compared to the control group. In order to do this, 21 female rats weighing 100 to 150 grams were applied. The rats were divided into three groups including control, VS (treated group by Herbal tea of Valeriana sisymbrifolia) and LA (treated group by Herbal tea of Lavandula angustifolia). Treatment groups (n = 7/group) had ad libitum access to the tea from Valeriana sisymbrifolia 0.3% (w/v) for VS Group and tea from Lavandula angustifolia 0.3% (w/v) for LA Group , during a period of 24 hours before the 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 analysed by one-way ANOVA following by Tukey test.* ***Finding:*** *The study indicated that the anxiolytic effect of the herbal tea of Lavandula angustifolia is stronger than herbal tea of Valeriana sisymbrifolia on the female rats.*

Keywords:
Anxiety; Anxiolytic; Valerian sisymbrifolia; Lavandula angustifolia; Rat; X-maze

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INTRODUCTION

Anxiety is a natural human reaction that involves both mind and body [1]. Anxiety is defined by a diffuse, unpleasant, vague sense of apprehension. It is often concomitant by autonomic symptoms, such as perspiration, palpitations, headache, and tightness in the chest [2]. Pharmacological treatment plays an important role in the therapeutic concept Benzodiazepines have been the most widely used anxiolytics in general practice for many years [3] and are relatively safe drugs for a short term treatment of anxiety despite their drug dependence potential and side effects [4, 5]. 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 [6, 7]. There are so many herbal teas to have anxiolytic effects. *Lavandula angustifolia* (LA) is part of the Labiatae family and belongs to the Lavender genus which is a natural growth in the Mediterranean region [8]. Lavender is reported to be an effective medical plant treating inflammation, depression, stress, seizure and of migraine headache [9-11]. Lavender is also reported to be an effective medical plant in treatment of restlessness in case of anxious mood. Intake administration of LA has been shown to the anxiolytic effect in clinical studies [12-14]. *Valeriana sisymbrifolia* (VS) (Valerianaceae family) is a medicinal plant used in complementary and alternative medicine for its sedative and anxiolytic properties [15, 16]. Valerian's effects on the central nervous system have been well documented and attributed to many of it active compounds: valepotriates, baldrinals, valerenic acid, valerenal, valeranone, and other constituents in the essential oils [15, 17-22]. Albeit, the anxiolytic properties of valerian have been demonstrated in animals [23, 24]. This study evaluated the effectiveness *Valeriana sisymbrifolia* versus *Lavandula angustifolia* and which is more effective for anxiolytic effects.

MATERIALS AND METHODS

This was an experimental study in which 21 female Wistar 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±2 °C, 40–60% humidity, 12 h light: 12 h dark cycle (lights on at 08:00 h). Animals are divided into three groups including control, VS (treated group by Herbal tea of VS) and LA (treated group by Herbal tea of LA). The Used dosage was considered based on leaflet in the pocket of the herbal tea (it was equivalent to 3g/lit/24h) and The VS rhizome and LA flowers were used for this study. VS and LA Groups rats (n = 7/group) had ad libitum access to the tea from VS 0.3% (3gram per 1000 ml w/v) in drinking water and tea from LA 0.3% (w/v), respectively, for a period of 24 hours before the 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 arms are across from each other and so are the closed arms 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 [25, 26]. In the day of the test, the animals were transferred to the laboratory in the afternoon between

17:00 p.m. and 20:00 p.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 testing 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 [1, 25-29].The total number of entrances into two arms are considered as a locomotor activity [30]. 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 ($p< 0.05$).

RESULTS

The ANOVA showed that there was a significant difference in rat behavior on time spent in the open arms of EPM between VS and LA groups compared to control group. Tukey test analysis showed a significant increase in time spent on open arms in treatment 2 group compared to the control group ($p<0.05$) but the time spent on open arms in the treatment1 group compared to control group was not significant [Fig. 1]. The number of entries into the open arms in treatment 2 increased significantly, [Fig. 2]. Time spent on closed arms for the treated group by Herbal tea of LA decreased significantly but this decrease was not significantly in the treated group by Herbal tea VS [Fig. 3]. Number of closed arms entries and total number of open and closed arms increased but not significantly [Fig. 4 and 5].

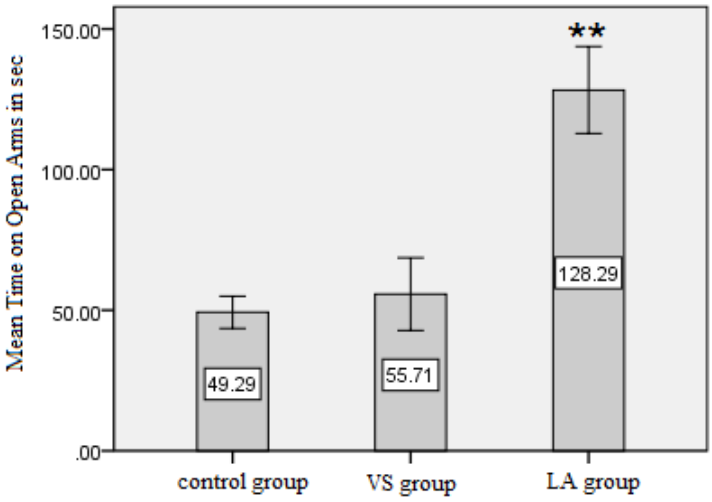

Fig. 1: The period of staying in open arms for LA group is significantly more than the control group using ANOVA following by Tukey test. **shows the significant difference ($P<0.001$)

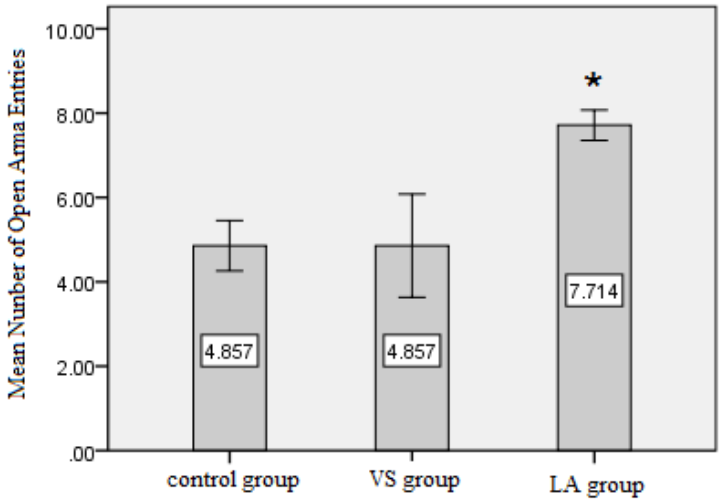

Fig. 2: The number of entrances into the open arm arms for LA group is significantly more than the control group using ANOVA following by Tukey test. *: shows the significant difference ($P<0.05$)

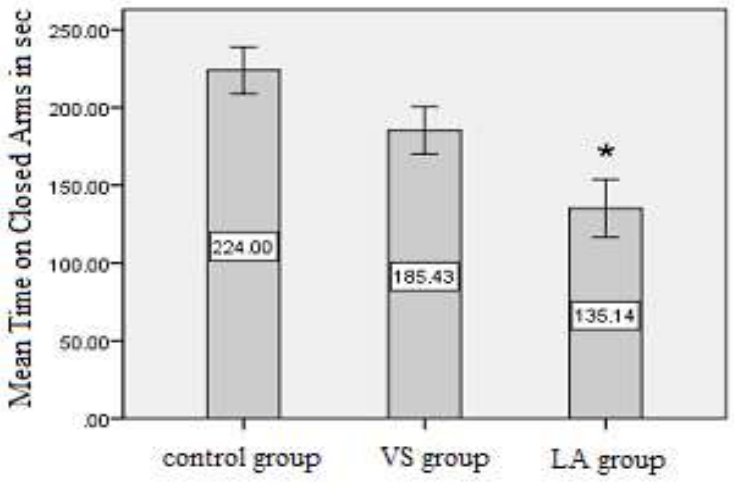

Fig. 3: The period of staying in closed arms for LA group is significantly less than the control group using ANOVA following by Tukey test. *: shows the significant difference (P<0.05)

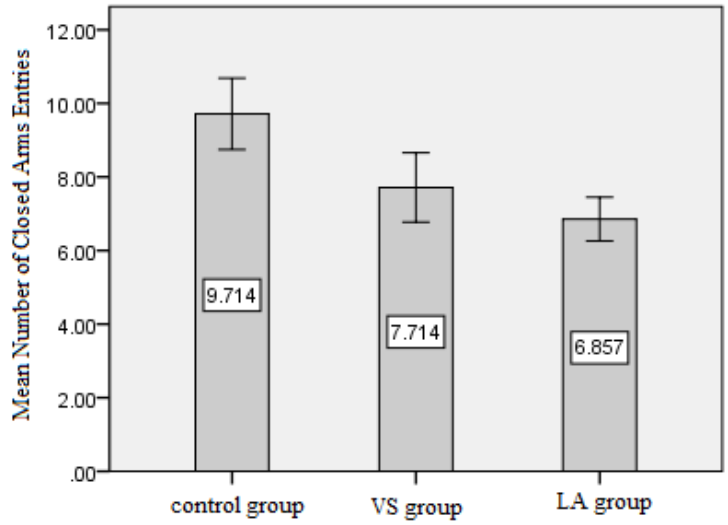

Fig. 4: The number of entrances into closed arms in the treatment groups

DISCUSSION

An increase in the time and the proportion of the entrances into the open arms without a changed locomotor activity are regarded as a powerful marker for an anxiolytic substance effect [29]. The close arm entries are selectively correlated with the locomotor activity [31]. The drugs that cause stimulation and increase the locomotor activity were reported to increase the number of close arm entries [32]. In the elevated plus maze, an anxiolytic or anxiogenic like-effect is evaluated by the relation of entries into the 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 in the time spent and number of entries into the open arm without changing locomotor activity was regarded as a powerful marker for the anxiolytic effect [29]. The enhancement of total arm entries might suggest a nonspecific locomotor stimulant effect which is the co-load on "locomotor activity" and "anxiety", whereas closed arms entries load highly and selectively on locomotor activity [31, 33]. Increase time spent in open arms, percent entries in open arms, total entries and closed arms entries indicated anxiolytic effect. The present study showed the treated groups by of herbal tea of VS and LA induced anxiolytic behavior but did not increase locomotor activity and this indicates herbal tea of LA has anxiolytic effects stronger than herbal tea of VS. The active components of LA are thought to be linalool, linalyl acetate, cineole, terpinen-4-ol and camphor [34-37]. The presence of linalool, linalyl acetate in the plant extract supports the claim that the extract has a sedative effect [38]. Some studies reported the parable mechanisms. Chronic Injection of Lavender oil altered dopamine D3 receptor subtype homeostasis in the olfactory bulb and induced behavioral change [39]**.** Also, Lavender oil potent anxiolytic properties via modulating voltage dependent calcium channels [35]. Linalool, a monoterpene compound prevalent in essential oil of Lavender, interferes with glutamatergic transmission [36]. Lavender oil is also suggested to modulate GABAergic neurotransmission, especially on GABAA receptors, and enhance

inhibitory tone of the nervous system [40-43]. Cholinergic system is suggested to play a role in lavender analgesic, antianxiety, antidepressant, and anticonvulsant effects of lavender [43, 44].

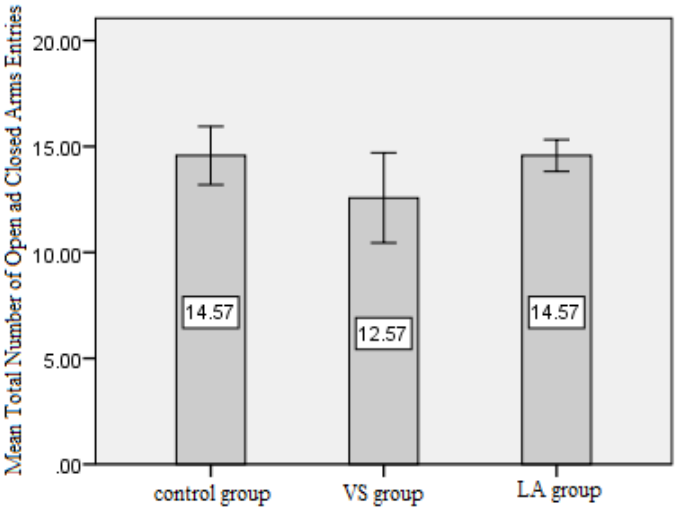

Fig. 5: The total number of entrances into open and closed arms in the treatment groups

Previous studies showed the binding of valerian extract to GABAA receptors in rat cortical membrane preparation [18]. It has been shown that valerian extract, aqueous or hydro-alcoholic, contained GABA and other amino acids that could displace labeled muscimol [18], 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 [45, 46]. Additionally, derivatives of valerenic acid inhibit the local catabolism of GABA by inhibition of the enzyme GABAse, which could also increase GABA concentration [47]. 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 [18]. 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 had not anxiolytic effects. The previous studies have shown anxiolytic effects of valerian in female rats aged six to ten months [24] and in the male mice [48] while in this study female rats aged two to three months were used. Perhaps this contradiction is because of the age testing, used dosage, method of extraction, route of administration and/or sex-dependent. However, the relationship between sex hormones and anxiety behaviors should be discussed. For example the relationship between estrogen and anxiety behavior in different findings may reflect several experiences. Frick et.al. [49] observed in their laboratories that female rats spent less time in elevated plus-maze in open arms. This indicates that exists more anxiety more in female rats. But they had not considered the sexual cycle and it also was not regarded in this study. However, Galeeva et.al. [50] indicated that explore in open arms was reduced in female rats in Diestrus phase, i.e. when the level of estrogen is in its minimum state, there is more anxiety; therefore, the reduction of estrogen results in more anxiety and this estrogen includes the anxiolytic effect. Again, in another experiment, the opposite was shown so that the ovariectomized female mice receiving estrogens in comparison with ovariectomized mice that did not receive any estrogen, showed an increased anxiety behavior [51]. However the effects of estrogen are exerted through two receptors consist of alpha and beta. but an anxiolytic effect of estrogen is more focused on beta receptors [52]. Also, some of the results show that the beta hormone receptors of estrogen are a potential facilitator for serotonin and dopamine neuro-transmitters. Hence, according to different reports by other scholars estrogen increases anxiety behavior. There is a possibility that estrogens on beta receptors are active in a time phase more than other times. However, it seems that the effects some of the herbal medications are sex-dependent [53]. Hence, more research is needed to investigate the anxiolytic effects of *Valeriana sisymbrifolia* in the female rats.

CONCLUSION

The results of this study showed that herbal tea of LA in female rats has anxiolytic effects compared to herbal tea of valerian and this effect was significantly than control and valerian groups. But valerian had not anxiolytic effects.

CONFLICT OF INTEREST
There is no conflict of interest.

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