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Comparison of Anxiolytic-like effects of *Echium amoenum* in the male and female rats

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ABSTRACT

Anxiety disorders are the most common mental illness in the world and became a very important area of research interest in Psychopharmacology. Based on a traditional belief, Echium amoenum (EA) (Boraginaceous) dried flowers are used in Iran as an anxiolytic remedy and also as a mood enhancer. The present study was conducted with the aim of comparing the Anxiolytic-like effects of EA in the male and female rats. This study was carried out to compare the anxiolytic effects of the herbal tea of EA 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 with herbal tea of EA) and 14 female rats weighing 100 to 150 grams were divided into two groups including control2, treatment2 (treated rats by herbal tea EA). Treatment groups rats (n = 7/group) had ad libitum access to the tea of Echium amoenum 0.3% (w/v), 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. All the data were given as Means±S. E. M. Data were analyzed by one-way ANOVA following by Tukey test. The study revealed that EA herbal tea in female rats has anxiolytic effects while in themale rats has sedative effects.

Keywords: Anxiety; Anxiolytic; *Echium amoenum*; Rat; Elevated plus maze

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INTRODUCTION

Mood, anxiety, and sleep disorders are prevalent and highly comorbid psychiatric conditions [1] that have been treated with botanical medicines since antiquity. Contemporaneously, herbal medicine and Complementary and Alternative Medicine (CAM) use is widespread among sufferers of mood and anxiety disorders. Data from a nationally representative sample of 2055 people interviewed during 1997–1998 revealed that 57% of those suffering anxiety attacks, and 54% of those with severe depression reported using herbal medicine and CAM therapies during the previous 12 months to treat their disorder [2]. And are relatively safe drugs for a short-term treatment of anxiety despite their drug dependence potential and side effects [3, 4]. However, the realization that benzodiazepines present a narrow safety margin between the anxiolytic effect and those causing unwanted side effects has prompted much research to evaluate new compounds in the hope that other anxiolytic drugs will have less undesirable effects [5, 6]. *Echium amoenum* (EA) or Boraginace is a wild annual herb and known in Iran as Ox-tongue. It is one of the important medicinal plants in Iranian traditional medicine [7, 8]. Petals of EA have been advocated for a variety of effects such as demulcent, anti-inflammatory and analgesic, especially for common cold, anxiolytic , sedative and other psychiatric symptoms including obsession in folk medicine of Iran [7-10]. The plant grows in the northern mountains of Iran [8]. Moreover, it has been recommended for mood enhancement [11]. The phytochemical studies on E. amoenum revealed that this plant have anthocyanidine, flavonoid aglycons, traces of alkaloids [12], volatile

oils (0.05%) [13], rosmarinic acid [3] and phytosterol compounds[14]. In this study, we examined anxiolytic property of the EA on the male rats in compared to female rats.

MATERIALS AND METHODS

This was an experimental study in which 14 male rats weighing 150 to 200 grams and 14 female rats weighing 100 to 150 grams were randomly chosen and examined. All animals were housed under standard environmental conditions of temperature, relative humidity and light (at 23±2 °C, 40—60% humidity, and 12 h light: 12 h dark cycle (lights on at 08:00 h).Male rats were divided into two groups including control1, treatment1 (treated rats by herbal tea *Echium amoenum*) and also female rats were divided into two groups including control2, treatment2 (treated rats by herbal tea *Echium amoenum*). Treatment groups rats (n = 7/group) had ad libitum access to the tea from *Echium amoenum* 0.3% (w/v), 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 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[15, 16].On the day of the test, the animals were transferred to the laboratory in the afternoon between 17:00 p.m. And 21:00 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 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[15-20].The total number of entrances into two arms are considered as a locomotor activity[21]. 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 ($p< 0.05$).

Findings of the study

ANOVA following by Tukey test showed that there is a reduction in time spent in the open arms of EPM between treatment1 compared to control1 group. But time spent on the open arms increased in the treatment2 group compared to control group (Fig. 1). The number of entries into the open arms in treatment 1 and 2 groups, respectively decreased and increased but not significantly (Fig. 2). Time spent on closed arms had not significant changes (Fig. 3). And Number of closed arms entries and total number of open and closed arms decreased, significantly, in the male rats treated by herbal tea of EA(treatment1 group) (Fig 4, 5).

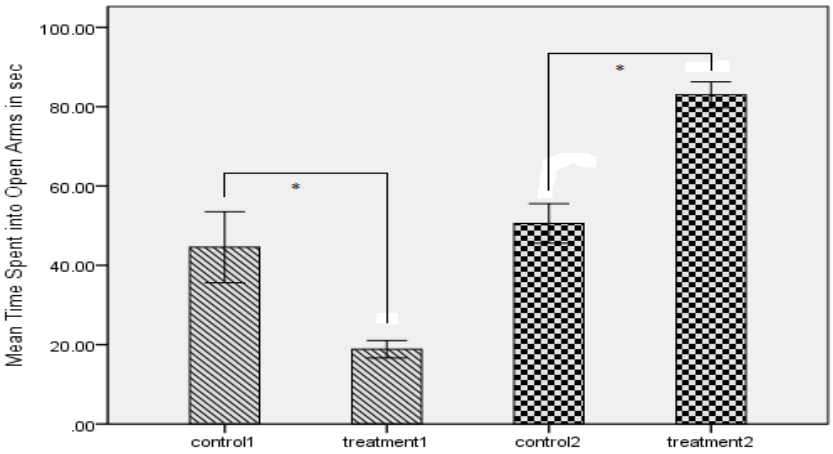

Fig. 1: shows the mean time spent in open arms for treatment1and 2 groups was, respectively, less and more compared with the control1and 2 groups, significantly using ANOVA followed by Tukey test

**: shows the significant difference (P<0. 05)*

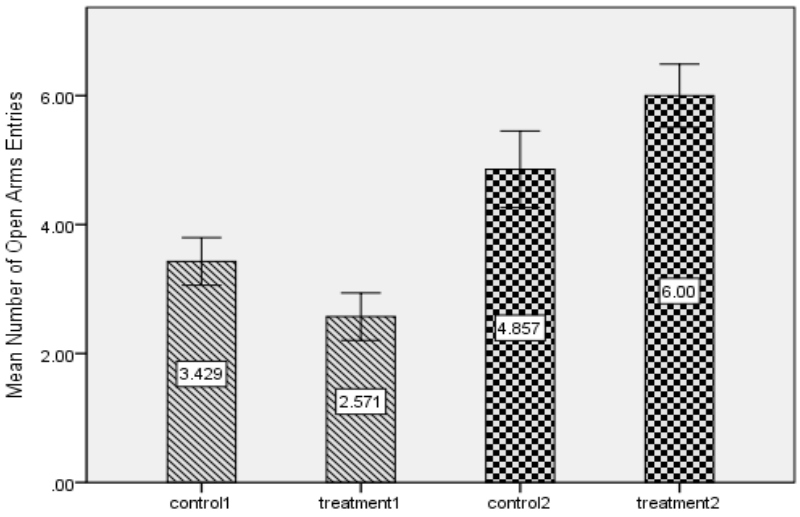

Fig. 2: shows the number of entries into the open arms

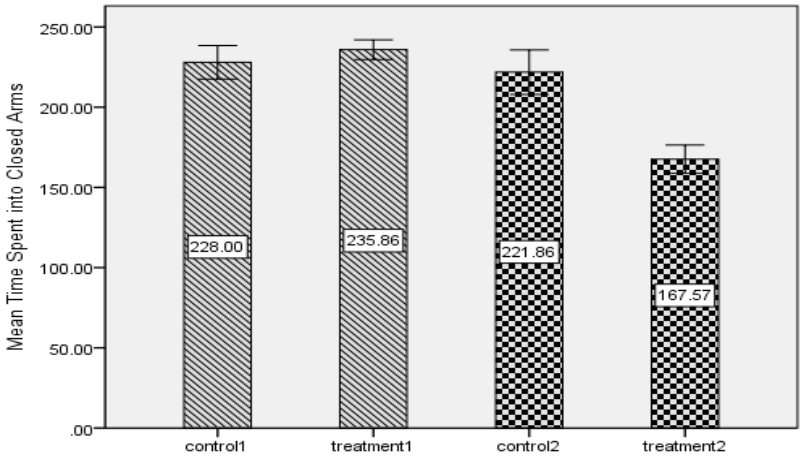

Fig. 3: shows the mean time spent into the open arms

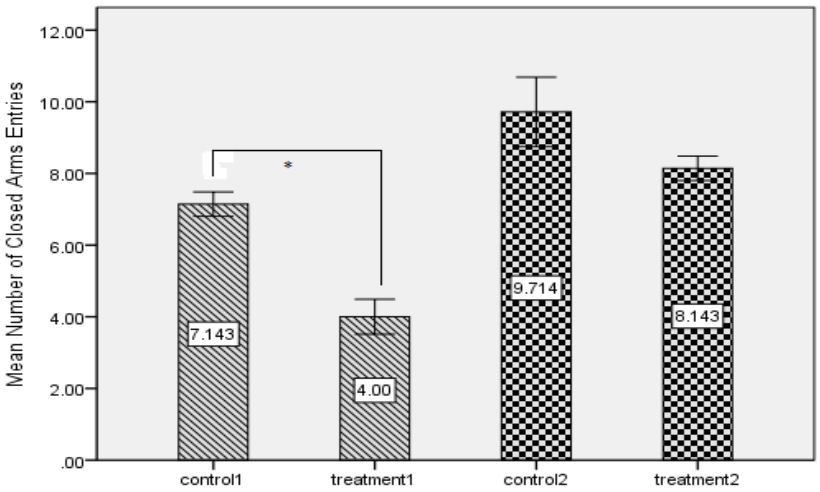

Fig. 4: shows that the number of entrances into closed arms in treatment1 group was significantly less than control 1 group
***: shows the significant difference (P<0. 05)**

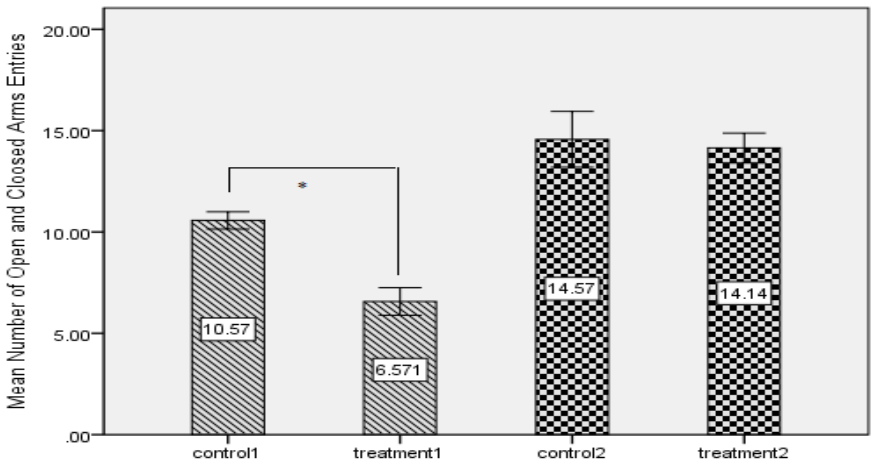

Fig. 5: shows the total number of entries into open and closed arms in treatment1 group was significantly less than control 1 group
***: shows the significant difference (P<0. 05)**

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 [20].Closed arms entries are selectively correlated with the locomotor activity [22]. The drugs that cause stimulation and increase the locomotor activity were reported to increase the number of close arm entries [23]. In the elevated plus maze, an anxiolytic or anxiogenic-like result is measured 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 command 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 [20]. 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 in locomotor activity [22, 24]. Increase time spent in open arm, percent entries in open arm, total entries and closed arm entries indicated anxiolytic effect. The findings of the study show that the male rats in the treatment1 group spent less time in the open arms than the control1 groups. Also, the number of entrances of rats of treatment1 group into closed arms was less than the control 1 group which indicates a reduction of locomotor activities of the animal[21] The reduction in locomotor activities is dependent on sedative properties of the materials present in EA. The previous studies have shown that the EA aqueous extract is effective on anxiety models in mice [10, 25] but the reason why these anxiolytic effects were not observed in this study on the male rats might be because of 1-excessive sedative effects of EA (due to flavonoid compounds) on the male rats in exerting dose. Therefore, led to a reduction in locomotor activities and finally resulted in the reduction of entrances into open arms and so the period of staying in the open arms significantly decreased in the treatment 1 group.

2- Phytosterols reduce cholesterol levels by competing with cholesterol absorption in the gut via one or several possible mechanisms [15, 16, 26]. Awad et al.[27]have reported a 33% reduction in serum testosterone in rats fed a diet containing 2% phytosterols with 0.2% cholic acid. And a 55% reduction in aromataze activity was the only effect observed in the testes. So decrease of time spent into open arms in the male rats might be due to decrease of testosterone hormone.

3- the previous studies have shown that aqueous extract of EA enhances level CSF serotonin[4]. Medications that increase serotonin levels are helpful after 3-4 weeks. So there are side effects in the first stages of treatment including anxiogenic effects.

RESULTS

The results of this study showed that Herbal tea of *Echium amoenum* in male rats has sedative effects stronger than female rats and it seems that the anxiolytic effect of EA is a sex-dependent and probably this different effect in two sexes is related to phytoestrol components of the EA.

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