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SEDATIVE EFFECT OF INFUSIONS FROM FIVE *LAMIACEAE* MARTINOV SPECIES

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Abstract

The increased emotional stress and anxiety in the modern human life are common causes of mental health problems which substantially grown during the COVID-19 pandemic. Timely intake of phytosedatives could mitigate the impact of stressful situations and reduce the risk of psychosomatic diseases. Essential oil-bearing plants belonging to the *Lamiaceae* Martinov family are valuable sources of bioactive compounds possessing sedative effects. The aim of the study was to evaluate the sedative effects of the infusions obtained from five unofficial *Lamiaceae* Martinov species. Infusions were daily administered to rats intragastrically in a prophylactic mode. The observations of behavioral reactions were carried out on the 1st, 4th and 7th days of the experiment using "open field" test. The sedative effect of infusions after their single administration to animals on the 1st day of the experiment was not observed. Starting with 4 days of the experiment, a noticeable sedative effect was established for the infusions from *Dracocephalum moldavica* and *Ocimum americanum* herbs. The noticeable sedative effects of the *Dracocephalum moldavica* and *Ocimum americanum* infusions are regarded as a result of synergistic properties of a lot of their biologically active compounds. Further research would help to reveal the mechanism of their sedative effect.

Keywords: *Agastache foeniculum, Dracocephalum moldavica, Monarda fistulosa*, *Ocimum americanum, Satureja hortensis*, herb, infusion, open field test

Introduction

The increased emotional stress and anxiety in the modern human life are common causes of mental health problems [1]. The amount of mental disabilities has grown significantly during the COVID-19 pandemic [2]. As synthetic sedatives can cause the development of addiction, hepatotoxicity and other side effects, it is a growing need in the developing of natural anxiolytics [3, 4].

Timely intake of phytosedatives could mitigate the impact of stressful situations and reduce the risk of developing psychosomatic diseases [5, 6]. For instance, dental fear and pain could be effectively decreased by intake the mild sedatives of the natural origin [7, 8].

Phytochemicals such as essential oils, alkaloids and phenolic compounds have been frequently reported to possess sedative, anesthetic, and antinociceptive properties [9].

Essential oil-bearing plants belonging to the *Lamiaceae* Martinov family are valuable sources of volatile compounds and polyphenols possessing promising sedative effects [10–15]. Sedative curatives were developed from the aerial parts of *Melissa officinalis* L., *Mentha × piperita,* etc. [16]. Infusions based on abovementioned herbal raw materials are known as a convenient form of daily drinking. They have long been used to treat and prevent the disorders of digestive system, respiratory tract, and as sedatives [17, 18]. The pleasant organoleptic characteristics support using them as teas.

A number of biologically active substances of the *Lamiaceae* species are hydrophilic, which allows to extract them with hot water [17, 18].

We supposed that the list of teas with anxiolytic effects could be expanded by a comprehensive study of aqueous extracts from raw materials of unofficial medicinal plants from the *Lamiaceae* family. The task of expanding the range of sedative phytopreparations could be successfully solved by using herbal raw materials harvested under the cultivation conditions (according to [19]).

The aim of the study was to evaluate the sedative effects of the infusions obtained from five *Lamiaceae* herbs cultivated in Ukraine.

Materials and Methods

Plant material and preparing of infusions

The herbs of five *Lamiaceae* species (*Agastache foeniculum* (Pursh) Kuntze, *Dracocephalum moldavica* L., *Monarda fistulosa* L., *Ocimum americanum* L., and *Satureja hortensis* L.) were harvested from the experimental plots in Ternopil region (Ukraine). The herbs were harvested during the flowering stage and dried in the shadow at 25–35°C.

Each infusion was prepared using 5.0 g of dry raw material. It was ground to a particle size passing through a 2 mm sieve and poured 200 mL of purified boiling water. Then it was for infused 15 min in a boiling water bath. The obtained extract was cooled for 30 min at room temperature, filtered and placed in a 200 mL volumetric flask, making up to the mark with purified water.

Sedative activity

Infusions were daily administered intragastrically through a tube. They were applied in a prophylactic mode (1 h before the placement of animal in the "open field"). "Open field" device consisted of a wooden field of 1m^2 [20]. The floor was divided into 25 marked small squares of equal (20 × 20 cm) dimensions with the holes at their intersections.

Male albino rats from the Vivarium of I. Horbachevsky Ternopil National Medical University (Ukraine) were provided with standard diet and free access to water. All the experimental animals were conformed to "Ethical Principles and Guidelines for Experiments on Animals" [21].

Each animal was placed in the center of the "open field" and tested once for 3 min. There were recorded the discrete behavioral reactions: the motor activity (number of crossed squares), approximate research activity (number of vertical struts on the hind limbs and inspected "mink" holes), and indicators of anxiety (number of acts of grooming, fecal bolus and urination) [20].

The observations of behavioral reactions were carried out on the 1st, 4th and 7th days of the experiment. 42 animals were divided into 7 groups (n=6): 1) intact control group (received purified water); 2-6) experimental groups (received infusions of 5 herbs at a dose of 100 mg/kg, in terms of dry residue: 2 - *Dracocephalum moldavica*; 3 - *Ocimum americanum*; 4 - *Agastache foeniculum*; 5 - *Monarda fistulosa*; 6 - *Satureja hortensis*); 7) reference drug

Diazepam (0.5 mg/kg) group. Diazepam (5 mg/mL) was obtained from the Elegant (India).

Statistical analysis

Statistical analyses were performed using Statistica 12 software (StatSoft Inc., USA). The data were expressed as mean ± standard error of the mean (SEM).

Results and Discussion

The results of screening studies of sedative activity of herbal infusions of five *Lamiaceae* species with different duration of intake are presented in Table 1.

As can be seen from the data in Table 1, the sedative effect of infusions after their single administration to animals on the 1st day of the experiment was not observed. The motor activity, as well as emotional manifestations of animals, were high. The significant difference between animals from the group of intact control and those receiving infusions were not detected. Animals of experimental groups and intact control groups moved mainly along the edge of the "open field" chamber, which is a sign of fear of exposure to unfamiliar conditions. It should be noted that the research behavior of animals, which is assessed by the amount of inspected holes, was maximally detected during the first minute of the animal's stay in the "open field". Later it gradually decreased.

Starting with 4th day of the experiment, a sedative effect was established for infusions from *Dracocephalum moldavica* and *Ocimum americanum* herbs (see Table 1). Its maximum was on the 7th day, as the number of horizontal and vertical movements of rats in the "open field" and the number of acts of grooming, urination and defecation significantly reduced. The *Agastache foeniculum*, *Monarda fistulosa* and Satureja *hortensis* infusions affected only the certain indicators of animal behavior. On the 7th day of the experiment, the number of horizontal movements of animals in the "open field" under the action of daily infusion declined, compared with the control, as follows: 1.59 times for *Dracocephalum moldavica*, 1.52 for *Ocimum americanum*, 1.36 *Agastache foeniculum, 1.31 for Monarda fistulosa,* and 1.28 for *Satureja hortensis*. The significant decrease in the approximate research activity and the manifestation of emotional reactions of rats was observed.

As can be seen from the abovementioned results, infusions from the raw materials of *Dracocephalum moldavica* and *Ocimum americanum* showed a pronounced sedative effect on the 4th and 7th days of the experiment. The the herbs of other species were effective only on the 7th day, and not by all criteria. It discovers the prospect for further research of the sedative properties of the *Dracocephalum moldavica* and *Ocimum americanum* herbs.

Sedative effects of *Dracocephalum moldavica* and *Ocimum americanum* could be regarded as a result of synergistic properties of a lot of biologically active compounds [22]. A number of pharmacologically active components with sedative action was previously established in the herbs of studied species [13, 14, 18].

As is known, the components of essential oils are partially extracted with water. The technology of preparing aromatic waters from essential oil-bearing plants is based on this feature [23, 24]. It was found that linalool and linaloool-containing essential oil were the alternative of traditional treatments for social stress-induced mental illnesses such depression and as anxiety [25-27]. Linalool and other volatile terpenoids of the *Ocimum* species can modify the function of $GABA_A$ receptors [25]. Sharifi-Rad et al. [27] described the valuable health-promoting sedative activities of geranyl acetate, geraniol and many other volatiles which were previously detected in the investigated species [14].

The prevailing of rosmarinic acid among the phenolic compounds of studied species revealed by the chromatographic methods [18, 28]. Rosmarinic acid (55.68 mg/g of infusion) was also the most abundant component of the *Melissa officinalis* tea [29]. Rosmarinic acid could potentiate the pentobarbital-induced sleeping through the activation of $GABA_A$-ergic systems [15, 30]. Generally, a lot of polyphenols and other bioactive compounds possess the free radicals scavenging effect which can prevent the neurodegenerative diseases [30-39].

The sedative effect of studied infusions may be enhanced due the containing water soluble amino acids [40–43]. Such amino acids as glycine, glutamic and γ-aminobutyric acids are the famous inhibitory neurotransmitter in the central nervous system.

Thus, the conducted research demonstrates the prospects of phytochemical and pharmacologycal studies of the infusions prepared from the *Dracocephalum moldavica* and *Ocimum americanum* herbs. Further research would help to reveal the mechanism of their sedative effect.

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Table 1. The influence of infusions prepared from the herbs of five *Lamiaceae* species on the spontaneous behavior of rats in the different days of the experiment ("open field" test, *n* = 6)

Group	Number of squares crossed	Tentative research activity		Indicators of anxiety (emotional reactions)		
		Vertical racks	Examined holes	Defecations	Urinations	Grooming
1st day of the experiment						
Control	30.17±1.45	8.17±0.39	4.17±0.15	1.67±0.08	0.50±0.02	1.83±0.09
Dracocephalum moldavica	25.83±1.32[2]	7.83±0.23[2]	3.83±0.21[2]	1.0±0.03[1,2]	0.50±0.02[2]	1.67±0.06
Ocimum americanum	26.0±1.07[2]	7.83±0.28[2]	3.83±0.24[2]	0.83±0.04	0.67±0.03[1,2]	1.67±0.07
Agastache foeniculum	26.83±1.09[2]	8.0±0.35[2]	4.0±0.23[2]	1.16±0.05[1,2]	0.50±0.02[2]	2.0±0.09[2]
Monarda fistulosa	27.0±1.32[2]	8.17±0.33[2]	3.83±0.27[2]	1.0±0.06[1,2]	0.67±0.03[1,2]	1.83±0.07[2]
Satureja hortensis	28.50±1.26[2]	8.33±0.34[2]	4.17±0.29[2]	1.16±0.08[1,2]	0.50±0.02[2]	2.0±0.04[2]
Diazepam	17,83±0,82[1]	6,33±0,29[1]	3,33±0,19[1]	0,83±0,04[1]	0,33±0,02[1]	1,50±0,06[1]
4st day of the experiment						
Control	29.33±1.17	7.83±0.25	3.83±0.22	1.33±0.06	0.50±0.03	2.0±0.18
Dracocephalum moldavica	23.67±1.05[1,2]	5.83±0.16[1,2]	3.67±0.13[2]	0.83±0.02[1]	0.33±0.02[1,2]	1.67±0.05[2]
Ocimum americanum	23.5±1.09[1,2]	5.67±0.14[1,2]	3.67±0.15[2]	0.83±0.03[1]	0.50±0.03[2]	1.50±0.07[1 2]
Agastache foeniculum	25.17±0.94[1,2]	6.0±0.19[1,2]	3.83±0.16[2]	1.0±0.03[1]	0.33±0.02[1,2]	1.50±0.06[1,2]
Monarda fistulosa	25.83±1.07[2]	6.33±0.29[1]	3.83±0.13[2]	1.0±0.04[1]	0.50±0.03[2]	1.67±0.04[2]
Satureja hortensis	26.17±0.85[2]	7.17±0.32[2]	4.0±0.18[2]	0.83±0.03[1]	0.50±0.02[2]	1.83±0.09[2]
Diazepam	12.50±0.67[1]	4.17±0.21[1]	2.50±0.09[1]	0.50±0.02[1]	0[1]	1.17±0.0,6[1]
7st day of the experiment						
Control	30.67±1.33	8.33±0.36	4.0±0.15	1.16±0.04	0.50±0.05	1.83±0.09
Dracocephalum moldavica	19.33±0.87[1,2]	5.33±0.22[1,2]	3.17±0.14[1,2]	0.67±0.03[1,2]	0[1]	1.17±0.08[1,2]
Ocimum americanum	20.17±1.08[1,2]	5.67±0.27[1,2]	3.17±0.17[1,2]	0.67±0.02[1,2]	0.17±0.01[1,2]	1.33±0.09[1,2]
Agastache foeniculum	22.50±1.12[1,2]	6.0±0.34[1,2]	3.0±0.18[1,2]	0.83±0.03[1,2]	0.33±0.03[1,2]	1.50±0.06[1,2]
Monarda fistulosa	23.33±1.26[1,2]	6.33±0.28[1,2]	3.67±0.11[2]	1.0±0.04[2]	0.50±0.01[2]	1.67±0.07[2]
Satureja hortensis	24.0±1.14[1,2]	6.87±0.27[1,2]	3.83±0.16[2]	1.0±0.05[2]	0.33±0.02[1,2]	1.50±0.06[1,2]
Diazepam	8.50±0.29[1]	3.0±0.12[1]	1.33±0.08[1]	0[1]	0[1]	0.33±0.01[1]

Note:[1] – the differences are statistically significant for the values of the control group ($p \le 0.05$); [2] – the differences are statistically significant for the values of the reference standard group ($p \le 0.05$)