Anxiolytic and antidepressant activities of *Pelargonium roseum* essential oil on Swiss albino mice: Possible involvement of serotonergic transmission

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The anxiolytic and antidepressant activities of the Reunion Geranium (*Pelargonium roseum* Willd) essential oil (EO) were evaluated in male Swiss albino mice by intraperitoneal administration of 10, 20, and 50 mg/kg bw using elevated plus maze (EPM), open-field test (OFT), and forced swimming test (FST). Moreover, we evaluated whether the 5-HT₁A and GABAₐ–benzodiazepine receptor systems are involved in the anxiolytic effects through the coadministration of WAY-100635 (a selective 5-HT₁A receptor antagonist) and flumazenil (an antagonist of benzodiazepine). GC–MS revealed the monoterpenic alcohols citronellol (35.9%) and geraniol (18.5%) as the main components of the *P. roseum* EO. EO was effective in increasing the total number of entries and time spent in the open arms of EPM whereas number of rearing in OFT was significantly decreased in comparison with the control. In the FST, immobility time decreased in EO treated mice. Pretreatment with WAY-100635, but not Flumazenil, was able to reverse the effects of the EO in the EPM and FST, indicating that the EO activity occurs via the serotonergic but not GABAergic transmission. Overall, results of this work showed significant anxiolytic and antidepressant activity of *P. roseum* EO and confirmed the traditional uses of *Pelargonium* species as calming agents.

KEYWORDS
5-HT₁A and GABAₐ–benzodiazepine receptor, antidepressive-like activity, essential oil, *Pelargonium roseum*

1  INTRODUCTION

Anxiety is one of the most common mental illnesses that affect all age groups with prevalence of approximately one eighth of the world population, at some point in their life experiencing this disorder (Grundmann, Nakajima, Kamata, Seo, & Butterweck, 2009). Pharmacotherapy is the first line treatment of this disorder but imposes some problems including sedation, muscle relaxation, and amnesia also in chronic treatments may result in tolerance, psychomotor effects, and dependence (Grundmann et al., 2009). Another increasingly prevalent mental disorder is depression. It has been shown that available antidepressants are only effective for one half to one third of patients and often cause adverse effects that diminish their beneficial results (Deng et al., 2015).

These considerations highlighted the importance of searching novel psychopharmacological drugs that possess prompt onset of action as well as fewer side effects. In this regard, natural products represent promising candidates for drug discovery and pharmacological treatments of these pathologies (Benelli, Maggi, & Nicoletti, 2016; Tabari & Tehrani, 2017). Among them, essential oils (EOs) are complex mixtures of volatile compounds characterized by low molecular weight, insolubility in water, and capability to easily cross the blood–brain barrier (Pavela & Benelli, 2016; Benelli & Pavela, 2018). Some of them have a long tradition of use in aromatherapy as well as in folk medicine, Chinese medicine, and alternative medicines (Dobetsberger & Buchbauer, 2011). Many EOs have shown pronounced effects on the central nervous system (CNS), such as analgesic, anxiolytic, sedative, relaxant, anticonvulsice, and neuroprotective (Dobetsberger & Buchbauer, 2011; Rakotosaona et al., 2017).
Pelargonium roseum Willd., also known as Reunion Geranium or Geranium-Rose, is a species belonging to the Geraniaceae family, native to Southern Africa and distributed and cultivated in many parts of the world owing to its pleasant rose-like scent. Leaves of P. roseum are covered with glandular trichomes (capitate trichomes) secreting an EO giving a pleasant rose scent (Baser & Buchbauer, 2015; Carmen & Hancu, 2014; Lis-Balchin, Hart, Deans, & Eaglesham, 1996). Several bioactivities including antimicrobial, antifungal, insecticidal, and anti-inflammatory have been attributed to the P. roseum EO (Carmen & Hancu, 2014; Lis-Balchin, Steyrl, & Kreno, 2003; Rezaie et al., 2008; Tabari, Youssefi, Esfandiari, & Benelli, 2017).

In the traditional medicine, the infusion of Reunion Geranium is used to control stress and anxiety (Lis-Balchin, 2003; Zargari, 1990). Moreover, the EOs of Pelargonium spp. as well as Geranium-based herbal preparations are currently in use as popular aromatherapy agents to relieve stress, anxiety, and depression (Dobetsberger & Buchbauer, 2011; Lemon, 2004; Setzer, 2009; van der Watt, Laugharne, & Janca, 2008).

However, to our knowledge, the neuropharmacological properties of P. roseum EO have not yet been elucidated. Therefore, this study investigated the behavioral effects of P. roseum EO using elevated plus maze (EPM), open-field test (OFT) and forced swimming test (FST) on mice. Moreover, this study also examined whether the 5-HT_{1A} and GABA_{A}–benzodiazepine receptor systems are involved in the anxiolytic effects of P. roseum EO in EPM and FST, through the coadministration of the EO with WAY-100635, a selective 5-HT_{1A} receptor antagonist, and flumazenil, an antagonist of benzodiazepine.

2 | MATERIAL AND METHODS

2.1 | Essential oil extraction and analysis

Fresh leaves of P. roseum were collected from plants grown in a garden placed in Kashan, 34.0351°N, 51.0671°E, Iran. The botanical identification was performed by Professor Rahimian, and the voucher specimen was deposited at the Sari University of Agriculture and Natural Resources (Sari, Iran) under the codex 4621. Leaves (50 g) were immersed in double their volume of distilled water and subjected to hydro-distillation using a Clevenger type apparatus. The oil yield was 0.96%. The chemical analysis was carried out on an Agilent 7890A gas chromatograph equipped with 5975C mass spectrometer. The separation of EO constituents was achieved on a HP5 column (5% phenylmethylpolysiloxane, 30 m length, 0.25 μm film thickness, J & W Scientific, Folsom, CA). The temperature program was as follows: 60 °C held for 3 min, then raised to 150 °C at 3 °C/min and held for 1 min, after that up to 260 °C at 3 °C/min and held for 3 min. The oil sample was diluted to 1% with n-hexane, and 2 μl of the solution was injected into the GC–MS system 3 times. The carrier gas was He at a flow rate of 1.0 ml/min. The injector and detector temperatures were 230 and 250 °C, respectively. The identification of the EO compounds was based on the comparison of their retention indices (RIs, calculated using a homologue series of n-alkanes) and mass spectra with those contained in the commercial libraries NIST 98.1, ADAMS, and 7 Mass Finder 3.1, as well as those contained in our homemade library. The quantitative values of the P. roseum EO constituents were taken from the peak integration without using correction factors.

2.2 | Animals

Male Swiss albino mice (25–30 g) purchased from Pasteur Institute of Iran, North Research Center (Amol, Iran) were used in this study. The animals were kept under controlled lightening (12-hr light/dark cycle) and at room temperature. Food and water were provided ad libitum. The experimental procedures were approved by the Animal Care and Use Committee of the Pasteur Institute of Iran (letter ID 94022-18); they were consistent with the Principles of Laboratory Animals Care (NIH Publication no. 85–23, revised 1996). At least 24 hr before testing mice were introduced to the experiment room.

2.3 | Chemicals

Buspironne HCI (Sigma-Aldrich, Germany) and Diazepam (Darupakhsh, Tehran, Iran) were used as standard anxiolytics. WAY-100635 (N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-ethyl]-N-(2-pyridyl) cyclohexane carboxamide trihydrochloride), a 5-HT_{1A} receptor antagonist, was obtained from Sigma (Sigma-Aldrich, Germany). Flumazenil (Sigma-Aldrich, Germany), a GABA–benzodiazepine antagonist was kindly provided by Dr. Bagherpour (anesthesiologist, Sari, Iran). Tween 80® (1%) was used as solvent for all treatments. All samples were prepared before testing and administered intraperitoneally in a volume of 0.1 ml/10 g bw.

2.4 | Experimental design and treatments

As there was no popularly based dose record, appropriate doses of the P. roseum EO were determined in previous preliminary tests, and 10 mg/kg bw was determined as the lowest dose that showed significant anxiolytic and antidepressant activities. To evaluate the anxiolytic effects of the P. roseum EO, at first, the mice (n = 8 per group) were randomly assigned to six experimental groups as follows: vehicle (CON), diazepam 1 mg/kg (DZP), buspirone 10 mg/kg (BSP), P. roseum EO 10 mg/kg (EO10), P. roseum EO 20 mg/kg (EO20), and P. roseum EO 50 mg/kg (EO50); all the drugs were injected 30 min prior to behavioral testing. In the second experiment, for the detection of possible mechanisms of anxiolytic and antidepressant activities, antagonists of GABA and 5-HT_{1A} transmissions were used by pretreatment with flumazenil or WAY-100635. For this purpose, mice were assigned to 12 experimental groups (n = 7 per group) as follows: vehicle + vehicle (CON), vehicle + diazepam 1 mg/kg (DZP), vehicle + flumazenil 3 mg/kg (FLU), flumazenil 3 mg/kg + diazepam 1 mg/kg (FLU + DZP), vehicle + buspirone 10 mg/kg (BSP), vehicle + WAY-100635 1 mg/kg (WAY), WAY-100635 1 mg/kg + buspirone 10 mg/kg (WAY + BSP), flumazenil 3 mg/kg + buspirone 10 mg/kg (FLU + BSP), WAY-100635 1 mg/kg + diazepam 1 mg/kg (WAY + DZP), vehicle + P. roseum EO 20 mg/kg (EO20), WAY-100635 1 mg/kg + P. roseum EO 20 mg/kg (WAY + EO20), and flumazenil 3 mg/kg + P. roseum EO 20 mg/kg (FLU + EO20). Between two consecutive injections, 15-min interval was adjusted. Thirty minutes after the second injection, the behavioral effects of the different treatments were evaluated by using EPM and
FST. The doses were selected based on the results of a pilot study performed in our laboratory, which revealed that EO of *P. roseum* at higher doses (200 and 500 mg/kg ip) produced marked sedation and altered locomotor activity.

### 2.5 Open-field test

The open-field apparatus consisted of a 30 × 30 × 15 cm acrylic glass, divided into nine squares. The procedure consists of subjecting an animal to an unknown environment from which escape is prevented by surrounding walls (Prut & Belzung, 2003). This device is used to evaluate exploratory activity and anxiety behavior in rodents. For each mouse, the following parameters, number of squares crossed with the four paws, number of grooming behavior, and number of rearing were recorded during 5 min (Neto et al., 2013). After each test, the equipment was washed with a 70% ethanol and dried.

### 2.6 Elevated plus maze

The test for mice consisted of two closed arms (30 × 5 × 25 cm³) and two perpendicular open arms (30 × 5 cm²) connected by a central platform (5 × 5 cm²) (Costa et al., 2014). The test is devised based on the natural aversion of rodents to an unprotected and elevated field. Anxiety level is measured by the number of entries into and the length of time spent in the aversive area (Carola, D’Olimpio, Brunamonti, Mangia, & Renzi, 2002). Thirty minutes after treatments, the mouse was placed at the central platform with its nose directing towards one of the close arms, and then the number of entries in open and closed arms and time spent in each of them was recorded during 5 min (Neto et al., 2013). After each test, the equipment was washed with a 70% ethanol and dried.

### 2.7 Forced swimming test

The FST test, also known as the behavioral despair test, is used for evaluation of depression-like behavior and hopelessness in mice. To perform this, test animal was set in a tank containing fresh water to a height of 20 cm and temperature of 25 °C, and immobility time (floating with only small movements necessary to keep the head above water) was examined for 5 min. The immobility time is postulated to indicate behavioral despair as an experimental model of depression (Melo et al., 2010).

### 2.8 Statistical analysis

The data were subjected to analysis of variance followed by Student–Newman–Keuls as post-hoc test. All statistical analyses were made using SPSS software V. 18 (SPSS Inc., Chicago). All results were expressed as mean ± standard error values. Values of *p* < .05 were considered statistically significant.

### 3 RESULTS

#### 3.1 Chemical composition of *P. roseum* EO

The chemical constituents of *P. roseum* EO were identified by GC–MS analysis and are shown in Table 1. Forty-two components were identified in the *P. roseum* EO, accounting for 99.6% of the total.

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<th>No.</th>
<th>Component*</th>
<th>Calculated RIb</th>
<th>Literature RIc</th>
<th>Abundance (%)d</th>
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<td>932</td>
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<td>Geranyl tiglate</td>
<td>1,695</td>
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</table>

Total identified (%) 99.6

Note: RI, Retention Indices.

*Compounds are listed in order of their elution from a HP-SMS column.

Linear retention index on HP-SMS column, experimentally determined using homologous series of C₈-C₃0 alkanes.

Linear retention index taken from Adams.

Relative percentage values are means of three determinations with a RSD% in all cases below 10%.
composition. The *P. roseum* EO composition was dominated by oxygenated monoterpenes, accounting for 75.3% of the total. Among them, the linear monoterpene alcohols as citronellol (35.9%) and geraniol (18.5%) were the most abundant components. Linalool (5.7%), iso-menthone (4.2%), citronellyl acetate (3.5%), and menthone (2.6%) were other minor representatives of this group. Sesquiterpene hydrocarbons (19.8%) gave a minor contribution to the *P. roseum* EO, with δ-selinene (5.5%), (E)-caryophyllene (2.6%), δ-cadinene (2.5%), and β-bourbonene (2.1%) as the most representative compounds. The chemical composition herein detected was consistent with that reported by Carmen and Hancu (2014) and slightly different from that found by Dabiri, Sefidkon, Yousefi, and Bashiribod (2011).

### 3.2 Effects of EO in the OFT

This test was carried out to evaluate possible effect of *P. roseum* EO on exploratory behavior of mice. As shown in Figure 1a, administration of *P. roseum* EO, diazepam and buspirone did not change the overall locomotor activity significantly (*p* > .05), but number of rearing and grooming behavior was significantly reduced in diazepam, buspirone, *P. roseum* EO 20, and *P. roseum* EO 50 treated mice (Figure 1b,c; *p* < .05).

### 3.3 Effects of EO on the EPM test

The results of the anxiolytic activity of *P. roseum* EO in the mice EPM are shown in Figure 2. Among different treatments, a significant difference in the number of open arm entries (NEOA) and the time spent in the open arms was observed. Results showed that the number of open arm entries was significantly increased, 3.37 and 2.82 times in groups treated with EO 20 and 50, respectively, as compared with the control (*p* < .001; Figure 2a). Results about the time spent in open arms (TSOA) showed a significant increase 1.55 and 1.81 times in *P. roseum* EO 20 and 50 treated mice, respectively, in comparison with the control (*p* < .01; Figure 2b). In DZP and BSP treated mice, the same behavioral alterations were observed in comparison with the control (*p* < .001; Figure 2a,b).

### 3.4 Effect of EO on the FST

The administration of *P. roseum* EO at all doses resulted in significant alteration in FST parameter (Figure 3). Immobility time significantly decreased in BSP (60.56%), EO10 (35.2%), 20 (60%), and 50 (75.88%) treated groups in comparison with the control (*p* < .01; Figure 3).

### 3.5 Role of GABA or 5-HT1A transmission on EO anxiolytic activity in EPM test

To determine whether the anxiolytic activity of the EO occurs through the GABAergic or serotonergic transmission systems, mice before receiving the EO (20 mg/kg bw, selected based on the results of the first series of experiments) were pretreated with antagonist of these systems, flumazenil and WAY-100635. As shown in Figure 4a,b, *P. roseum* EO, DZP, and BSP produced a significant increase in the NEOA and TSOA, whereas FLU and WAY in comparison with the control, did not show any significant difference (*p* > .05). Pretreatment with FLU not only was unable to reverse the effects of BSP but also could not block the effects of *P. roseum* EO. As it could be expected, FLU and WAY antagonized the effects of DZP and BSP in the EPM, respectively (*p* < .01 for NEOA and *p* < .001 for TSOA vs. DZP and BSP, respectively). Pretreatment with WAY either in WAY + BSP or WAY + *P. roseum* EO significantly reversed the anxiolytic effects of BSP and *P. roseum* EO (*p* < .01 for NEOA and *p* < .001 for TSOA).

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**FIGURE 1** Effects of essential oil from *Pelargonium roseum* on (a) number of squares crossed, (b) rearing, and (c) grooming in the open-field test (OFT). Values are presented as mean ± standard error of the mean for number of eight mice (per group). *p* < .05 versus control and essential oil 10 mg/kg (analysis of variance followed by Student–Neuman–Keuls test). CON = vehicle; DZP = diazepam; BSP = buspirone.
expected BSP decreased the immobility time of the animals in the FST and pretreatment with WAY blocked these effects (p < .01). Administration of FLU and WAY per se did not cause any alteration in performance of mice in the FST (p > .05).

4 | DISCUSSION

The use of plant EOs always has a defined place in the traditional medicine, and nowadays, many researchers have shown interest to investigate their potential biological effects and possible uses in conventional medicine (Benelli et al., 2016; Rakotosaona et al., 2017). Numerous EOs and their main compounds have been recognized as active on the CNS and have a potential to affect the conditions such as anxiety, depression, and epilepsy (Fajemiroye et al., 2012; Rakotosaona et al., 2017). In Iranian folkloric medicine, the EO of Pelargonium roseum is commonly used for several conditions, including nervous disturbance (Zargari, 1990). A number of studies have reported several bioactivities including antibacterial, antioxidant, and anti-inflammatory effects for this EO (Carmen & Hancu, 2014; Lis-Balchin et al., 2003; Rezaie et al., 2008). However, to the best of our knowledge, there are no reports of the CNS effects of Pelargonium roseum EO, as well as which neurotransmitter systems are largely affected by the EO itself.

In the present research, the sedative and anxiolytic effects of Pelargonium roseum EO were examined in mice by using open field, elevated plus maze, and forced swimming test, which are validated models to test the effects of a given drug on CNS. Our findings showed that Pelargonium roseum EO has anxiolytic and antidepressant effects without changing locomotor activity in mice. Locomotor activity of animals and effects of Pelargonium roseum EO on them were evaluated by the open-field test. Diazepam and buspirone were used as reference anxiolytics, and different doses of Pelargonium roseum EO were used for determining anxiolytic actions. Diazepam (DZP), buspirone (BSP), and EO did not decrease the locomotor activity of mice, but number of rearing and grooming behaviors significantly decreased in DZP, BSP, Pelargonium roseum EO20, and EO50 treated groups (p < .05). Our results are in line with those reported by Chioca et al. (2013) who reported anxiolytic-like effects of the lavender (Lavandula angustifolia Mill.) EO that contains linalool and linalyl acetate as main components in mice without significantly altering spontaneous locomotor activity. Blanco, Costa, Freire, Santos, and Costa (2009) described that treatment of mice with the essential oil of Cymbopogon citratus (DC.) Stapf did not cause any changes in parameters observed in the open field such as ambulation, rearing, freezing, and grooming. The main constituents of C. citratus were geranial (40.8%), neral (36.3%), and β-myrcene (13.2%). Because it is recognized that rearing is a function of the excitability level of the central nervous system (de Almeida, Costa, de Almeida, de Sousa, & de Freitas, 2012), reduction of rearing in the EO treated mice can reveal the central effects of Pelargonium roseum.

In this study, an obvious anxiolytic-like effect of Pelargonium roseum has been noticed as well. When placed in a new environment, mice demonstrate fear and anxiety. EPM has been designed based on the natural fear of elevation and openness in rodents. Increases in open arm parameters are indicators of anxiolytic-like effects (File, 2001). Data obtained from the EPM showed that Pelargonium roseum EO was significantly able to increase the number of entries as well as the time spent in

3.6 | Role of GABA or 5-HT1A transmission on EO antidepressant activity in FST test

Pretreatment with WAY but not FLU reversed the effects of Pelargonium roseum EO on the immobility time in the FST (Figure 5). As it could be
the open arms. Similar findings have been reported from several EOs, including *C. citratus*, *Citrus limon* (Burn), *Spiranthera odoratissima* A. St. Hil., and *L. angustifolia* (Blanco et al., 2009; Chioca et al., 2013; Galdino et al., 2012; Lopes Campêlo et al., 2011). The *C. limon* EO contains 28 volatile constituents among which monoterpenoids such as limonene, linalool, citronellal, neral, and geranial are the predominant components (Lopes Campêlo et al., 2011). β-caryophyllene is the main sesquiterpene component of *S. odoratissima* A. St.-Hil. EO. Administration of *S. odoratissima* EO (500 mg/kg) and β-caryophyllene (100 and 200 mg/kg) in mice, increased entries into and time spent on the open arms in the EPM test (Galdino et al., 2012).

The acute injection of *P. roseum* EO decreased the immobility time in a dose-dependent manner in the FST test. Immobility time is the main parameter indicating antidepressant activity in the FST procedure. The results suggest antidepressant effect of *P. roseum* EO. In contrast with our findings, EOs of *C. citratus*, containing citral (71.29%) as the main compound and *Citrus × aurantium* L. containing limonene (98.66%), have been reported as unable of modifying immobility time...
in the FST test (Costa et al., 2013; de Almeida Costa et al., 2011). Whereas, it was shown that C. limon EO, like the standard antidepressant imipramine, can decrease the immobility time in the FST test (Lopes Campêlo et al., 2011). Phytochemicals from Asparagus racemosus Willd., a medicinal plant commonly used in the traditional Indian medicine and Ayurveda, have been reported to possess significant antidepressant activity on rodents using models for depression research, in which this species reduces immobility time in the FST. It has been demonstrated that this activity is mediated through the serotonergic and noradrenergic systems (Singh, Garabadu, Muruganandam, & Krishnamurthy, 2009).

In common with the EO of P. roseum, which showed concurrent anxiolytic and antidepressant activity, these effects have also been reported from the aqueous extract of Cecropia glaziovii Sneath, and bioactive glycowithanolides isolated from Withania somnifera (L.) Dunal (Bhattacharya, Bhattacharya, Sairam, & Ghosal, 2000; Rocha et al., 2007). The dual anxiolytic and antidepressant activity in one therapeutic compound is highly beneficial and leads to a better response especially in pharmacotherapy of comorbid anxiety/depression disorders. Depression and anxiety are not two distinct entities and frequently these disorders occur concomitantly in the same patient. About 85% of patients with depression also experience remarkable symptoms of anxiety. Moreover, depression coexists in approximately 90% of patients with anxiety disorders. Patients with comorbid depression and anxiety often have more severe symptoms, lower response to treatment, and poorer prognosis than patients with only one disorder (Gorman, 1996). These considerations may highlight the significance of compounds that can be simultaneously effective on anxiety and depression. The EO of P. roseum, due to its anxiolytic and antidepressant like effects, can be regarded as a natural remedy for alleviating symptoms of comorbid anxiety/depression disorder.

Because P. roseum EO showed anxiolytic and antidepressant effects, we decided to determine the possible underlying mechanism. The anxiolytic-like effect of EO in the EPM was significantly blocked by pretreatment with WAY-100635 but not by flumazenil. WAY-100635, a selective 5-HT1A receptor antagonist, reversed EO effects on the number of entries as well as time spent in the open arms, suggesting that this EO might act through the serotonergic system. These findings could indicate that the anxiolytic effects of P. roseum are likely mediated by 5-HT receptors. In agreement with our results, it has been shown that EOs extracted from L. angustifolia, S. odoratissima, and Citrus × aurantium exert their anxiolytic-like effects via serotonergic system (Chioca et al., 2013; Costa et al., 2013; Galdino et al., 2012). The administration of WAY-100635 also reduced the antidepressant effect of EO in the FST test. In line with this finding, Lopes Campêlo et al. (2011) reported the involvement of the serotonergic system in the antidepressant effect of C. limon (Lopes Campelo et al., 2011).

The major chemical constituent of P. roseum EO was the linear monoterpene alcohols citronellol (35.9%) and geraniol (18.5%). Both compounds have been shown to be active on CNS. Indeed, Brito et al. (2012) reported that citronellol reduces nociception and inflammation in rodents (Brito et al., 2012). Deng et al. (2015) demonstrated antidepressant activity of geraniol in chronic unpredictable mild stress model in mice. They also reported that geraniol ameliorates CNS inflammation (Deng et al., 2015). Also, Rekha, Selvakumar, Sethupathy, Santha, and Sivakamasundari (2013) reported neuroprotective efficacy of geraniol and theorized that this compound can be a lead for the development of novel therapeutic agents for the treatment of neurodegenerative disorders such as Alzheimer (Rekha et al., 2013). These data support our findings on the CNS bioactivity of P. roseum EO, which can be attributed to its major constituents. Moreover, further studies are needed to compare the CNS effects and the action mechanism of the crude EO with those of its major components and find meaningful synergisms among them. The P. roseum EO contained 5.7% of linalool. This linear monoterpenoid may play an important role in synergizing the effect of citronellol and geraniol. Linalool was proven to exert important antidepressant and sedative effects (Guzmán-Gutiérrez, Gómez-Cansino, García-Zebadúa, Jimenéz-Pérez, & Reyes-Chilpa, 2012). Linalool is able to reduce locomotion in mice without influencing the motor coordination (Linck et al., 2009). Its sedative effects may be explained by its antagonist effects on N-methyl-D-aspartate receptors (Silva Brum, Emanuelli, Souza, & Elisabetsky, 2001), whereas its contribution to the antidepressant-like effect may derive from interaction with the monoaminergic system (Guzmán-Gutiérrez, Bonilla-Jaime, Gómez-Cansino, & Reyes-Chilpa, 2015).

Overall, the results of this study showed significant anxiolytic and antidepressant activity of P. roseum EO, thus confirming the traditional uses of Pelargonium species as calming agents and suggest possible involvement of serotonergic transmission in these effects. Our findings highlight the importance of the nature arsenal in providing novel therapeutic agents with rapid onset of action and fewer adverse effects for the treatment of disorders such as anxiety and depression.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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