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Evaluation of antidepressant effect of ethanolic extract of *Rosa damascena* using forced swimming test

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Abstract

Objective: *Rosa damascena* mill L (*R. damascena*) is a medicinal plant mostly known in the world for its perfume. It also has beneficial effects on stress, tension and depression. In this experiment antidepressant effect of ethanolic extract of *R. damascena* by forced swimming test (FST) was evaluated.

Material and Methods: Animals received ethanolic extract (15, 60 and 90 mg/kg, i.p), imipramine (15mg/kg, i.p; positive control), or saline (negative control). Thirty min post- injection, immobility and swimming times were measured and compared in the different studied groups.

Results: Intraperitoneal injection of lower concentration of extract (15 mg/kg) did not change swimming and immobility times compared to the control group. The higher concentrations of extract (60 and 90 mg/kg) significantly increased immobility time and decreased swimming time. Therefore ethanolic extract at tested doses had no antidepressant effect in this study.

Conclusion: Although ethanolic extract did not have antidepressant effect, we cannot rule out this effect altogether. In our opinion, antidepressant effect is masked by CNS depression effect of ethanolic extract of *R. damascena*.

Keywords: *Rosa damascena*, Mice, Immobility time, Antidepressant effect, Ethanolic extract

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Introduction

Depression is an important health care problem in the world that is characterized by several signs such as intense sadness, despair, and recurrent thoughts of death or suicide. Prevalence of this disorder is about 13-20% of the population (Licinio and Wong, 1999). Approximately two third of depressed patients has suicide thoughts and 10-15% of whom attempt suicide before the age of 40 (Moallem et al., 2007). Although several synthetic drugs are available for treatment of depression, side effects such as dry mouth, hypotension, fatigue, sexual dysfunction and drowsiness limit the use of these treatments (Dhingra and Sharma 2006). In addition, the success rate of medication is low and at least 40% of the patients do not respond to the antidepressant drugs (Freitas et al., 2010). Therefore, researches for new antidepressant drugs with fewer side effects are needed.

Nowadays, medicinal plants are largely investigated for treatment of depression (Nathan 2001; Sakakibara et al., 2006; Machado et al., 2009). Several plants such as *Crocus sativous*, *Echium vulgar*, *Rosmarinus officinalis*, *Hypericum reflexum* and *Ginkgo biloba* (Hosseinzadeh et al., 2003; Sakakibara, Ishida et al. 2006; Sanchez-Mateo, Bonkanka et al. 2007; Machado et al., 2009) showed antidepressant activity.

Another plant that may have antidepressant function is *Rosa damascena Mill (R.damascena)*. This plant is an erect shrub from the Rosaceae family with1 to 2 meter height (Shafei et al., 2003). *R. damascena* is a medicinal plant that is mostly known in the world for its perfume effect (Zargari 1992; Nikbakht and Kafi 2004; Boskabady et al. 2011). However, in traditional medicine, it has been used for treatment of abdominal and chest pain, strengthening the heart (Zargari 1992; Boskabady et al., 2011), menstrual bleeding, and digestive problems (Zargari 1992). It also has beneficial effects on stress, tension and depression (Momeni et al., 1991). In recent studies antibacterial, anti-HIV, hypnotic, and analgesic, laxative. bronchodilatory and antittussive effects from flower of this plant have been reported (Shafei et al., 2003; Boskabady et al., 2006; Nyeem et al., 2006; Rakhshandah and Hosseini ,2006; Kheirabadi et al., 2008; Boskabady et al., 2011). In a previous study drop of *R. damascena* has shown antidepresant effect in comparison with amphetamine in rats. (Zarghami et al., 2002). In addition, we showed antidepresant function of aqueous extract of *R. damascena* (Dolati et al., 2011). Because active components of any plant differ depending on the extracting solvents used, we supposed that effect of aqueous and ethanolic extracts on depression are different. Therefore, in this study antidepressant effects of three doses of ethanolic extract from *R. damascena* in comparison with imipramine by using swimming test (FST) in mice were evaluated.

Material and Methods

Plant and extracts

R. damascena was collected from Kalate –Nader (an area near Mashhad, east of Iran) and identified by botanists in the Herbarium of the School of Pharmacy, Mashhad University of Medical Sciences (Herbarium No: 254-1804-01).

For preparation of ethanolic extract of *R. damascena,* 60g of dried flower was ground to a fine powder and extracted with 300 ml ethanol (50%) by the soxhlet apparatus. The ethanol used for obtaining extract was then removed under reduced pressure. The final extracted materials weighed 15g. Concentrations of the extract were prepared by dissolving final product in distilled water. An aqueous solution of Tween 80 at 5% was added for dissolving ethanolic extract.

Animals

Male albino mice (25-30 g) were housed in a controlled room (temperature; 22±2°C,

light/dark cycle; 12h). Animal had free access to food and water. Experiments were carried out between 9:00 and 17:00. The animals were placed in the experimental room 24 h before the test for acclimatization.

FST procedure in mice

The forced swimming test was done according to the previous study (Moallem et al., 2007). Briefly, animals were placed in Pyrex cylinders (10 × 45 cm) which were filled with water at 24-25 °C with a 30-cm depth and behaviors were monitored. Saline, imipramine and three doses of ethanolic extract were administered intraperitoneally 30 min prior to the test session. The duration of test was 6 min. After two min, immobility and swimming time was measured during the last 4 min (Hosseinzadeh et al., 2007). Immobility was assigned when no additional activity was observed other than that required to keep the animal's head above the water and swimming time assigned when animal did active movement of extremities and circling in the container.

Experimental groups

The following groups (n=6 for each group) were used:

1- Saline as the negative control
2- Imipramine (15mg/kg) as the positive control
3- Ethanolic extract group (15mg/kg)
4- Ethanolic extract group (60mg/kg)
5- Ethanolic extract group (90mg/kg)

Statistical analysis

All the data were expressed as mean ± SEM. Comparison between data obtained from three concentrations of extract were performed by one-way ANOVA followed by Tukey's HSD test. $p<0.05$ was considered significant.

Results

Effects of saline on the forced swimming test

Injection of saline did not exhibit significant effect on immobility time and swimming time in the forced swimming test compared to pre injection status. Therefore, all experimental groups were compared with saline as the control group.

Effects of imipramine on the forced swimming test

The administration of imipramine (15mg/kg, i.p) as a positive control, in mice significantly decreased immobility time (21.5±2.90 sec *vs* 75.25±5.8 sec, $p<0.001$) and increased swimming time (218.16±3.2 sec *vs* 166.5±7.3 sec, $p<0.001$)) compared to the control group. The effects of imipramine on immobility and swimming time are shown in figures 1, 2.

Effects of ethanolic extract of *Rosa damascena* on the forced swimming test

Three different doses of ethanolic extract (15, 60 and 90mg/kg, i.p) of *R. damascena* were used to investigate the antidepressant effect of this plant. Our results showed that ethanolic extract at the dose of 15 mg/kg did not changed immobility time (75.8±7.2 sec *vs* 70.1±5.2 sec, $p>0.05$; n=6) and swimming time significantly (159.17±9.8 sec *vs* 171.7±3.6 sec, $p>0.05$; n=6) compared to the control group in mice (Figure 1, 2). However, these effects were statistically different compared to imipramine.

The dose of 60 mg/kg of ethanolic extract significantly increased immobility time (70.23±4.2 sec *vs* 75.25±5.8 sec, $p<0.05$; n=6) and decreased swimming time (158.28±3.3 sec *vs* 166.5±5 sec, $p>0.05$; n=6) compared to the saline group.

The high dose (90 mg/kg) of extract also the same as dose of 60 mg/kg significantly increased immobility time (104.83±6.53 sec *vs*75.25±5.8 sec n=6; $p<0.001$) and decreased swimming time (135.16±6.53 sec *vs* 166.5±5 sec, $p<0.01$; n=6) compared to the saline group. Immobility and swimming times in 60 and 90 mg/kg also were statistically different compared to imipramine, ($p<0.01$ to $p<0.001$).

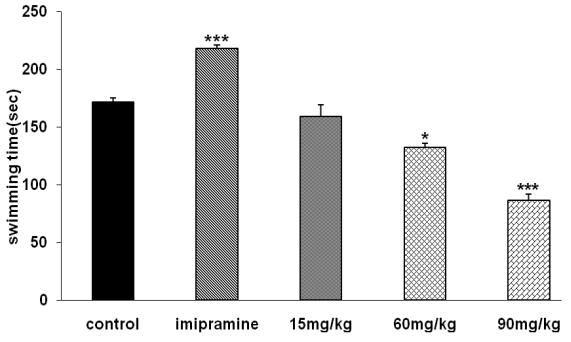

Figure 1. Effects of the imipramine (15 mg/kg, i.p) and three doses of ethanolic extract (15, 60 and 90 mg/kg, i.p) of *R.damascena* on swimming time in mice.
Data represent means±SEM. Comparisons were done by one-way ANOVA followed by Tukey's HSD test. * $p<0.05$;*** $p<0.001$ compared with control group

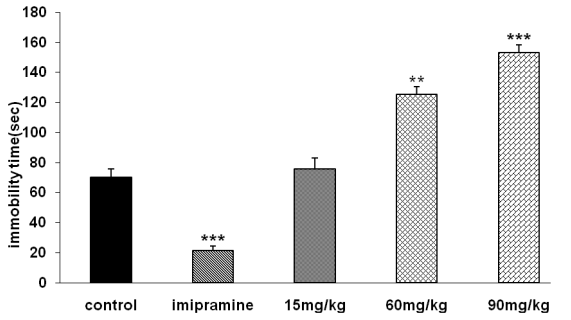

Figure 2. Effects of the imipramine (15 mg/kg, i.p) and three doses of ethanolic extract (15, 60 and 90 mg/kg, i.p) of *R. damascena* on immobility time in mice.
Data represent means±SEM. Comparisons were done by one-way ANOVA followed by Tukey's HSD test. ** $p<0.01$;*** $p<0.001$ compared with control group

Discussion

In this study, we evaluated the antidepressant effects of ethanolic extract of *R. damascena* using forced swimming test. For this purpose, duration of immobility and swimming times of the three doses of ethanolic extract from *R. damascena* in comparison with saline (negative control) and imipramine (positive control) were studied.

Results indicated that in lower dose of the extract (15 mg/kg) immobility and swimming times (Figure 2) did not changed compared to the saline group. However, higher concentrations of extract (60 and 90 mg/kg) significantly increased and decreased immobility and swimming times respectively compared to the saline group. Forced swimming test is the well- known behavioral model used for evaluation of antidepressant activity in rodents (Porsolt et al., 1977; Emamghoreishi and Talebianpour, 2009).

In this test when animal forced to swim in a restricted area initially has vigorous activity and then shows an immobile posture and its movement will be restricted to those movements that keep its head above water (Porsolt et al., 1977). Immobile behavior shows lowered mood (Emamghoreishi and Talebianpour 2009). The agents that decrease this behavior are presumed to have antidepressant effects (Porsolt et al., 1979).

Based on the hypothesis of depression, monoamines, serotonin and noradrenalin play important role in development of depression. According to this theory, impairment of monoaminergic neurotransmission and decreased level of serotonin and noradrenaline are most common causes of depression (Abdalla Salem, 2004) and classical antidepressant drugs such as imipramine by increasing synaptic level of monoamines show antidepresant effect (Porsolt et al., 1977; Hosseinzadeh et al., 2003; Emamghoreishi and Talebianpour, 2009).

In this study, the used doses of ethanolic extract of *R. damascena* didn't have effect on immobility and swimming times. However, with increasing doses of extract, immobility time increased and swimming time decreased. Base on these results, ethanolic extract of *R. damascena* has no antidepressant effect.

The CNS inhibition (hypnotic effect and decreased locomotors activity) of *R. damascena* has been shown in previous studies (Nyeem et al., 2006; Boskabady et al., 2011). One possible reason for this effect may be related to CNS inhibition of

extract that decreased swimming time and increased immobility time. Similar to our results Moallem et al 2007 reported that with increasing dose of aqueous extract from *Echium vulgare* immobility time increased (Moallem et al., 2007).

In addition, in a previous study, we showed that low dose of aqueous extract significantly increased swimming time and decreased immobility time. However, with increasing doses these effects reversed (Dolati et al., 2011).

The R. *damascena* contains several components such as phenolic acid, flavonoids, kaempferol, geraniol, and citranellol that have several pharmacological activities in the CNS (Yassa et al., 2009; Boskabady et al., 2011; Rakhshandah and Hosseini, 2006).

The responsible compound for antidepressant effect of *R. damascena* cannot be determined by the results of the current study but flavonoids, and kaempefrol showed antidepressant effect in previous studies (Velioglu and Mazza 1991; Moallem et al., 2007). Therefore, these compounds maybe responsible for the antidepressant effect. The flavonoids also have hypnotic effect and it is possible that concentrations of flavonoids in ethanolic extract are higher than that of aqueous extract and hypnotic effect is dominant compared to antidepressant effect. However exact mechanism of antidepressant effect of *R. damascena* is unknown and further experiments are needed to clarify this effect.

In summary, the used concentrations of ethanolic extract of R. damascena in this study didn't show any antidepressant effect.

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