Antidepressant-like effect of aqueous extract from *Rosa damascena* in mice

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**Abstract**

**Objective:** *Rosa damascena* mill L (*R. damascena*) is an ornamental plant that has several therapeutic (such as sedative and hypnotic) effects. It also heals depression, grief, nervous stress and tension. In the present study we evaluated antidepressant-like effect of *R. damascena* using forced swimming test (FST).

**Material and Methods:** Three doses of aqueous extract (15, 60 and 90 mg/kg) was injected intraperitoneally. After 30 min of injection, immobility and swimming times were measured and compared with control (negative control) and imipramine (positive control).

**Results:** The results showed that low dose (15mg/kg) of extract significantly increased swimming time and decreased immobility time. However, the two high doses of extract (60 and 90mg/kg) had no significant effect on these parameters.

**Conclusion:** These results proposed antidepressant-like effect of low concentration of aqueous extract of *R. damascena*.

**Keywords:** *Rosa damascena*, Mice, Immobility time, Antidepressant-like effect

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Introduction

Rosaceae families are the most common ornamental plants in the world that have been known as the king of flowers. *Rosa damascena* mill L (*R. damascena*) is the well-known Rosaceae family used for several medicinal purposes especially perfuming effects (Loghmani-Khouzani et al., 2007). People call this plant “flower of Prophet Mohammed” (Gole mohammadi); because they believe it’s nice aroma reminds them of Prophet Mohammad. In addition, its rose water is symbol of love and purity and also used to aid meditation and prayer (Nikbakht and Kafi, 2004; Loghmani-Khouzani et al., 2007).

This plant is cultivated all over the world including Iran (especially in Kashan) for preparing rose water and essential oil and other products (Yassa et al., 2009). The *R. damascena* also has been used for several medicinal purposes and various products and isolated constituents from flowers, petals and hips (seed-pot) of plant were studied in a variety of in vivo and in vitro studies (Boskabady et al., 2011). This plant contains several compounds such as terpenes, glycosides, flavonoids, anthocyanins, Carboxylic acid, myrcene, vitamin C, kaempferol, quarcetin, and Geranial (Zargari, 1992; Schiber et al., 2005; Moeina et al., 2010; Boskabady et al., 2011).

*R. damascena* in ancient medicine was used for strengthening the heart, treatment of menstrual bleeding, digestive problems (Shafei et al., 2003) and reduction of inflammation (Zargari, 1992). It also heals depression, grief, nervous stress and tension (Zargari, 1992; Libster, 2002). The rose inhibits the activity of the hypothalamus and pituitary systems in rat and can suppress the central nervous system. Rose oil of plant in high doses can lead to stress adjustment and the increased ability of the brain to compensate by going to steady state (Kaul et al., 2000).

Recent studies have shown that *R. damascena* has anti-HIV, antioxidant, antitussive, relaxant and antispasmodic effects (Shafei et al., 2003; Boskabady et al., 2011). In addition, it has been reported that *R. damascena* possesses sedative and hypnotic effects (Rakhshanadah and Hosseini, 2006).

Flavonoids and kaempferol compounds have antidepressant properties and plants such as Crocus sativus, Ginkgo biloba and Echium vulgare containing these compounds show antidepressant effect (Velioglu and Mazza, 1991; Moallem et al., 2007; Hosseinzadeh et al., 2007).

*R. damascena* is caontain of flavonoids and kaempefrol (Zargari, 1992; Schiber et al., 2005; Moeina et al., 2010). In addition, it is reported that drop of rose has antidepressent effect in rat (zarghami et al., 2002). Based on these evidence, in the present study antidepressant effects of aqueous extract of *R. damascena* by forced swimming test (FST) was 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).

The aqueous extract of plant was prepared as follows:

Sixty grams of the chopped, dried flowers of plant were extracted with 300 ml distilled water by the soxhlet apparatus. The solvent used for obtaining extract was evaporated by a rotary evaporator under reduced pressure at 50°C. The final extracted materials weighed 10g.

Concentrations of the extract were prepared by dissolving final product in distilled water.

Animals

Frothy male albino mice (25-30 g) were provided by animal house of Mashhad University of medical sciences. They were housed at a controlled temperature of 21-23°C with free access to food and water and constant 12 h light/dark cycle.
Experiments were carried out between 9:00 and 17:00 h. The animals were placed in the experimental room 24 h before the test for acclimatization.

**Experimental groups**
In this experiment the following groups (n=6 for each group) were used:
1- Saline as the negative control
2- Imipramine (15mg/kg) as positive control
3- Aqueous extract group (15mg/kg)
4- Aqueous extract group (60mg/kg)
5- Aqueous extract group (90mg/kg)

**Protocols**
The forced swimming test was used for the evaluation of antidepressant effect of *R. damascena* in mice. 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 aqueous 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.

**Statistical analysis**
All the data were expressed as mean ± SEM. Comparison of the data obtained in the presence of three concentrations of extract was made using ANOVA followed by Tukey’s HSD test. Significance was accepted at p<0.05.

**Results**

**The effects of saline administration on immobility and swimming time in mice**
Treatment with normal saline did not significantly change the immobility time (75.25± 5.8 sec vs 72.3± 4.85 sec) and swimming time (162. 8± 6.4 sec vs 165.5± 7.3 sec) in FST. Therefore, all experimental groups were compared with saline as the control group.

**The effect of imipramine on immobility and swimming times in mice**
The effect of imipramine (15mg/kg) on immobility and swimming time in FST in mice has been shown in Figures 1, 2. As shown, injection of imipramine significantly decreased immobility (21.5±2.90 sec vs 75.25± 5.8 sec, p<0.001) and increased swimming (218.16± 3.2 sec vs 166.5± 7.3 sec, p<0.001) times compared to the control group.

**The effect of aqueous extracts of Rosa damascena on immobility and swimming times in mice**
Three different doses of aqueous extract (15, 60 and 90mg/kg) of *R. damascena* showed different effects on FST. Aqueous extracts at the dose of 15 mg/kg significantly decreased immobility (16.8±1.97 sec vs 75.25± 5.8 sec p<0.001) and increased swimming (223.16± 3.9 sec vs 166.5± 7.3 sec, p<0.001) time in mice compared to the control group (Figure 1, 2). However, these effects didn't reach the statistically significant level compared to imipramine. The dose of 60 mg/kg of this extract didn't have statistically significant effect on immobility (70.23 ± 4.2 sec vs 75.25± 5.8 sec, p>0.05) and swimming (158.28±3.3 sec vs 166.5. ± 5 sec, p>0.05) times compared to the saline group. On the contrary, the dose of 90 mg/kg of this extract significantly increased immobility time (104.83±6.53 sec vs75.25± 5.8 sec, p<0.001) and decreased swimming time (135.16±6.53 sec vs 166.5. ± 5 sec, p<0.01) compared to the saline group. Immobility and swimming times in this dose also significantly increased and decreased compared to imipramine, respectively (p<0.001). In addition, there was significant difference in immobility and swimming times between low and high doses of the extract (p<0.001; Figures 1, 2)
Discussion
In this study, antidepressant-like effect of *R. damascena* has been studied. For this purpose, forced swimming test was used and duration of immobility time and swimming time of the three doses of aqueous extract from *R. damascena* in comparison with saline (negative control) and imipramine (positive control) were evaluated.

Our results showed that duration of immobility time only in lower concentration (15mg/kg) of the aqueous extract (Figure 1) was significantly decreased compared to the saline group and this effect was not statistically significant compared to imipramine. However, higher concentration of aqueous extract did not decrease immobility time significantly.

The symbol of depression is immobility and forced swimming test is a well known animal model for evaluating depression. In FST, mice forced to swim in a restricted space quickly abandon swimming and
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stand still. This behavior is named immobility and shows lowered mood. The agents that reduce this despair behavior are known as antidepressant drugs (Porsolt et al., 1979). In a new method of FST, in addition to immobility time, swimming time is also measured. Based on this method, drugs that inhibit norepinephrine reuptake, decrease immobility time without any significant effect on swimming time. Drugs that selectively inhibit serotonin reuptake decrease immobility and increase swimming time (Detke et al., 1997).

One of the important neurotransmitters involved in the depression are monoamines. It is well-known that low level of monoamines in synapses causes depression and classical antidepressants such as imipramine by inhibiting reuptake of monoamines (5-HT and noradrenalin) increase levels of these neurotransmitters and show antidepressant activity (Katzong, 2001; Sanchez-Mateo et al., 2007; Rojas et al., 2011). In this study, the lower dose of aqueous extract of R. damascena caused a significant reduction in immobility time and increased swimming time. The effect of this dose of extract was comparable to imipramine. Therefore we suggest that antidepressant-like effect of aqueous extract of R. damascena maybe mediated by reuptake inhibition of monoamine neurotransmitters (the same mechanism as imipramine). In addition, because low concentration of the extract significantly decreased immobility time and increased swimming time, therefore this dose may has serotonin reuptake inhibitory effect.

R. damascena contains several components such as flavonoids, kaempferol, geraniol, citranellol that have several pharmacological activities in the CNS.

The role of these compounds for antidepressant effect of R. damascena is not defined. However, it has been reported that plants containing compounds such as flavonoids, and kaempferol show antidepressant effect (Velioglu and Mazza 1991; Moallem et al., 2007). It has also been shown that kaempferol -a constituent of Crocus sativus petal- has antidepressant effect (Hosseinzadeh et al., 2007). In addition, it has been reported that flavonoids and kaempferol show inhibitory effect on mono-amino oxidase enzyme (MAO) in vitro (Butterweck et al., 2002; Moallem et al., 2007). Therefore, it can be suggested that flavonoids and kaempferol of R. damascena are important compounds which may be responsible for its antidepressant effect.

In previous study antidepressant effect the drop of R. damascena compare to amphetamine in rat also was evaluated (zarghami et al., 2002). Because antidepressant effect drop of this plant same to amphetamine, maybe aqueous extract of plant also same to amphetamine increased releasing of monoamines (zarghami et al., 2002). However, exact mechanism of this effect unknown and needs further studies.

In this study, we also found that increasing the dose of extract increased the immobility time and decreased swimming time. The same finding also has been shown in previous studies (Moallem et al., 2007). Mechanism of this effect is unknown. However, it has been shown that R. damascena has CNS depressant and hypnotic effects (Nyeem et al., 2006; Rakhshandah and Hosseini, 2006). Its ethanolic extract also reduced onset and duration of pentobarbital-induced hypnosis, and decreased locomotors activity in the open field test (Nyeem et al., 2006). These effects of R. damascena were attributed to its affinity to benzodiazepines and GABA receptors (Boskabady et al., 2011).

Therefore, we can suggest that in low dose, the extract affects monoamines reuptake in synapses and show antidepressant effect. However, with increasing dose of extract, affinity for binding to benzodiazepines and GABA receptors increases. Therefore, antidepressant effect of extract is masked by vigorous CNS depressant effect of the extract in high doses.

In summary our results showed that low dose of aqueous extract of R. damascena...
has antidepressant effect comparable to imipramine but high doses did not have any antidepressant effect.

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