Avicenna Journal of Phytomedicine
Received: July 18, 2011; Accepted: Aug 8, 2011
Vol. 1, No. 2, Autumn 2011, 91-97

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

Karim Dolati[1], Hassan Rakhshandeh[1], Mohammad Naser Shafei[2*]

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

1- Pharmacological Research Center of Medicinal Plants and Department of Pharmacology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, I. R. Iran
2- Neuroscience Research Center and Department of Physiology, School of medicine, Mashhad University of Medical Sciences, Mashhad, I. R. Iran
***Corresponding Author**: Tel: +985118002230; Fax: +985118828564
E-mail: shafeimn@mums.ac.ir

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 (Rakhshandah and Hosseini, 2006).

Flavonoids and kaempefrol 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 antidepresant 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 *vs*75.25± 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)

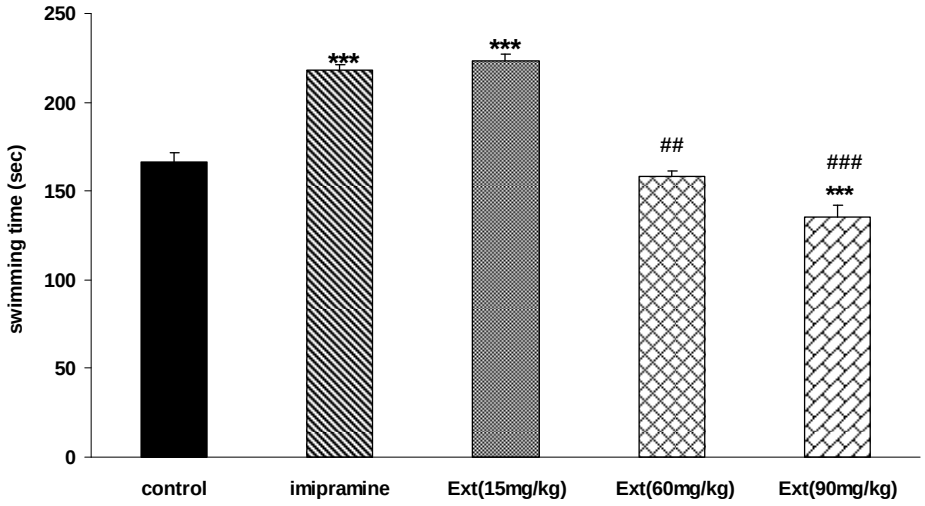

Figure 1. Effects of aqueous extract of *R. damascena* on swimming time in mice.
Data are expressed as means ±SEM (n= 6). ***p<0.001 *vs* control, # # # p<0.001 *vs* imipramine

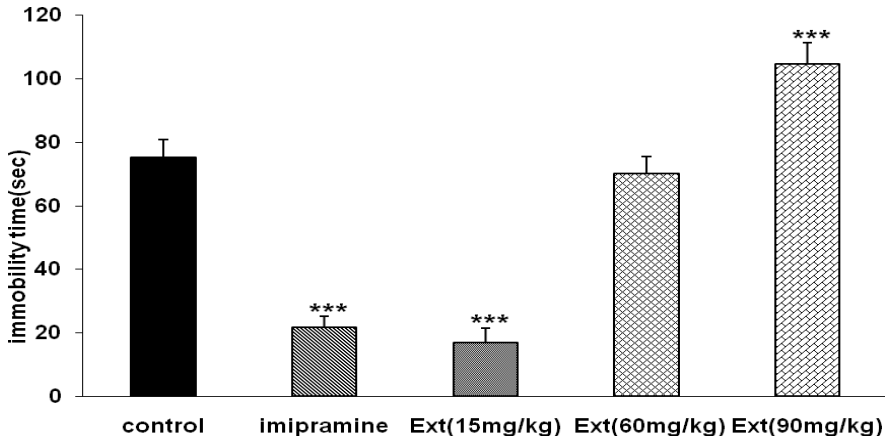

Figure 2. Effects of aqueous extract of *R. damascena* on immobility time in mice.
Data are expressed as means ±SEM (n= 6). ***p<0.001 *vs* control

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 (Figure1) 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

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 kaempefrol show antidepressant effect (Velioglu and Mazza 1991; Moallem et al., 2007). It has also been shown that kaempefrol -a constituent of Crocus sativus petal- has antidepressant effect (Hosseinzadeh et al., 2007). In addition, it has been reported that flavonoids and kaempefrol 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 kaempefrol 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.

Acknowledgments

This study was financially supported by Vice Chancellery of Research of Mashhad University of Medical Sciences.

References

Anchez-Mateo C, Bonkanka C, Prado B, Rabanal R. 2007. Antidepressant activity of some Hypericum reflexum L. fil. extracts in the forced swimming test in mice. Journal of ethnopharmacology, 112(1): 115-121.

Boskabady MH, Shafei MN, Saberi Z, Amini S. 2011. Pharmacological Effects of *Rosa Damascena*. Iranian Journal of Basic Medical Sciences, 14 (4): 213-218.

Butterweck V, Nahrstedt A, Evans J, Hufeisen S, Rauser L, Savage J, et al. 2002. In vitro receptor screening of pure constituents of St. John's wort reveals novel interactions with a number of GPCRs. Psychopharmacologia, 162(2) :193-202.

Detke MJ, Johnson J, Lucki I. 1997. Acute and chronic antidepressant drug treatment in the rat forced swimming test model of depression. Experimental and clinical psychopharmacology, 5(2):107.

Hosseinzadeh H, Motamedshariaty V, Hadizadeh F. 2007. Antidepressant effect of kaempferol, a constituent of saffron (Crocus sativus) petal, in mice and rats. Pharmacologyonline, 2: 367-370.

Katzong Bertram G. 2001. Basic and clinical pharmacology, New York: McGraw-Hill.

Kaul VK, Singh V, Singh B. 2000. *Damask rose* and marigold: prospective industrial crops. J Med Aromat Plant Sci, 22: 313-318.

Libster M. 1999. Delmar's integrative herb guide for nurses. Delmar, 360-370.

Loghmani-Khouzani H, Sabzi Fini O, Safari J. 2007. Essential oil composition of *Rosa damascena* mill cultivated in central Iran. Scientia Iranica, 14(4): 316-319.

Moallem SA, Hosseinzadeh H, Ghoncheh H. 2007. Evaluation of Antidepressant Effects of Aerial Parts of Echium vulgare on Mice. Iranian Journal of Basic Medical Sciences, 10: 189 - 196.

Moeina M, Karamib F, Tavallalib H, Ghasemia Y. 2010. Composition of the Essential Oil of *Rosa damascena Mill*. from South of Iran. Iranian Journal of Pharmaceutical Sciences, 6(1): 59-62.

Nikbakht A, Kafi M. 2004. A Study on the Relationships between Iranian People and *Damask Rose* (*Rosa damascena*) and Its Therapeutic and Healing Properties. Acta Hort, 2008; 790:251-254.

Nyeem M, Alam M, Awal M, Mostofa M, Uddin S, Islam N. 2006. CNS Depressant Effect of the Crude Ethanolic Extract of the Flowering Tops of *Rosa Damascena*. Iranian journal of pharmacology and therapeutics, 5(2): 171-174.

Porsolt RD, Bertin A, Blavet N, Deniel M, Jalfre M. 1979 . Immobility induced by forced swimming in rats: Effects of agents which modify central catecholamine and serotonin activity. European Journal of Pharmacology, 57(2-3): 201-210.

Rakhshandah H, Hosseini M .2006. Potentiation of pentobarbital hypnosis by *Rosa damascena* in mice. Indian journal of experimental biology, 44(11): 910.

Rojas P, Serrano-García N, Medina-Campos ON, Pedraza-Chaverri J, et al .2011. Antidepressant-like effect of a Ginkgo biloba extract (EGb761) in the mouse forced swimming test: Role of oxidative stress. Neurochemistry International.(in press)

Schiber A, Mihalev K, Berardini N, Mollov P, Carle R. 2005. Flavonol glycosides from distilled petals of *Rosa damascena* Mill. Z Naturforsch, 60: 379-384.

Shafei MN, Rakhshandah H, Boskabady MH. 2003. Antitussive effect of *Rosa damascena* in Guinea pigs. Iranian Journal of Pharmaceutical Research, 2: 231-234.

Velioglu Y, Mazza G .1991. Characterization of flavonoids in petals of *Rosa damascena* by HPLC and spectral analysis. Journal of agricultural and food chemistry, 39(3): 463-467.

Yassa N, Masoomi F, Rankouhi SER, Hadjiakhoondi A. 2009. Chemical

Composition and Antioxidant Activity of the Extract and Essential oil of *Rosa damascena* from Iran, Population of Guilan. Daru, 17:175-180.

Zarghami M, farzin D, bagheri K. 2002. Anti depressant effects of *Rosa damascena* on laboratory rats (a controlled experimental blind study). Journal of Mazandaran University of medical sciences, 11(33):27-33.

Zargari A .1992. Medicinal plants. Vol 2. 5th ed. TehranUniversity Press, Tehran, pp. 281-284.