



Mini Review

A Mini Review of Neuropharmacological Effects of *Rosa damascena* Herrm

Farimah Beheshti^{1,2}, Somaieh Ahmadabady³, Yousef Baghcheghi³, Akbar Anaeigoudari⁴, Mahmoud Hosseini⁵

¹Neuroscience Research Center, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

²Department of Physiology, School of Paramedical Sciences, Torbat Heydariyeh University of Medical Sciences, Torbat Heydariyeh, Iran.

³Student Research Committee, Jiroft University of Medical Sciences, Jiroft, Iran.

⁴Department of Physiology, School of Medicine, Jiroft University of Medical Sciences, Jiroft, Iran.

⁵Division of Neurocognitive Sciences, Psychiatry and Behavioral Sciences Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Article Info

Article History:

Received: 29 May 2021

Accepted: 20 August 2021

ePublished: 27 August 2021

Keywords:

-Nervous system

-Neuropharmacological

-*Rosa damascena* Herrm

Abstract

Background: *Rosa damascena* Herrm (*R. damascena*) is a species of the Rosaceae family. The *R. damascena* has been shown to improve depression, anxiety and grief. It also suppresses allergic reactions and migraine headache. In addition, amelioration of learning and memory deficits, delay in onset of seizure attacks, alleviation of pain and improvement of sleep disorders have been attributed to extract and essential oil of *R. damascena*. This review was conducted to integrate the neuropharmacological effects of *R. damascena*.

Methods: Employed scientific databases for collecting information were including PubMed, Scopus and Google Scholar.

Results: The results of animal and clinical trial studies indicate that the extract of *R. damascena* and its essential oil apply useful therapeutic effects on depressant and anxiety-like behaviors, epileptic seizures, learning and memory impairments, sleep disturbances and pain.

Conclusion: Based on scientific findings, the neuroprotective effects of *R. damascena* can be mainly linked to its antioxidant and anti-inflammatory properties.

Introduction

Rosa damascena (*R. damascena*) or Damask rose¹ is familiarized as Gole Mohammadi in Iran.² This plant is a member of the Rosaceae family.³ The people believe that Gole Mohammadi reminds them of Prophet Mohammad.⁴ This flowering plant is bred in Iran (mainly in Kashan).⁵ At the present time, more than 200 species of this plant have been recognized. Regardless of employing as a fancy plant in houses, gardens, and parks, *Rosa damascena* is basically used as a fragrance in industry and is famous due to its perfuming impacts.⁶ Additionally, *R. damascena* has been implicated for therapeutic purposes in traditional medicines.⁷ There is no review on neuropharmacological impacts of *R. damascena*.⁸ This literature review, therefore, was aimed to summarize the neuropharmacological impacts of *R. damascena*.

Search Method

A detailed survey was accomplished in the databases including Medline, PubMed, Scopus and Google Scholar from beginning of 1950 until the end of 2020 to identify the studies carried out on neuropharmacological effects of *R. damascena*. The keywords were *R. damascena*, neuropharmacological, neurotoxicity, neurodegeneration,

memory, learning, epilepsy, pain, anticonvulsant, antianxiety and anti-depressant.

Description and History

R. damascena is bush plant which grows roughly 1 to 2 meters upper floor and has extensive, ostentatious and beautiful blossoms. This plant is able to grow in different areas of the world. Middle East is known as a main source of Damask rose. The history of breeding of *R. damascena* is long in Iran. It has been defined that the crude refining of rose for oil production was begun from the late seventh century AD, and later it was circumfused in many areas of the world in fourteenth century. Although *R. damascena* is grown in multiple cities of Iran, Kashan is main place to bring up of this flowering plant. Iran was the primary maker of rose oil until the sixteenth century and sent out it to whole of global.⁸

Products

Rose water

Rose water is one of the most famous products of *R. damascena* which is used mainly in religious ceremonies.⁸ Generated rose water in Kashan has high quality and is employed annually to wash Kaaba (God House) in Mecca.

*Corresponding Author: Akbar Anaeigoudari, E-mail: Anaeiga317@gmail.com

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Rose water also has high worthiness in the food industry and some food products are aromatized by it.^{4,9}

Essential oil

Essential oil is extracted from the flowers of *R. damascena* and is full of linalool, geraniol, citronellol and nerol. The harvest time and temperature are considered as important factors affecting the quality of essential oil of *R. damascena*.¹⁰ The essential oil is pale, yellow and semisolid. Presence of saturated aliphatic hydrocarbons in oil makes it solid in room temperature.^{4,11} Essential oil is vended as an expensive product in various countries of the world.¹²

Dried flowers

Flowers of *R. damascena* are kept in two forms. Dried buds are mostly exported and dried petals are used for alleviation of gastrointestinal system problems including constipation. Dried flowers of this medicinal plant has been shown to cure asthma, cancer, infection, skin injuries and wounds. Iranian people consume the flowers of *R. damascena* with yogurt.^{4,13}

Other products

Besides products listed above, ethanolic, aqueous and chloroformic extracts are prepared from flowers, petals, and hips of *R. damascena*. These extracts are employed for research works.¹⁴

Chemical Compounds

Presence of glycosides, terpenes, flavonoids and anthocyanin has been confirmed in extract of *R. damascena*.^{15,16} Carboxylic acid, myrcene, vitamin C, quercetin and kaempferol also were extracted from *R. damascena*.¹⁷ Rose hips contain vitamins such as vitamin C, minerals, fatty acids, carotenoids and polyphenols. Phenolic compounds of *R. damascena* possess antioxidant, anticancer, anti-inflammatory, antimutagenic, and antidepressant properties.^{7,18} The essential oil of *R. damascena* contains a lot of nonterpenoid hydrocarbons. The essential oil also is rich of compounds such as linalool, geraniol, n-tricosane, 1-nonadecene, n-pentacosane, nerol and n-hexatriacontane.¹⁹

Traditional Remedies

In traditional medicine, rose water extracted from petals of *R. damascena* is used for preparation of food. The rose water has been suggested to have antimicrobial, antiseptic, antioxidant, anti-inflammatory, anti-aging and lenient effects. Dried flowers of *R. damascena* have been found to remedy digestive problems, to alleviate the pain in abdominal and chest, to reinforce heart and to reduce menstrual bleeding. People believe that rose hips purify blood, therefore they are used with bread.²⁰ Rose oil is prepared from petals of flower and can be used orally. The oil of *R. damascena* is used against anxiety, depression and grief. Reduction of thirst and amelioration of wound and

skin injuries have been attributed to oil of *R. damascena*. Vapor therapy of rose oil has been also suggested to be helpful in treatment of some allergies and headaches including migraine headache.¹³

Neuropharmacological Effects

Multiple pharmacological researches have been done on *R. damascena* to evaluate its impacts on the central nervous system (CNS). Beneficial effect of *R. damascena* on depression, anxiety, learning and memory, seizure, sleep and pain has been documented. Therefore, this review goes on address these issues.

Effect on depression and anxiety

Depression and anxiety are disorders with similar features such as nervousness, irritability, and problems in sleeping and concentrating.²¹ Elevated plus maze²² and open field²³ are experimental tests widely employed for evaluating the effects of compounds and drugs on anxiety. Hole cross test also is used to monitor the spontaneous activity of animals.²⁴ The results obtained from forced swimming test (FST) are used to assess the effect of antidepressant drugs.^{25,26} Using the mentioned tools, *R. damascena* has been reported to possess anxiolytic and anti-depression effects. The results of open field and hole cross tests indicated that oral administration of 250 and 500 mg/kg of the ethanolic extract of *R. damascena* led to a significant reduction in locomotion of animals.²⁷ Unlike these findings in an animal study on male rats, intraperitoneal infusion of 60 and 90 mg/kg of ethanolic extract of *R. damascena* increased immobility, decreased swimming times in FST whereas 15 mg/kg was not effective. The antidepressant effect of *R. damascena* extract was attributed to flavonoides and kaempferol presented in extract.²⁸ Researchers reported that 15 mg/kg of aqueous extract significantly enhanced swimming time and mitigated immobility time in rats. This antidepressant effect of *R. damascena* was comparable with imipramine. Regarding this subject, suppression of reuptake of monoamine neurotransmitters in the brain has been considered as a underlying mechanism for antidepressant effect of *R. damascena* extract.²⁹ It was documented that administration of 0.15 ml/kg rose oil as a vapor for 15 min every day for 28 days improved sucrose preference and attenuated depression like behavior induced by chronic mild stress in rats. In this study, antioxidant effect of the oil of *R. damascena* is mentioned as a basic factor in reduction of sickness behaviors in rats.³⁰ Researchers showed that 100–1600 mg/kg of *R. damascena* oil dissolved in olive oil palliated the avoidance rate in the discrete shuttle-type conditioned avoidance task in mice.³¹ In a clinical trial, 10 and 15 mg capsules of *R. damascena* extract improved depression and behavioral obstacles in old dementia patients. It has been suggested that these effects may be due to the inhibition of serotonin reuptake.³² The Anti-anxiety and anti-depressive effects of *R. damascena* were shown in Table 1.

Table 1. Anti-anxiety and anti-depressive effects of *R. damascena*

Preparation	Dose/Concentration	Type of study	Mechanism/Results
Ethanollic extract	250 and 500 mg/kg (oral)	<i>In vivo</i> (mice)	Decrease of locomotion and reduction of depressant actions ²⁷
Ethanollic extract	60 and 90 mg/kg (i.p)	<i>In vivo</i> (rat)	Increase of immobility and decrease of swimming times in FST ²⁸
Aqueous extract	15 mg/kg (i.p)	<i>In vivo</i> (rat)	Enhancement of swimming time and reduction of immobility time in FST ²⁹
Rose oil	0.15 ml/kg (inhalation)	<i>In vivo</i> (rat)	Improvement of sucrose preference and attenuation of depression like behavior induced by chronic mild stress ³⁰
Essential oil	100–1600 mg/kg (subcutaneous)	<i>In vivo</i> (mice)	Decrease of avoidance rate without affecting the response rate ³¹
Capsules	10 and 15 mg capsules (oral)	Clinical trial	Amelioration of depression and behavioral obstacles ³²

Effect on learning and memory

Oral administration of methanolic extract of *R. damascena* (300, 600, 1200 mg/kg/day for 1 month) improved amyloid β -related memory abnormalities in rats when they were examined by Morris water maze (MWM) and passive avoidance tests. Based on high performance liquid chromatography (HPLC) analysis, these effects may be resulted from antioxidant compounds presented in extract of *R. damascena* such as flavonoids and polyphenols.³³ Treatment with 50 and 250 mg/kg of hydroalcoholic extract of *R. damascena* for 2 weeks prevented scopolamine-induced memory deficits. In this research extract improved brain oxidative damage via decreasing malondialdehyde (MDA) and increasing thiol concentration.³⁴ Oral use of 1 g/kg of hydroalcoholic extract of *R. damascena* has been indicated to have positive impact on high-fat diet-induced learning and memory dysfunction in rats. It was hypothesized that antioxidant properties of *R. damascena* extract contribute in results of this study.³⁵ Inhibition of acetylcholinesterase has been documented to prevent memory deficits. In an *in vitro* study, 1000 μ g/ml of essential oil of *R. damascena* showed inhibitory impact on acetylcholinesterase and butyrylcholinesterase. Based on these findings, *R. damascena* can amplify memory abilities via the suppression of acetylcholinesterase and butyrylcholinesterase activity.³⁶ Improving impacts of *R. damascena* on learning and memory impairments have been concluded in Table 2.

Effect on seizure

Infusion of 750 mg/kg of essential oil of *R. damascena* before pentylenetetrazol (PTZ) increased the latency time

in beginning of seizures in rats. These anticonvulsant properties were linked to the effects of flavonoids of *R. damascena* on gamma aminobutyric acid (GABA)_A receptors.³⁷ It has been shown that 100, 500 and 1000 mg/kg of aqueous and ethanollic extracts of *R. damascena* could attenuate the severity of minimal clonic seizures (MCS) and generalized tonic-clonic seizures (GTCS) in mice kindled by PTZ.³⁸ Electroencephalography (EEG) recording also showed that administration of 50, 100 and 200 mg/kg of hydroalcoholic extract of *R. damascena* attenuated severity of seizures induced by PTZ in rats. One of the possible proposed mechanisms in results of this study is free radicals scavenging properties by the extract of this plant.³⁹ Injection of 750 and 1000 mg/kg of essential oil of *R. damascena* 30 min before PTZ administration in rats retarded the development of seizure stages and prevented kindling acquisition. The role of flavonoids of essential oil in the reduction of seizure severity via activating GABA_A receptors has been suggested in this research.⁴⁰ It has been revealed that seizures followed by PTZ administration can result in neuronal apoptosis in CA₁, CA₃ and dentate gyrus (DG) areas of hippocampus. Researchers reported that hydroalcoholic extract of *R. damascena* (50, 100 and 200 mg/kg) stopped neuronal death caused by PTZ in hippocampus of rats.⁴¹ In a clinical trial, sixteen children with refractory epilepsy received essential oil (5 mg/kg) of *R. damascena* for 3–6 weeks. Based on results, mean frequency of seizures significantly was lowered compared to the control. It was proposed that probably flavonoid compounds of *R. damascena* involve in these results via affecting benzodiazepine receptors.⁴² The anticonvulsant effects of *R. damascena* have been demonstrated in Table 3.

Table 2. Effects of *R. damascena* on learning and memory

Preparation	Dose/concentration	Type of study	Mechanism/ Results
Methanolic extract	300, 600, 1200 mg/kg/day (oral)	<i>In vivo</i> (rat)	Improvement of spatial memory and passive avoidance learning ³³
Hydroalcoholic extract	50 and 250 mg/kg (i.p)	<i>In vivo</i> (rat)	Amelioration of spatial memory, decrease of MDA and increase of thiol concentration ³⁴
Hydroalcoholic extract	1 g/kg (oral)	<i>In vivo</i> (rat)	Improvement of high-fat diet-induced learning and memory dysfunction ³⁵
Essential oil	1000 μ g/ml	<i>In vitro</i>	Inhibition of acetylcholinesterase and butyrylcholinesterase activity ³⁶

Table 3. Effects of *R. damascena* on seizure and epilepsy

Preparation	Dose/concentration	Type of study	Mechanism/Results
Essential oil	750 mg/ kg (i.p)	<i>In vivo</i> (rat)	Postponement in onset seizure via affecting GABA _A receptors ³⁷
Aqueous extract Ethanolic extract	100 and 500 mg/kg (i.p) 1000 mg/kg (i.p)	<i>In vivo</i> (mice)	Retardation in beginning minimal clonic seizures and generalized tonic-clonic seizures ³⁸
Hydroalcoholic extract	50, 100 and 200 mg/ kg (i.p)	<i>In vivo</i> (rat)	Attenuation of severity of seizures induced by PTZ ³⁹
Essential oil	750 and 1000 mg/ kg (i.p)	<i>In vivo</i> (rat)	Prevention of seizure attacks and delay in induction of kindling ⁴⁰
Hydroalcoholic extract	50, 100 and 200 mg/kg (i.p)	<i>In vivo</i> (rat)	Cessation of neuronal death caused by PTZ ⁴¹
Essential oil	5 mg/kg (oral)	Clinical trial	Improvement of refractory seizures ⁴²

Effect on sleep

Hypnotic effects of *R. damascena* were investigated in several studies. Aqueous and ethanolic extracts (500 and 1000 mg/kg) significantly elevated sleep time caused by pentobarbital which was similar to the effects of diazepam. These effects may be mediated via influencing GABA_A receptors.⁴³ In another study, hypnotic impact of the ethanol extract of *R. damascena* and its fractions was evaluated in mice. Results showed that 250 and 500 mg/kg of ethanol extract of *R. damascena* and its ethylacetate fraction exerted hypnotic effects in mice. These effects were attributed to enhanced level of GABA_A receptors activity.⁴⁴ In a clinical trial, the effect of *R. damascena* on sleep was examined. *R. damascena* was used for three subsequent nights and sleep quality was tested using the Pittsburgh Sleep Quality Index. *R. damascena* aromatherapy significantly improved the sleep quality.⁴⁵ The effects of *R. damascena* on sleep disorders have been presented in Table 4.

Analgesic effects

The effects of hydroalcoholic extract (250, 500 and 1000 mg/kg) of *R. damascena* and its oil (100, 200 and 400 µL/kg) on pain alleviation were examined in rats. The hydroalcoholic extract (500 and 1000 mg/kg) significantly alleviated abdominal twitches. In formalin test, the oil of the plant was not effective but hydroalcoholic extract

lowered paw licking time of both phases of formalin test dose-dependently. It is probable that analgesic effects of hydroalcoholic extract of *R. damascena* were carried out via the inhibition of C fibers.⁴⁶

In clinical trial, 88 patients with migraine headache received a combination of *Viola odorata L.* and *R. damascena* flowers and *Coriandrum sativum L.* fruits in 500 mg capsules three times a day and propranolol tablet (20 mg) twice a day. According to the results, the capsules alleviated headache in patients with migraine.⁴⁷ In another clinical trial, ethanolic extract (400 mg capsules) of *R. damascena* had analgesic and anti-inflammatory effects and reduced postoperative pain.⁴⁸ The effects of *R. damascena* on pain relief have been presented in Table 5.

Toxic Effects

There are not enough reports about toxic effects of *R. damascena*. In a study on dogs, researchers evaluated the nephrotoxic and hepatotoxic effects of this plant in doses of 90-1440 mg/kg during 10 days. The results indicated a slight increase in bilirubin concentration and alanine aminotransferase (ALT) in group treated with *R. damascena* with respect to control group. There was no remarkable difference in blood concentration of creatinine, urea and alkaline phosphatase (ALP) in dogs treated with *R. damascena* compared to those of control group.⁴⁹

Table 4. Effects of *R. damascena* on sleep

Preparation	Dose/Concentration	Type of study	Mechanism/Results
Ethanolic extract and aqueous extract	500 and 1000 mg/kg (i.p)	<i>In vivo</i> (mice)	Elevation of sleeping time induced by pentobarbital ⁴³
Ethanolic extract and ethylacetate fraction	250 and 500 mg/kg (i.p) 500 mg/kg (i.p)	<i>In vivo</i> (mice)	Prolongation of sleep time ⁴⁴
Drop	Aromatherapy	Clinical trial	Improvement of sleep quality ⁴⁵

Table 5. Analgesic effects of *R. damascena*.

Preparation	Dose/concentration	Type of study	Mechanism/Results
Hydroalcoholic extract	500 and 1000 mg/kg (oral)	<i>In vivo</i> (rat)	Inhibition of abdominal twitches and reduction of carrageenan-induced paw edema ⁴⁶
Capsule	500 mg capsules three times a day (oral)	Clinical trial	Improvement of headaches in patients with migraine ⁴⁷
Ethanolic extract	400 mg capsules (oral)	Clinical trial	Relief of postoperative pain and amelioration of inflammation ⁴⁸

Conclusion

Based on the present review, *R. damascena* extracts and products obtained from it in particular rose oil prevent the death of brain neurons and exert beneficial therapeutic effects on anxiety, depression, learning and memory impairments, seizure, sleep disorders and pain. The neuroprotective effect of *R. damascena* can be linked to its antioxidant and anti-inflammatory properties. In addition, presented ingredients in *R. damascena* extract can improve behavioral disorders resulted from brain neuronal damages via amplifying the effect of neurotransmitters such as GABA and inhibiting acetylcholinesterase and butyrylcholinesterase activity.

Author Contributions

FB: Collecting data and drafting the manuscript, SA: Collecting data and drafting of the manuscript, YB: Drafting of the manuscript, AA: Analysis of data, interpretation, submission of the manuscript and revision, MH: Drafting of the manuscript and revision. All authors read and confirmed the final version of the manuscript.

Conflict of Interest

The authors report no conflicts of interest.

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