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Original Article

ANTIDEPRESSANT-LIKE ACTIVITY OF AQUEOUS EXTRACT OF *ROSA DAMASCENA* IN MICE

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ABSTRACT

Objective: Plant-based drugs have the potential to be very effective substitutes for prescription antidepressants. *Rosa damascena* has therapeutic potential as an analgesic, anticonvulsant, antitussive, bronchodilatory, antibacterial, anti-diabetic, anti-inflammatory, antioxidant, and laxative. Given this context, the goal of the current study was to assess *Rosa damascena*'s potential antidepressant effects.

Methods: Maceration was used to create an aqueous extract of *Rosa damascena*. The Tail Suspension Test (TST) on BALB/c mice and the Forced-Swimming test (FST) on C57BL/6 mice were used to quantify the antidepressant activity. Mice were divided into three groups: control (saline), standard (citalopram and desipramine), and *Rosa damascena* aqueous extract (n = 6 per group). Intraperitoneally (1 ml/100 g) injections of drugs were administered. Analysis of variance was used to examine the data, and then LSD post-hoc tests were performed. The data are expressed as mean±SEM.

Results: Antidepressant-positive controls, citalopram and desipramine, significantly decreased the time of immobility in the FST and TST as compared to the vehicle control group ($p<0.001$). In FST, the immobility durations were significantly reduced by the *Rosa damascena* aqueous extract at a dose of 40 mg/kg compared to lesser doses of the same extract (10 and 20 mg/kg) ($p<0.001$). Similarly, the 40 mg/kg dose of *Rosa damascena* aqueous extract significantly reduced the length of immobility in TST ($p<0.001$).

Conclusion: The present findings demonstrate *Rosa damascena*'s antidepressant-like effects in mice. Further research is necessary to determine the underlying mechanism by which *Rosa damascena* generates effects akin to those of an antidepressant in light of this observation.

Keywords: *Rosa damascena*, Antidepressant-like effect, Forced-swimming test, Tail suspension test, Citalopram, Desipramine

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INTRODUCTION

Depression, an important psychiatric condition, is characterized by lethargy, shrinking self-esteem, restlessness, a change in appetite, and reduced attention [1]. Worldwide, depression affects a sizable percentage of adults [2]. While anybody can suffer from depression, certain individuals and populations are more prone to progressing with this disorder than others. Compared to other age groups, the pace of growth in depression was noticeably faster in younger age groups [3]. It is well documented that the main root of this ailment is the insufficiency of monoamines like Norepinephrine (NE) and serotonin (5-HT) in the brain.

Many pharmacological antidepressants, such as monoamine oxidase inhibitors, Tricyclic Antidepressants (TCA), and selective Serotonin Reuptake Inhibitors (SSRI), have been used extensively to treat depression [4]. However, because of a number of side effects, including weight gain, disturbed sleep, and sexual dysfunction, all of these medications used to treat depression disrupt the course of treatment [5]. One of the best and safest sources of medicine is found in nature. Based on the information at hand, it is now plausible that herbal medicine can be used to treat almost every condition found in nature. Because of this, the evaluation, classification, and documentation of different medicinal herbs and their chemical constituents with respect to a variety of illnesses, such as anxiety, analgesia, and depression, have received a great deal of attention [6].

Plant-based medicines have the potential to be excellent substitutes for the chemical antidepressants that are now on the market because they are often linked to satisfactory protection without adverse effects. Many studies conducted recently have focused on classifying the antidepressant potential of these herbal drugs and the classification of their therapeutically active ingredients [7-9].

Given that there are around 400,000 species of higher plants in the world and that only a small percentage of these have been examined, it is clear that plants will continue to be a great source of leads for drug discovery [10, 11]. By locating novel chemical entities for medication development, studies targeted at dissecting natural compounds from herbal sources can quicken the drug discovery process. Little research has been done on finding botanical medications for depression despite significant efforts being made to find medications for other illnesses.

Oman is home to over a thousand terrestrial plant species, many of which are indigenous and have therapeutic benefits [12]. One of the indigenous species in the Al-Jabal Al-Akhdar mountain range of the Al-Dakhiliya Governorate, Sultanate of Oman, is *Rosa damascena*. *Rosa damascena* is a perennial bushy shrub that grows to a height of one to two meters. Its leaves are imparipinnate, with five to seven leaflets per leaf. [13]. Numerous studies have examined the various activities of *Rosa damascena*, including its analgesic, anticonvulsant, antitussive, bronchodilatory, antibacterial, anti-diabetic, anti-inflammatory, antioxidant, and laxative properties [14-16].

In Oman, *Rosa Damascena*, locally known as Damask rose, is utilized as a therapeutic agent for cosmetics and aromatherapy due to its high vitamin and antioxidant content [17]. However, a thorough investigation of this plant's neuropharmacological effect is lacking, which inspired us to look into *Rosa Damascena's* antidepressant effects in two behavioral antidepressant models, the Forced-Swimming Test (FST) and the Tail Suspension Test (TST).

MATERIALS AND METHODS

Animal

Two strains of mice, each weighing 22-30 g, were used for two different tests. For the FST, C57BL/6 mice were employed. Based on a previous publication on this strain of mice [18], this strain was chosen for the FST. However, based on a previous report that showed the immobility periods across the strains of mice and proved the good sensitivity of the BALB/c strain of mice, male BALB/c mice were chosen for the TST [19]. All the animals used in the current study were supplied by the Animal Facility Units of the

University of Nizwa. The animals were kept at a temperature of 22 C in groups of six (6) and given unlimited access to food and water. They also experienced a 12-hour light/dark cycle. After receiving approvals (Approval Number: CGSR/AEC/02/2020 dated June 15, 2020) from the University of Nizwa Animal Ethics Committee, all animal studies were carried out.

Plant material

The Fawah Factory in Al-Jabal Al-Akhdar, Al-Dakhiliya Governorate, Sultanate of Oman, is the source of the *Rosa Damascena* rose water. The *Rosa damascene* (voucher specimen number: UCRD53) was harvested from the same mountain range (23°09'56.7"N 57°29'56.0"E) and used by the maker of rose water. Usually, the flowers of this shrub are used to make rosewater [20].

Chemicals

Solvents used in the current study were dimethyl sulfoxide (Fisher Chemicals) and sodium hydrogen phosphate (Merck, Germany). SSRI, citalopram and TCA, desipramine (Sigma-Aldrich) were used for behavioral studies.

Instruments

A rotary evaporator (Model RE 801, Yamato Scientific) was utilized to prepare the crude extracts of rose water from *Rosa damascena*.

Preparation of the aqueous extract of *Rosa damascena*

To prepare the aqueous fraction, 250 ml of rose water from *Rosa damascene* were used. A rotary evaporator operating under reduced pressure at 42 ◦ C and roughly 250 rpm was used to evaporate the rose water solvent. After being weighed, the dried extracts were transferred into vials for additional processing [21]. To prepare extract concentrations, the final product was dissolved in 10% DMSO.

Experimental protocol for the FST

Thirty minutes before the FST, mice were received an intraperitoneal (i.p.) injection of citalopram (10 mg/kg, n=6), desipramine (20 mg/kg, n=6), vehicle control (saline, n=6) and the aqueous extract of *Rosa damascena* (10, 20, 40 mg/kg, n=18). Following treatment, mice were placed one at a time into clear plastic cylinders measuring 23 cm in height and 10 cm in diameter that are filled with 8 cm of water at 25 °C. A video camera positioned around 30 centimeters above the cylinder recorded each mouse for a duration of six minutes. The first two minutes of this time were used for acclimatization, and the latter four minutes of each testing session were used to determine immobility [22]. Three independent raters quantified the immobility time. When an animal is immobile, it means that it cannot move except to maintain its head and nose above the water's surface [23]. All mice were first-time swimmers and none were used for multiple FSTs.

Experimental protocol of the TST

Thirty minutes before the FST, mice were received an intraperitoneal (i.p.) injection of citalopram (10 mg/kg, n=6), desipramine (20 mg/kg, n=6), vehicle control (saline, n=6) and the aqueous extract of *Rosa damascena* (10, 20, 40 mg/kg, n=18). Every mouse was hanged upside down by its tail and fastened to a metal bar attached to a ring stand using adhesive tape 2-4 cm from the tip of the tail. The mice were suspended 35 cm above a layer of protecting sponge. Every mouse was hung and taped with a video camera at the same level as the animal for six minutes. Three separate raters quantified the amount of time spent immobile during the final four minutes of each testing session. The unmoving period of the mouse was considered immobility [24]. All mice were used once for TSTs.

Data analysis

Every data point was expressed as mean±SEM. One-Way Analysis of Variance (ANOVA) was used to do the statistical analysis of the data. Additional multiple comparisons were carried out using the LSD test as the post hoc test whenever the ANOVA showed significant results. All assessments were finished using SPSS software (version 21). Statistical significance level was $p<0.001$.

RESULTS

The time of immobility in FST was decreased in a dose-dependent manner by the SSRI antidepressant positive control citalopram (fig. 1). According to LSD post-hoc analysis, citalopram at doses of 5 and 10 mg/kg reduced immobility by 30% and 44%, respectively, compared to the vehicle control group ($p<0.001$). Desipramine, the TCA positive control, likewise considerably lowered the duration of immobility in FST (fig. 2). Desipramine at a dose of 20 mg/kg was found to reduce immobility by 35% as compared to the vehicle control, according to LSD post-hoc analysis ($p<0.001$). *Rosa damascena* aqueous extract was found to reduce immobility in FST in a dose-dependent manner (fig. 3). Furthermore, in contrast to the vehicle control, the *Rosa damascena* extract at a dose of 40 mg/kg ($p<0.001$) showed a 33% reduction in immobility, according to LSD post hoc analysis.

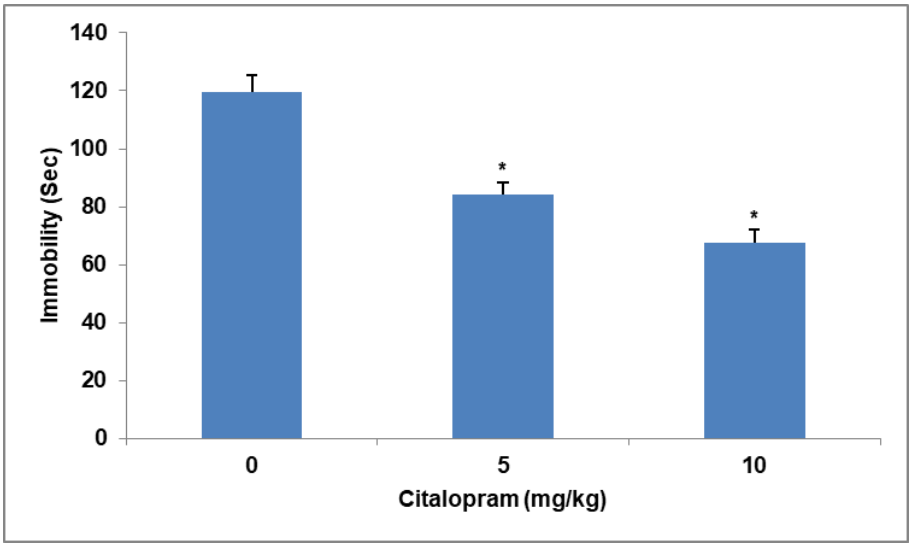

Fig. 1: Dose response of the SSRI positive control, citalopram, in the FST. DMSO (10%) served as the vehicle control (0 mg/kg). Vehicle control or citalopram (n=6 per group) was injected 30 min before the test. Data were evaluated using analysis of variance, followed by LSD post-hoc tests, where *p<0.001 was considered significantly different from the vehicle control. The data are expressed as mean±SEM

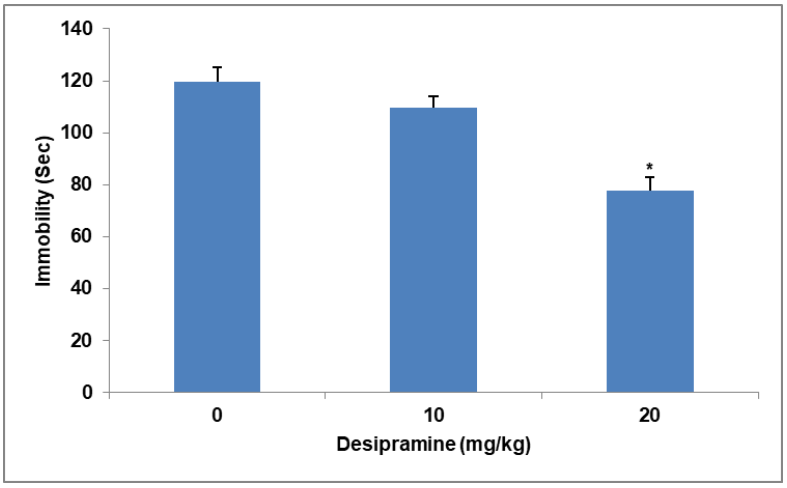

Fig. 2: Dose response of the TCA positive control, desipramine, in the FST. DMSO (10%) served as the vehicle control (0 mg/kg). Vehicle control or desipramine (n=6 per group) was injected 30 min before the test. Data were evaluated using analysis of variance, followed by LSD post-hoc tests, where *p<0.001 was considered significantly different from the vehicle control. The data are expressed as mean±SEM

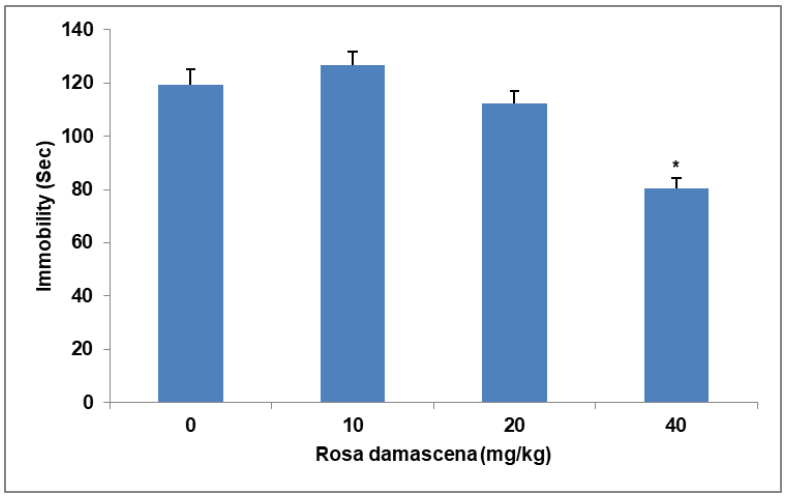

Fig. 3: Dose response of Rosa damascena (DMSO as vehicle control) in the FST. DMSO (10%) served as the vehicle control (0 mg/kg). Vehicle control or *Rosa damascena* (n=6 per group) was injected 30 min before the test. Data were evaluated using analysis of variance, followed by LSD post-hoc tests, where *p<0.001 was considered significantly different from the vehicle control. The data are expressed as mean±SEM

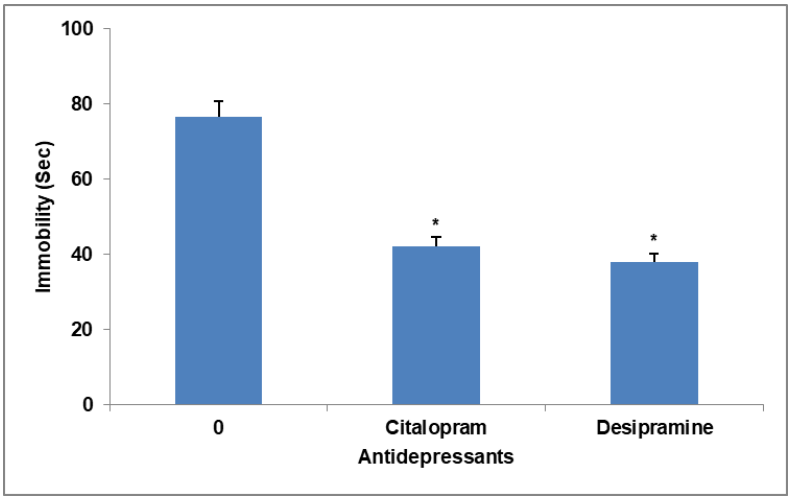

Fig. 4: Effects of citalopram (10 mg/kg) and desipramine (20 mg/kg) in the TST. DMSO (10%) served as the vehicle control (0 mg/kg). Vehicle control, citalopram, or desipramine (n=6 per group) was injected 30 min before the test. Data were evaluated using analysis of variance, followed by LSD post-hoc tests, where *p<0.001 was considered significantly different from the vehicle control. The data are expressed as mean±SEM

In TST, citalopram, an SSRI antidepressant positive control, shortened the immobility period (fig. 4). According to LSD post-hoc analysis, citalopram at a dose of 10 mg/kg reduced immobility by 45% as compared to the vehicle control group ($p<0.001$). Desipramine, the TCA positive control, likewise significantly decreased immobility in TST (fig. 4). According to LSD post-hoc analysis, desipramine at a dose of 20 mg/kg reduced immobility by 50% as compared to the vehicle control ($p<0.001$). *Rosa damascena* aqueous extract reduced immobility in TST in a dose-dependent manner (fig. 5). Additionally, the LSD post hoc analysis showed that the extract of *Rosa damascena* at a dose of 40 mg/kg ($p<0.001$) reduced immobility by 39% as compared to the vehicle control.

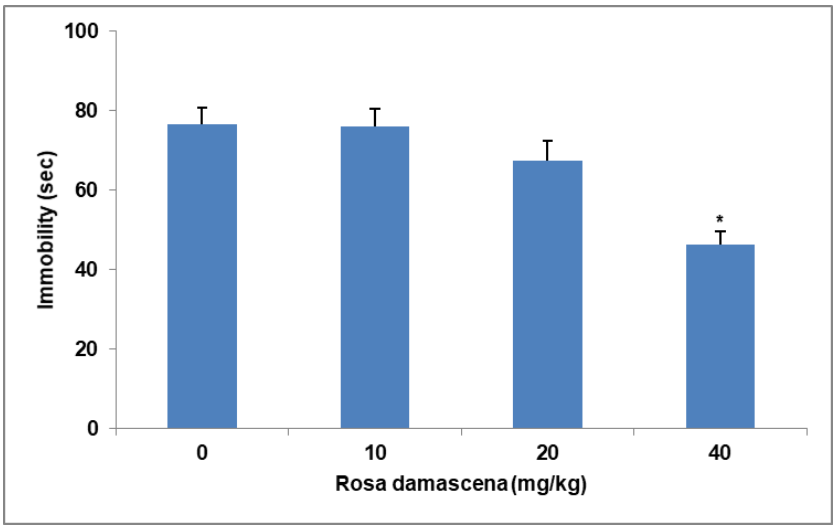

Fig. 5: Dose response of *Rosa damascena* (DMSO as vehicle control) in the TST. DMSO (10%) served as the vehicle control (0 mg/kg). Vehicle control or *Rosa damascena* (n=6 per group) was injected 30 min before the test. Data were evaluated using analysis of variance, followed by LSD post-hoc tests, where *p<0.001 was considered significantly different from the vehicle control. The data are expressed as mean±SEM

DISCUSSION

In today's world population, neurological illnesses such as anxiety and depression are quite common and come with a significant morbidity rate. The modern world demands that we address these problems and develop effective medications. While there are many medications on the market, they are all associated with some limitations, so it is imperative to seek out alternative medications to treat these conditions. Increased oxidative stress is one of the potential contributing elements to the multiple physiological phases of depression [25]. Oxidative stress occurs as soon as the human body's flawed antioxidant system is unable to control the oxidative mediators. Many metabolic diseases as well as other health issues have developed as a result of such.

The information that was available suggested that the brain is harmed by oxidative stress due to its increased oxygen consumption and weakened resistance to reactive oxygen species. Reactive oxygen species production is a major contributor to neurodegeneration and is clearly seen in the course of depression [26]. Reports that are currently available suggest that *Rosa* genus extracts and active ingredients can lessen oxidative stress [27, 28]. The present researchers were motivated to investigate the antidepressant impact of *Rosa damascena*, an indigenous plant found in Al-Jabal Al-Akhdar, Al-Dakhilia Governorate, Sultanate of Oman, due to these features and the antidepressant effects of constituents and extracts from the *Rosa* genus.

The aim of the present investigation was to assess the possible antidepressant properties of *Rosa damascena* aqueous extract by means of mouse behavioral models. It is difficult to establish a reliable animal behavioral model to determine an effective antidepressant treatment [29]. In practicality, rodent FST and TST are widely accepted animal models for assessing behavior similar to that of antidepressants. These behavioral experiments have evaluated immobility, which is analogous to human behavior. According to findings that are now available, antidepressants can shorten the period of immobility in experimental animals [22]. The purpose of immobility in mice during FST is to recreate a state of hopelessness, which is meant to mimic depressive illnesses in humans. Moreover, antidepressant drugs have the ability to reduce the duration of immobility. This model has a unique correlation between the clinical efficacy of antidepressants and their effectiveness in the FST [30].

In the present research, the FST demonstrated that an aqueous extract of *Rosa damascena* proved its ability to act as an antidepressant, suggesting it could be the leading medication for depression treatment. *Rosa damascena*'s capacity to exhibit antidepressant-like effects in the FST is demonstrated through its ongoing reduction in the immobility time as the dose increases. Additionally, the aqueous extract of *Rosa damascena* showed antidepressant properties in both the FST and TST, similar to well-known antidepressants such as citalopram and desipramine. Citalopram shows its effects by blocking the reabsorption of 5-HT; on the other hand, desipramine works by preventing the reabsorption of both 5-HT and NE. These two types of chemical antidepressants are commonly employed in research. The positive results seen with citalopram and desipramine in the FST are due to the enhanced availability of these neurotransmitters at the synapse following the blocking of the reuptake process [31, 32].

The basic beliefs about depression were developed over more than half a century ago, indicating that signs of depression often arise from the lack of essential brain chemicals such as 5-HT, dopamine (DA), and NE at the synapse [33]. Research has also demonstrated that natural plant extracts can improve a person's general resistance to stress across various measures and lessen their reaction to stress by managing the levels of certain chemicals. This suggests that plant extracts might have the potential to act as antidepressants by restoring these neurotransmitters to their typical levels [34].

Rosa damascena's chemical components may be responsible for its possible beneficial effects on stress, anxiety, depression, and sleep disturbances. Among these, specific components, especially flavonoids and kaemferol, appear to have antidepressant properties. Various researchers have suggested that flavonoids and kaemferol exhibit antidepressant effects by blocking monoamine transporters

and monoamine oxidase enzymes [35, 36]. Furthermore, there is a significant overlap in the antidepressant actions and antioxidant potential [37]. Additionally, it has been noted that plant species generally lessen oxidative stress, which in turn increases serotonergic neurotransmissions in synapses to form the basis of their antidepressant potential [38]. Therefore, by adjusting its antioxidant properties, the *Rosa damascena* aqueous extract may show potential as an antidepressant. However, additional research is necessary to elucidate *Rosa damascena*'s mechanism of action within the central nervous system.

CONCLUSION

This study found that *Rosa damascena* had antidepressant-like effects in two common antidepressant models: the TST and the FST. According to the present studies, the aqueous extract of *Rosa damascene* showed considerable antidepressant effects that were comparable to those of citalopram and desipramine, two common antidepressants. Further research is required to elucidate the mode of action of *Rosa damascena* in generating antidepressant effects. The present research also warrants further studies to isolate the active components in *Rosa damascena,* which may produce antidepressant-like effects.

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AUTHORS CONTRIBUTIONS

As the lead researcher, Jamaluddin played a key role in developing the idea and planning the research. In addition, he wrote the manuscript and explained the findings. The studies were carried out, the findings evaluated, and paper writing assistance was provided by Afaf and Sadri.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interest

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