

Evaluation of The Antidepressant-like Effect of The Aqueous Extract of *Prunus Mahaleb* L. Seed kernels in Mice

Awatif M. Al-Saaedi

University of Thi-Qar/ College of Science/ Biology Department

Thi-Qar/ Iraq

e-mail: awatifhistology_bio@sci.utq.edu.iq

<https://doi.org/10.32792/utq/utjsci/v8/1/6>

Abstract— Depression is a common psychiatric condition where 21% of the world population suffers from it. *Prunus mahaleb* is widely used in folk medicine to treat many diseases, but the antidepressant effect of this plant is not well investigated. The present study aims to evaluate the antidepressant-like activity of the aqueous extract of *Prunus mahaleb* seed kernels. For assessment of the antidepressant effect of aqueous extract of *Prunus mahaleb* at 200 and 400mg/kg, two models for depression were used in this study, forced swim test and tail suspension test. Aqueous extract of *Prunus mahaleb* seed kernels has a significant ($p < 0.05$) antidepressant-like effect at two doses 200 and 400 mg/kg in mice. Herbal medicine can play a significant role in treating depression; however, further studies are necessary to detect the pure compounds in *Prunus mahaleb* extract that responsible for the antidepressant activity and to understand their mechanism of action.

Keywords— Depression, *Prunus mahaleb*, antidepressant

I. INTRODUCTION

Depression is a common and disabling psychiatric condition, where 21% of the world population suffers from it. According to the reports of World Health Organization, mood disorders are the second leading cause of disability-adjusted life years and also the leading cause of years lived with disability in different ages (Raymond, 2012; Kumar *et al.*, 2014; Abdul Mannan, *et al.*, 2015).

Unfortunately, some synthetic drugs used to treat depressed people have adverse effects, including fatigue, gastrointestinal or respiratory problems, anxiety, agitation, drowsiness, and cardiac arrhythmias besides the drug-drug interactions. These reasons create an opportunity for medicinal plants to use as alternative drugs for depression treatment (Talha *et al.*, 2011).

Herbal therapies may be a successful way to treat depression since a large number of herbal preparations have appeared psychotherapeutic activities. The search for new pharmacotherapy from medicinal herbs and constituents isolated from plant extracts for psychiatric disorders,

including depression, has advanced expressively over the previous decade (Zhang, 2004).

Prunus mahaleb L. (white mahaleb) is a member of Rosaceae family. This plant is native to the Mediterranean region. It is a tall shrub or a small tree up to 12 m in height. It produces a marginal fruit crop with cherry-like dark purple drupes and a very bitter taste. Culinary use of *P. mahaleb* seed kernels is restricted to the Southeastern part of Europe and West Asia (Oskoueian *et al.*, 2012; Gerardi *et al.*, 2016; Ravindran, 2017).

P. mahaleb has a great value in folk medicine to treat different diseases such as blood pressure, diarrhea, asthma, nausea, and kidney stone also it is used as a tonic for sensory organs and the heart and for relief of pain arising from liver and gastrointestinal troubles. Also, in Arabia, *P. mahaleb* kernels are used as a sedative (Shams and Schmidt, 2008; Oskoueian *et al.*, 2012), but the antidepressant activity of *P. mahaleb* is not clearly investigated. The present study was designed to evaluate the antidepressant-like activity of the aqueous extract of *P. mahaleb* seed kernels in mice.

II. MATERIALS AND METHODS

A. Plant material and extraction

Dried *P. mahaleb* seed kernels were collected from the markets of Nasiriyah city in Thi-Qar province, south of Iraq, and were authenticated as *P. mahaleb* in the laboratories of University of Thi-Qar/ College of Science. Seed kernels were ground for the extraction process. Aqueous extract of *P. mahaleb* seed kernels was prepared according to the method of (Akomolafe *et al.*, 2017) with some modification. Thirty grams of powdered seed kernels have to be soaked in 250 mL distilled water at 25 ± 2 °C for 72 h in a beaker and was stirred by a magnetic bar and stirrer hot plate. Seed suspension was filtered with the help of Whatman No. 1 filter paper. The solvent was removed by rotary evaporator, and the obtained extract was dried at room temperature. The dried extract was stored at 4°C in a dark vial until the antidepressant activity was investigated.

B. Animals

Forty two-month-old BALB/c mice (weighting about 20-25 grams) of both sexes were purchased from the High Institute for Infertility Diagnosis and Assisted Reproduction Technologies, AL-Nahrain University/ Baghdad/ Iraq. The animals were housed and were maintained under standard hygienic conditions at $20^{\circ}\text{C} \pm 2^{\circ}\text{C}$ with a 12-hour day/night cycle and access to water and food ad libitum. Animals were treated in accordance with the Ethical Committee of College of Science/ Thi-Qar University.

C. Antidepressant activity tests

1) Forced swimming test (FST)

The FST was performed according to the method of (Porsolt et al., 1977). Twenty mice were divided into four groups (n=5 and were set to receive orally: group 1: distilled water (control), group 2: Imipramine Hydrochloride as a standard drug (30 mg/kg), group 3 and 4: *P. mahaleb* seed kernels extract (200 mg/kg) and (400 mg/kg) respectively, 1 h. before the test. Mice were placed in an acrylic cylinder (30 cm height x 20 cm diameter) filled with water at $25 \pm 1^{\circ}\text{C}$ to a depth of 15 cm after 1 h. of the treatment. All animals were forced to swim for 5 min and the duration of immobility (when they remained floating, motionless in the water, making only those movements necessary to keep its nose above water was observed and measured during the final 4 min. A significant decrease in the duration of immobility is an indicator of an antidepressant-like activity.

2) Tail suspension test (TST)

Twenty mice were also divided into four groups. They were treated orally with: Group 1: distilled water (control), group 2: 30 mg/kg Imipramine hydrochloride (standard), group 3 and 4: 200 and 400 mg/kg of *P. mahaleb* seed kernels respectively 1 h. before the study. Mice were suspended on the edge of the table, 50 cm above the floor, with the help of adhesive tape placed approximately 1 cm from the end of the tail. The total duration of immobility induced by tail suspension was recorded by observation during the last 6 min of the 10 min period. The animal was considered to be immobile when it did not show any movement, hanged passively, and completely motionless (Steru et al., 1985).

D. Statistical analysis

The results are presented as mean \pm SEM. The statistical analysis was performed using one-way analysis of variance (ANOVA) followed by LSD post hoc test as appropriate using SPSS 14 software. Differences between groups were considered significant at a level of $p < 0.05$.

III. RESULTS AND DISCUSSION

The antidepressant-like effect of the aqueous extract of *P. mahaleb* seed kernels was illustrated in the table (1). The standard drug and also *P. mahaleb* extract at doses of 200 and 400 mg/kg produced a significant decrease in immobility time in the two models at $P < 0.05$ when compared with the control group.

TABLE (1): ANTIDEPRESSANT-LIKE EFFECT OF *P. MAHALEB* IN MICE.

Groups	Treatment (orally)	Forced Swim test Immobility Duration (Sec)	Tail suspension test Immobility Duration (sec)
1	distilled water	125.2000 \pm 4.95a	155.22 \pm 1.88a
2	Imipramine hydrochloride (30mg/kg)	55.4000 \pm 1.80b	63.80 \pm 1.77b
3	200 mg/kg of the extract	55.6000 \pm 2.15b	91.61 \pm 2.65c
4	400 mg/kg of the extract	45.2000 \pm 1.88c	82.20 \pm 3.397d

Value are means \pm S.E.M. Different letters refer to a significant difference at $P < 0.05$

FST has not traditionally been considered as a consistently sensitive model for detecting selective serotonin reuptake inhibitor activity, while these antidepressants are generally active in the TST (Castagn et al., 2011; Kiranmayi et al., 2018).

The main biochemical causes of depression are metabolic disorders of monoamine neurotransmitters that are involved in noradrenaline, serotonin, and dopamine signaling (Naughton et al., 2000; Li et al., 2013).

The antidepressant activity of plant preparations was linked to their content of flavonoids and Coumarin because of their antioxidant effect. Hesperidin, Chrysin, Naringenin, and Astilbin are examples of flavonoids that have antidepressant activity (Singh et al., 1992; Bubols et al., 2013; Guan and Liu, 2016; Hritcu et al., 2017).

Seed kernels of *P. mahaleb* have a high content of coumarins (Ieri et al., 2012). This may be the cause of the antidepressant effect of the kernels extract in this study.

It could be concluded that the aqueous extract of *P. mahaleb* seed kernels has antidepressant-like activity; further studies are necessary to detect the pure compounds in *P. mahaleb* extract that responsible for the antidepressant activity and to understand their mechanism of action.

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