



Exploring the Antidepressant Effect of Aqueous Alcoholic Extract of Purslane Plant (*Portulaca Oleracea*) on Asthma-induced Depression in Mice: Insights from Open Field and Forced Swimming Tests

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ABSTRACT

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Asthma is one of the most common chronic diseases in which inflammation plays an essential role in its pathophysiology. One of the secondary effects of asthma is depression, which is probably due to overlapping pathogenic mechanisms. One of the important mechanisms in the treatment of depression and asthma is to pay attention to removing inflammation and reducing oxidative stress. Purslane exerts its anti-inflammatory and antioxidant effects through NF κ B and NOS pathways. This study aims to investigate the effect of the aqueous-alcoholic extract of the purslane plant on depression caused by experimental asthma using an Open Field Test and Forced Swimming Test in small laboratory mice.

To investigate the aqueous-alcoholic extract of the purslane plant on depression caused by experimental asthma, 40 Syrian NMRI male mice were divided into 4 groups: control, asthmatic, and asthmatic receiving the extract at a dose of 50 mg/kg and 100 mg/kg. Syrian mice were injected and inhaled ovalbumin to develop asthma, and the control group received PBS solution in the same way. The treated groups received the extract at the same time as asthma induction.

The results show that depression symptoms increased significantly after asthma induction. These symptoms were significantly reduced after the administration of purslane extract in a dose-dependent manner. The results indicated a significant increase in depression in the asthmatic group samples compared to the control group and also a significant decrease in depression in the groups treated with purslane extract compared to the asthmatic group.

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INTRODUCTION

Asthma is one of the most common chronic diseases in the world, which causes numerous changes in the shape and function of the respiratory system and other body systems, including the immune system, nervous system, and endocrine system (1), and is associated with symptoms such as depression and anxiety (2). According to the statistics of the World Health Organization, the number of asthma patients in the whole world is 300 million and it is expected to reach 400 million by 2025 (3). The average prevalence of asthma in Iran is 13.14%, which is higher than the world average (4). Asthma is a very complex and heterogeneous disease, and genetic factors along with

environmental factors play a role in it (5-7).

Studies show that respiratory diseases are associated with the persistence of depression and anxiety, so it is not surprising that there are common pathogenic mechanisms between them (8). Research has shown that patients with asthma are more at risk of depression, and this has been observed to varying degrees in studies (9-14). In asthma, the disorder of nitric oxide metabolism leads to an increase in the production of oxygen-free radicals by eosinophils and other leukocytes. On the other hand, the concentration of natural antioxidants such as glutathione and vitamins C and E decreases in blood cells and lavage fluid (15). Following the reduction of antioxidant

factors, mitochondrial dysfunction and inflammation in asthma, complications such as depression come to a person. The inflammasome is another reason for the development of systemic inflammation that leads to the increase of IL-1 β in these two diseases (16). Increased levels of inflammatory markers including IL-6, IL-4, IL-1 and TNF α , C-reactive protein and CD163 (macrophage activation index) have been associated with decreased lung function (17-19).

Purslane is the 8th most used plant in the world, which has a long history of use as an edible and medicinal plant in the list of the World Health Organization. Studies that have recently been conducted on the isolation of homoisoflavonoids and related compounds from purslane indicate that this plant family has biomedical properties such as cough relief, antioxidant, anti-allergic, anti-inflammatory, antihistamine, etc. This plant contains glutathione, coenzyme Q10-omega-3, vitamins (A, B1, B2, C, E), noradrenaline, dopamine and flavonoids such as quercetin and apigenin. Melatonin is also one of the active and unique molecules that can be found in abundance in purslane, and part of the antioxidant properties of purslane extract is due to the presence of this substance (20- 28).

Many studies have been conducted on the anti-inflammatory and antioxidant effects of purslane in various diseases, but so far no research has been done on its effect on depression caused by asthma. This study aims to investigate the effect of the aqueous-alcoholic extract of the purslane plant on depression caused by experimental asthma using an Open Field Test and Forced Swimming Test in small laboratory mice.

MATERIALS AND METHODS

Animals

In this research, 40 Syrian NMRI male mice with an approximate weight of 25 to 30 grams were obtained from the Razi Serum Institute of Mashhad. The samples were kept in 12 hours of light and darkness with free access to water and food at a temperature of 21-23 °C in PVC cages in the animal room of the Islamic Azad University of Mashhad, Faculty of Basic Sciences.

The animals were randomly divided into 4 groups (n = 10), 1) control, 2) asthmatic, 3 and 4) asthmatic receiving water-alcoholic extract of purslane at the rate of 50 and 100 mg per kilogram of body weight. Intraperitoneal face in 6 times. To standardize the test conditions, the samples of the control group received PBS solution intraperitoneally.

Method of preparation of aqueous-alcoholic extract of purslane plant

The purslane plant was identified by herbarium

code 10033 by the Islamic Azad University of Mashhad, Faculty of Basic Sciences. Extraction was done by the Soxhlet method. To prepare the extract, 100 grams of dried purslane leaves were used. The solvent consisted of 250 ml of distilled water and 250 ml of 98% ethanol. The extraction continued until the solvent became colorless. Finally, about 24 grams of dry extract was obtained (due to the presence of oily and carotenoid compounds, purslane extract is not completely dry and powder-like). This extract with a certain dose was dissolved in PBS solution and injected intraperitoneally into the animals.

Experimental asthma induction method

To induce asthma, ovalbumin solution (1 mg/kg of ovalbumin powder along with 100 mg of aluminium hydroxide powder and 0.5 ml of PBS solution) was injected intraperitoneally into the samples for three consecutive days. Also, the animals, from day 6 to day 21 In addition to intraperitoneal injection, received this solution by inhalation with the help of a nebulizer and an aerosol device It was used in the inhalation chamber (29, 30).

Behavioral tests

Open Field Test (OFT): This test is used to evaluate behavioral responses such as motor activity, hyperactivity and exploratory behavior as well as measure anxiety. OFT is an indicator of the activity of the dopaminergic and glutamate systems. To perform this test, a white wooden cube with dimensions of 70 x 70 cm with a wall of 40 cm and divided into 25 squares of 14 x 14 cm was used. The behavior of the samples after 21 days of asthma induction was recorded by a video camera and the following parameters were measured for 5 minutes: 1) the duration of residence in central houses (O.F.C.T), 2) the number of central squares travelled (O.F.C.N), 3) duration of residence in environmental houses (O.F.P.T) and 4) several environmental squares travelled (O.F.P.N).

Forced Swimming Test (FST): This test is one of the most common tests to check the level of depression and its possible mechanism. For this purpose, a glass cylinder with a height of 45 cm and a diameter of 30 cm was used, which contained water of 24 \pm 1 degrees Celsius up to a depth of 30 cm. The duration of immobility (F.S.T.F) was measured and recorded with a chronometer for 5 minutes (31).

Data analysis

The results were analyzed using SPSS software and the Kolmogorov-Smirnov test was used to determine the normal distribution of the data. Data measurement was done based on one-way ANOVA followed by the Tukey post hoc test. The data were drawn as a

graph (Mean±SEM) and $p < 0.05$ was considered as a statistically significant difference.

RESULTS

Placement time in central houses (O.F.C.T)

The average O.F.C.T in the control group is 41.86 ± 4.53 seconds and in the asthmatic group it is 12.13 ± 4.8 seconds, and there is a significant difference between these two groups at $p < 0.01$. This average is 24.62 ± 4.27 seconds in samples treated with a dose of 50 mg/kg, which is not significantly different compared to the asthmatic group. This rate in the samples treated with a dose of 100 mg/kg is equal to 37.88 ± 9.16 seconds, which has a significant increase in $p < 0.01$ compared to the asthmatic group (Fig 1).

Number of shifts in central houses in open box test (O.F.C.N)

The average O.F.C.N in the control group is 29.43 ± 3.7 and in the asthmatic group is 2 ± 0.9 , and there is a significant difference between these two groups ($p < 0.001$). This average in samples treated with a dose of 50 mg/kg is equal to 13.33 ± 2.57 , which is significantly increased compared to the asthmatic group ($p < 0.001$). This amount in the samples treated with a dose of 100 mg/kg is equal to 15.13 ± 3.73 , which has a significant difference ($p < 0.001$) compared to the asthmatic group (Fig 2).

At the time of establishment in O.F.P.T environmental houses

The average O.F.P.T in the control group is 258 ± 4.53 seconds and in the asthmatic group it is 288.88 ± 4.53 seconds, and there is a significant difference between these two groups ($p < 0.01$). This average in samples treated with 50 mg/kg dose is 277.8 ± 3.74 seconds, which is not significantly different compared to the asthmatic group. This amount in samples treated with 100 mg/kg dose is equal to 268.7 ± 8.45 seconds, which has significantly decreased compared to the asthmatic group at $p < 0.05$ (Fig 3).

The number of displacements in peripheral houses in the open box test (O.F.P.N.)

The average O.F.P.N in the control group is 125.71 ± 8.66 and the asthmatic group is 79.37 ± 5.78 , and there is a significant difference between these two groups ($p > 0.001$). This average in the samples treated with a dose of 50 mg/kg is 99 ± 10.006 , which is not significantly different compared to the asthmatic group. This amount in the samples treated with 100 mg/kg of purslane is 102.82 ± 4.95 , which has a significant increase in $p < 0.05$ compared to the asthmatic group (Fig 4).

The duration of immobility in the forced swimming test (F.S.T.F)

The average immobility time in the control group

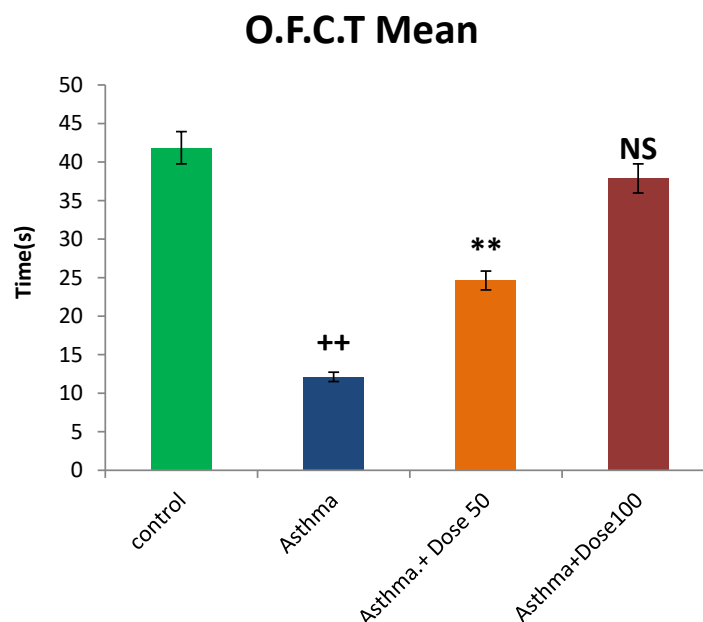


Fig1. Comparison of mean \pm standard error, O.F.C.T of control, asthmatic and O.F.T group samples ++ represents the significance of the difference between the asthmatic group and the control group ($p < 0.01$).

** The significance of the difference between the asthmatic group and the recipient of purslane extract for the treatment of depression caused by it is ($p < 0.01$).

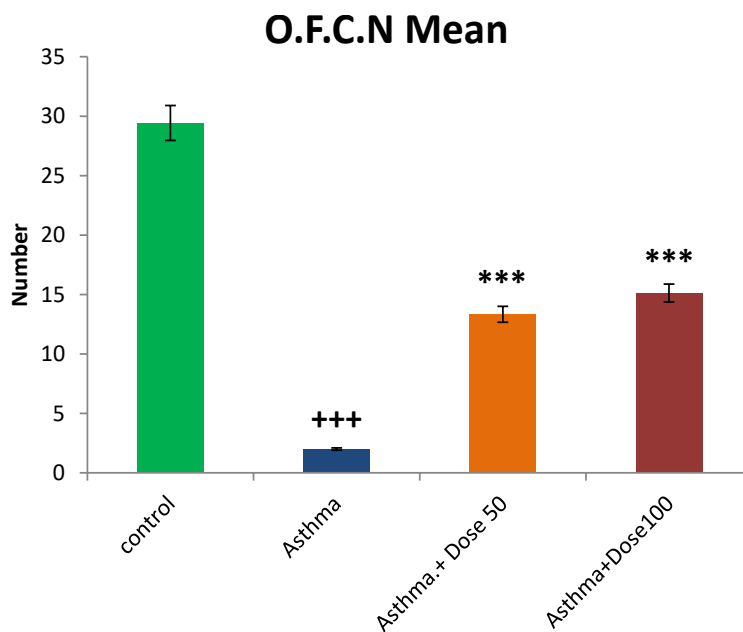


Fig 2. Comparison of mean ± standard error, O.F.C.N of control, asthmatic and treated group samples in O.F.T. +++ represents the significance of the difference between the asthmatic group and the control group ($p > 0.001$). *** Indicates the significance of the difference between the asthmatic group and the recipient of purslane extract for the treatment of depression caused by it, at the level of ($p < 0.001$).

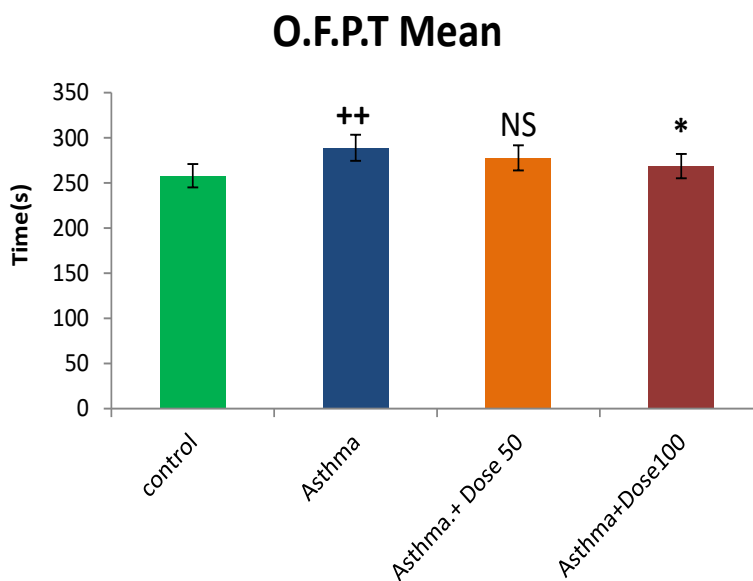


Fig 3. Comparison of mean ± standard error, O.F.P.T of control, asthmatic and treated samples in O.F.T. ++ represents the significance of the difference between the asthmatic group and the control group ($p < 0.01$). * The significance of the difference between the asthmatic group and the recipient of purslane extract for the treatment of depression caused by it is ($p < 0.05$). = NS indicates no significant difference.

is 12.22 ± 5.82 seconds and in the asthmatic group is 77.33 ± 20.13 seconds, and there is a significant difference between these two groups at $p < 0.001$. This average is 33.71 ± 12.15 in the samples treated with 50 mg/kg dose, which is a significant difference at $p < 0.05$ compared to the asthmatic group. This amount in

samples treated with 100 mg/kg dose is equal to 18.33 ± 3.48 seconds, which has a significant difference of $p < 0.001$ compared to the asthmatic group (Fig 5).

DISCUSSION

According to the results of this study, it was

O.F.P.N Mean

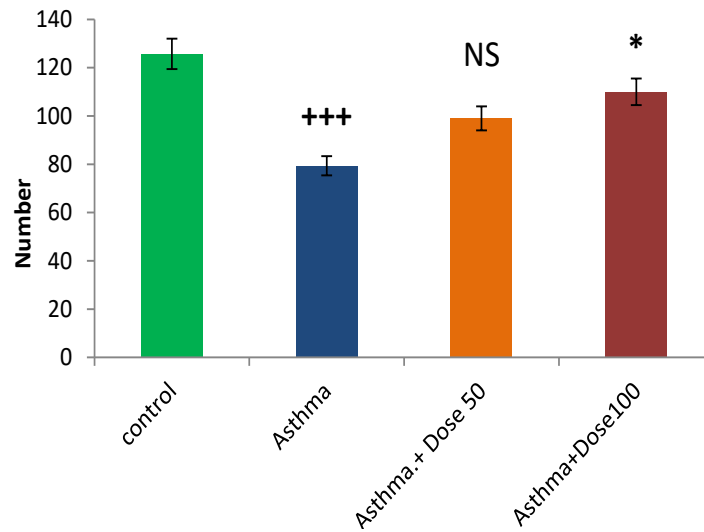


Fig 4. Comparison of mean \pm standard error, O.F.P.N of control, asthmatic and treated group samples in O.F.T. +++ represents the significance of the difference between the asthmatic group and the control group ($p > 0.001$). * The significance of the difference between the asthmatic group and the recipient of purslane extract for the treatment of depression caused by it is ($p < 0.05$). = NS indicates no significant difference.

F.S.T.F Mean

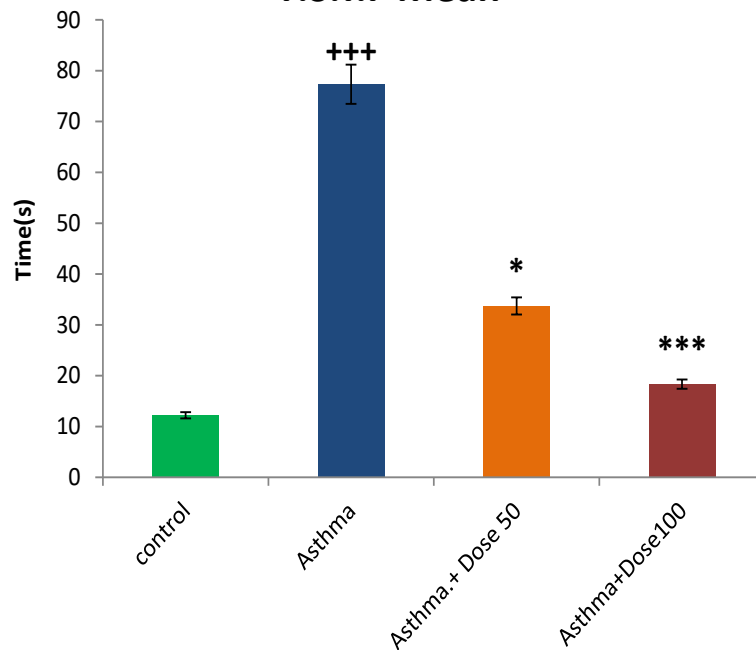


Fig 5. Comparison of mean \pm standard error, F.S.T.F of control, asthmatic and treated samples in F.S.T. +++ represents the significance of the difference between the asthmatic group and the control group ($p > 0.001$). * The significance of the difference between the asthmatic group and the recipient of purslane extract for the treatment of depression caused by it is ($p < 0.05$). *** Indicates the significance of the difference between the asthmatic group and the recipient of purslane extract for the treatment of depression caused by it, at the level of ($p < 0.001$).

observed that the aqueous-alcoholic extract of purslane can significantly reduce the symptoms of depression

factor that controls the expression of inflammatory mediators such as iNOS, COX-2, IL-8, IL-6, IL-1 β ,

caused by asthma induction. The results of FST and OFT indicate an increase in depression and anxiety in asthmatic samples compared to the control group, which is consistent with other studies. According to the results of this study, the improvement of these symptoms was observed after intraperitoneal administration of purslane aqueous-alcoholic extract. According to the research of Milady et al., the anti-anxiety effects of purslane have been reported to be dose-independent (32).

Recent research has shown that plants that are rich in antioxidant compounds can show anti-anxiety and anti-depressant effects (33). The body's antioxidant defense system includes enzymatic components such as catalase and non-enzymatic components such as vitamins E and C (34). Coenzyme Q10 acts as a strong antioxidant in scavenging free radicals and plays a role in the production of other key antioxidants such as vitamins C and E (35). Omega-3 fatty acids inhibit the production of IL-1 β and TNF- α , which are inflammatory mediators in asthma and depression. It also reduces the production of leukotrienes by blocking the metabolism of arachidonic acid. Leukotrienes are potent inducers of bronchospasm, airway edema, mucus secretion, and inflammatory cell migration in asthma (36). Due to their antioxidant and anti-inflammatory properties, flavonoids play a role in modulating Th2-induced inflammation (37). Flavonoids are inhibitors of monoamine oxidases A or B, with quercetin having MAO-A inhibitory activity (38, 25). Also, studies have shown that apigenin is a flavonoid compound with sedative, anti-anxiety and anti-depressant properties that exerts its pharmacological properties by binding to GABA-A receptors (27).

According to the results obtained in this research, depression in the samples with experimental asthma has decreased to a favorable extent, which is probably due to the presence of antioxidants that are abundant in the purslane plant.

According to the results of OFT, experimental asthma induction has led to a decrease in the duration of presence and the number of movements of asthmatic group samples in central houses compared to the control group, which is probably a sign of depression. This decrease in motor activity is probably caused by the decrease in dopamine in the brain (37). Aqueous-alcoholic extract of the purslane plant has led to an increase in the presence of samples in central houses and a decrease in the presence of samples in peripheral houses, which may be due to its effects through synaptic modulation of monoaminergic neurotransmitters in brain regions (36). Also, in this research, we see a significant increase in immobility in the FST in the asthma group compared to the control group, which

probably indicates the occurrence of depression due to asthma induction, which is in line with other studies.

One of the important mechanisms in the treatment of asthma and depression is to pay attention to removing inflammation and reducing oxidative stress. The inflammasome is a multi-protein complex that plays a role in the development of systemic inflammation that causes airway depression and hypersensitivity (16). Its activation is a two-step process that leads to the production of IL-1 β through the activation of the NF κ B pathway (39). NF κ B is an oxidative-sensitive factor that controls the expression of inflammatory mediators such as iNOS, COX-2, IL-8, IL-6, IL-1 β , and TNF α . NF κ B is a transcription factor that plays an important role in proliferation, apoptosis, inflammation and immunity. Melatonin is one of the important antioxidants of purslane, which acts as an anti-inflammatory agent by modulating the NF κ B signaling pathway. Also, melatonin modulates the inflammatory pathway by inhibiting the release of TNF- α (40, 39). On the other hand, studies show that antidepressants reduce oxidative stress by inhibiting the expression of pro-inflammatory cytokines such as TNF α (41).

According to the results obtained in this research, the purslane plant has been able to reduce the amount of depression caused by asthma induction due to the presence of these compounds. According to the epidemiological studies and overlap of the common mechanisms between asthma and depression and the antioxidant and anti-inflammatory effects of purslane, while improving the symptoms of depression, it probably also improves the symptoms of asthma. Based on this, the use of purslane in asthmatic patients can be considered a candidate for replacing synthetic drugs after conducting confirmatory studies.

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Authors's Contribution

Ali Neamati: data curation; editing and review. Najmeh Khatun Dehnavi: investigation and writing. All authors read and confirmed the final manuscript.

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Ethics approval and consent to participate

Not applicable.

Conflict of Interest

The authors declared no conflict of interest.

Consent for publication

Not Applicable.

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