

# A review Study on Pharmacological Activities, Chemical Constituents, and Traditional Uses of *Echium amoenum*

Hossein Azizi<sup>1</sup>, Saloumeh Ghafari<sup>1</sup>, Roshanak Ghods<sup>1,2</sup>, Asie Shojaii<sup>2,3</sup>, Mahboubeh Salmanian<sup>1</sup>, Jafar Ghafarzadeh<sup>1</sup>

<sup>1</sup>Department of Traditional Medicine, School of Persian Medicine, <sup>2</sup>Research Institute for Islamic and Complementary Medicine, <sup>3</sup>Department of Traditional Pharmacy, School of Persian Medicine, Iran University of Medical Sciences, Tehran, Iran

## ABSTRACT

*Echium amoenum* Fisch. and Mey. (*Boraginaceae*) is a plant which is used widely in Iranian folk medicine, especially for anxiety and depression. In this study, published scientific reports about the composition and pharmacological properties of this plant were reviewed. The electronic databases including Google Scholar, PubMed, ScienceDirect, Scopus, Web of Science, and Scientific Information Database were searched from 1970 to May 2016 and the data were summarized. Efficacy of *E. amoenum* (especially petals of *E. amoenum*) was studied in different *in vitro*, *in vivo*, and clinical evaluations. Furthermore, some chemical compounds such as rosmarinic acid, echimidine, and cyanogenic glycosides were isolated from *E. amoenum* petals. According to the results, *E. amoenum* showed various biological activities such as antimicrobial, antiviral, antioxidant, antidiabetic, analgesic, immunomodulatory, and anxiolytic effects. Clinical studies on *E. amoenum* showed effectiveness of this plant in depression and anxiety disorders. More clinical trials are recommended for evaluating different beneficial effects of this plant in human models and synthesis of new drugs from the active ingredients of this plant in the future.

**Key words:** Biological activities, clinical, depression, chemical compound, *Echium amoenum*, *in vivo*, *in vitro*

## INTRODUCTION

*Echium amoenum* Fisch. and Mey. is a medicinal plant that belongs to *Boraginaceae* family.<sup>[1]</sup> This plant called “Gav Zaban” in Persian and “Lesan-al-sour” in Iranian traditional medicine. There are different species of *Echium* all around the world, but only four species of it are available in Iran.<sup>[2]</sup>

*E. amoenum* is a biennial or perennial herb indigenous to the narrow zone of the northern part of Iran and Caucasus, where it grows at highlands at the altitude ranging from 60 to 2200 m.<sup>[3]</sup> The petals of *E. amoenum* have been widely recommended for a variety of effects, such as sedative, anxiolytic, demulcent, anti-inflammatory, analgesic, antioxidant, and tranquilizing effects, and it is used as a decoction among the Iranian people in folk medicine.<sup>[4-10]</sup> Despite the various studies which were conducted on *E. amoenum*, there is no comprehensive review about the chemical constituents and pharmacological activities of *E. amoenum*. Hence, in continuation of previous review studies on medicinal plants of Iranian traditional medicine, in this article, all published studies about *E. amoenum* were reviewed.<sup>[11-13]</sup>

## METHODS

All published articles about the chemical constituents and pharmacological activities of *E. amoenum* were searched in different

databases including Google Scholar, PubMed, ScienceDirect, Scopus, and Scientific Information Database from 1970 up to May 2016. The agricultural studies and investigations on tissue culture were excluded.

## *Echium amoenum* in Iranian traditional medicine

*E. amoenum* was called “Lesan-al-sour” in Iranian traditional medicine. The temperament of it has been mentioned as warm and dry. The flowers of *E. amoenum* are used for the treatment of concern, cough, dyspnea, sore throat, grippe, and pneumonia in Iranian traditional texts. Some other effects such as efficacy in melancholy, obsession, fear, and icterus have been mentioned for this plant. Its flowers are known as exhilarant and tonic for heart, liver, spirit, and brain. It was also mentioned for the treatment of nephrolithiasis.<sup>[8,14,15]</sup>

## Chemical constituents

Evaluation of the composition of volatile oil from *E. amoenum* petals (yielded 0.05%) showed that it consists of 26 components. The major components, except aliphatic alkanes, which belong to sesquiterpenes, are  $\alpha$ -cadinene (24.25%), viridiflorol (4.9%),  $\alpha$ -muurolene (4.52%), ledene (3.8%),  $\alpha$ -calacorene (3.04%),  $\beta$ -cadinene (2.9%).<sup>[16,17]</sup>

There are some compounds isolated from the extract of *E. amoenum*. Four pyrrolizidine alkaloids including echimidine, echimidine isomer, 7-angeloylretronecine, and 7-tigloylretronecine were isolated from dried petals of *E. amoenum*. The total alkaloid content of *E. amoenum* was 0.01%.<sup>[18]</sup> The major phenolic component isolated from ethyl acetate extract of *E. amoenum* petals was rosmarinic acid, a potent antioxidant

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### Correspondence:

Dr. Asie Shojaii,  
Department of Traditional Pharmacy, School of Persian Medicine, Iran University of Medical Sciences, Tehran, Iran and Research Institute for Islamic and Complementary Medicine, Iran University of Medical Sciences, Tehran, Iran.  
E-mail: shojaii.a@iums.ac.ir

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compound with antiviral and anti-inflammatory activities.<sup>[19,20]</sup> Other compounds which have been reported of *E. amoenum* petals were cyanidin, delphinidin, anthocyanidins, gamma-linolenic acid, alpha-linolenic acid,  $\delta$ -6-fatty acyl desaturase,  $\delta$ -8-sphingolipid desaturase, and flavonoids<sup>[3,17,19,20]</sup> [Figure 1].

Evaluation of the nutritional composition of *E. amoenum* showed the presence of calcium, phosphorous, iron, and Vitamin C, in the concentration of 704, 356, 68, and 51 mg per 100 g of *E. amoenum* extract, respectively. Furthermore, the extract contained carotenoids and anthocyanin.<sup>[21]</sup>

## Pharmacological studies

### *In vitro* and *in vivo* studies

#### Antiviral activity

Antiviral activity of *E. amoenum* was evaluated against bacteriophage 3C by agar overlay method. The results showed that antiviral effect of the extract was heat resistant and was not eliminated by autoclaving at 110°C for 1 h. Although the activity of the freeze-dried extract was reduced during 90 days of storage at 4°C, the activity of working solution was diminished in a 1-week period at 4°C.<sup>[22]</sup>

In another study, antiviral effect of *E. amoenum* extract was evaluated against HSV-1 by cytopathic effect inhibition assay. The extract showed significant antiviral activity and the most antiviral activity exhibited 1 h after virus inoculation. Antiviral activity of this plant was reduced after 2 and 3 h. The extract was inhibitor of virus replication at concentration higher than 400 µg/mL [Table 1].<sup>[23]</sup>

#### Antimicrobial activity

Antibacterial activity of *E. amoenum* was evaluated against *Staphylococcus aureus* 8327 using agar well diffusion, disc diffusion, and minimum inhibitory concentration (MIC) methods. MIC of the extract was 6.2 µg/mL. The findings indicated concentration-dependent antibacterial activity of *E. amoenum* against *S. aureus* 8327 and the antibacterial activity was heat resistance.<sup>[19,22,24]</sup> In contrast to this study, another study did not show significant activity of *E. amoenum* extract against these bacteria.<sup>[22]</sup>

In a study by Bonjar, methanolic extract of *E. amoenum* was tested against *Micrococcus luteus*, *Serratia marcescens*, *Klebsiella pneumonia*, and *Bordetella bronchiseptica* by disc diffusion and MIC methods. The result showed that the extract was effective against *B. bronchiseptica* with MIC 15 mg/mL.<sup>[25]</sup>

Another antimicrobial evaluation was assessed at various concentrations of seed oil of *E. amoenum* (10–1000 mg/mL) against *S. aureus*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Candida albicans*, and *Aspergillus niger* by MIC method using Mueller-Hinton broth

and Sabouraud dextrose broth mediums. The results revealed that *E. amoenum* seed oil raised the growth of *A. niger* and *S. epidermidis*, but it inhibits the growth of *P. aeruginosa* and *C. albicans*; however, it did not show any effect on *S. aureus*.<sup>[26]</sup> Trypanocidal activity of *E. amoenum* against *Trypanosoma cruzi* was investigated, and minimum lethal concentration was calculated. The results showed that different extract of *E. amoenum* did not show any significant activity against epimastigotes of *T. cruzi*.<sup>[27]</sup>

#### Immunological effect

In a study by Asadollahi *et al.*, photoimmunological properties of *E. amoenum* in bovine neutrophils (polymorphonuclear neutrophil [PMN]) were tested to determine the *E. amoenum* effect on bovine neutrophils photoredox and phagocytosis by *in vitro* model system. Bovine PMN was isolated from healthy dairy cows which were preincubated with *E. amoenum* extract, and the impact on phagocytosis-dependent and -independent cellular chemiluminescence, phagocytosis, fluorescence-backed PMN H<sub>2</sub>O<sub>2</sub> production, and necrosis was tested. The findings showed that phagocytosis and killing of *Escherichia coli* and *S. aureus* by PMN which cured with *E. amoenum* were higher than control PMN.<sup>[28]</sup>

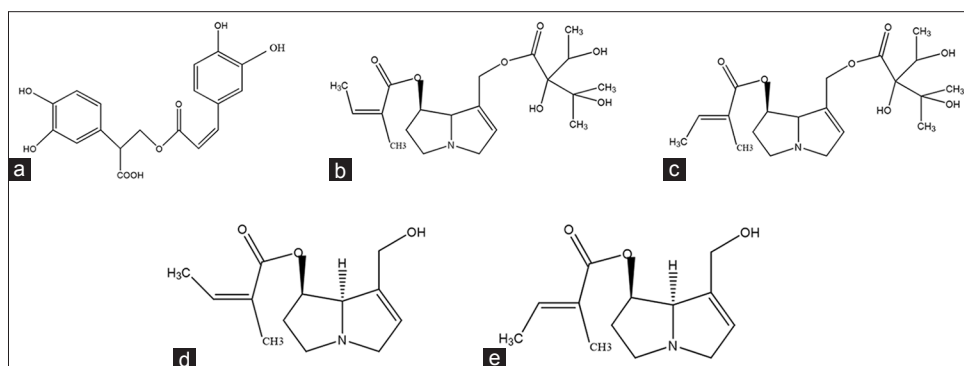
In a study by Nadi *et al.*, the ability of *E. amoenum* extract on secretion of TNF- $\alpha$  by noninfected and infected mouse macrophage was evaluated by ELISA technique. At the end of the study, concentration of TNF- $\alpha$  in noninfected and infected macrophage culture which cured with various concentrations of *E. amoenum* extract was prominently higher than the control.<sup>[29]</sup>

Effect of *E. amoenum* on cellular or humoral immune response was tested by lymphocyte proliferation assay and two-way mixed lymphocyte reaction. The results revealed that *E. amoenum* did not show stimulatory activity on either lymphocytes or thymocytes in proliferation assay, but the extract at concentration of 50–400 µg/mL had a costimulatory effect on mitogenic lymphocyte proliferation.<sup>[30]</sup>

#### Antioxidant effect

Antioxidant assays such as free radical scavenging, reducing power, and total antioxidant activity were carried out for ethanol, methanol, acetone, 80% methanol, and 80% ethanolic extracts. Antioxidant activity of different extracts of *E. amoenum* was examined by 2,2-diphenyl-1-picrylhydrazyl and reducing power assay. *E. amoenum* showed the highest antioxidant activity in hot water extract (100°C) and water extract (30°C). The highest and least activity was observed in water and acetone extract, respectively, in all assays.<sup>[21]</sup>

In another study, anthocyanin-rich extract from the petals of *E. amoenum* (25–1000 µg/mL) was tested for total antioxidant capacity.



**Figure 1:** Structures of some chemical compounds isolated from *Echium amoenum*. (a) Rosmarinic acid; (b) echimidine; (c) echimidine isomer; (d) 7-Angeloyl retronecine; (e) 7-Tigloyl retronecine

**Table 1:** *In vitro* and *in vivo* studies of *Echium amoenum*

Biological activity	Sample	Effective dose	Reference	
<i>In vitro</i> studies				
Antiviral	Aqueous extract	5 mg	[22]	
Antimicrobial activity	Aqueous extract	50-400 µg/ml	[23]	
	Aqueous extract	5, 10 mg	[22]	
	Seed oil	Equal to or higher than 1 mg/l	[26]	
	Methanol extract	20 mg/ml	[25]	
	Hexane, methanol extract	200 and 100	[27]	
Immunological activity	Ethanol extract	-*	[24]	
	DPBS extract	300 µg/ml	[28]	
	Aqueous extract	0.5, 5, 50 µg/ml	[29]	
	Hydro alcoholic extract	50-400 µg/ml	[30]	
Antioxidant	Ethanol, methanol, aqueous extract (100°C), aqueous extract (30°C), hydromethanolic extract (80%), hydroethanolic extract (80%)	0.4, 0.6, 0.8, 1 mg	[21]	
	Acetone extract	5, 10, 15, 20 mg		
Genotoxicity (effect on DNA damage)	Anthocyanin-rich extract	100-1000 µg/ml	[31]	
Cytotoxic effect	Hydroalcoholic, aqueous extract	25 mg/ml	[27]	
	Hexane extract	-	[32]	
	Ethyl acetate extract	10-1000 mg/ml		
	Methanol extract	-		
Animal studies	Anthocyanin-rich extract	25-1000 µg/ml)	[31]	
	Anxiolytic effect			
	Aqueous extract	125 mg/kg	[6]	
	Ethanol extract	50 mg/kg	[36]	
	Aqueous extract	125 mg/kg	[39]	
	Tolerance to anxiolytic effect	Hydroalcoholic extract	25, 50 mg/kg	[41]
	Anticonvulsant effect	Methanolic extract	6.25 mg/kg	[42]
	Immunomodulatory properties on BALB/c mice	Alcoholic extract, aqueous extract	5, 15, 75 mg/kg	[43]
	Effect on cerebral ischemia	Total anthocyanin extract	200 mg/kg	[44]
	Effect on blood pressure and heart beat	Decoction	400, 600 mg/kg	[45]
	Effect on wound healing	Ointment	1.5% of aqueous extract (5%, w/v)	[46]
	Antidiabetic effect	Hydroalcoholic extract	400, 600 mg/kg	[47]
	Analgesic effect	Methanolic extract	10 mg/kg	[7]
Effect on acute pancreatitis:	Hydroalcoholic extract	400 mg/Kg	[48]	
Hepatotoxicity	Aqueous extract	-	[49]	
	Dried infusion**	-	[33]	
	Hydroalcoholic extract	100, 200 mg/kg	[35]	
Liver/kidney function	Hydroalcoholic extract	400 mg/kg	[37]	
Effect on cataract	Hydroalcoholic extract	400 mg/kg	[37]	

\*.-=Not effective significantly in any of tested doses, \*\*Infusion of *Echium amoenum* petals in water which filtered and dried. DPBS=Dulbecco's phosphate-buffered saline

Results revealed that the extract significantly decreased intra- and extra-cellular hydroperoxides concentration and increased ferric reducing antioxidant power value in both intra- and extra-cellular fluid at different concentration range.<sup>[31]</sup>

### Genotoxicity and cytotoxicity

Cytoprotective and antioxidant effect of *E. amoenum* was tested on human vascular endothelial cells under H<sub>2</sub>O<sub>2</sub>-induced oxidative stress. In conclusion, *E. amoenum* at the concentration of 100–1000 µg/mL decreased the cell death.<sup>[31]</sup>

The probable effect of *E. amoenum* extract on DNA of hepG2 cells was assessed using the comet assay. The result showed genotoxicity of *E. amoenum* at the concentration of 25 µg/mL.<sup>[27]</sup>

In a study by Gohari et al., *E. amoenum* extract was tested to evaluate its cytotoxicity on *Salina artemia* Larvae, by Brine shrimp cytotoxicity bioassay. This study revealed moderate cytotoxicity effect of *E. amoenum*.<sup>[32]</sup>

### Anxiolytic effect

Different extracts of *E. amoenum* were evaluated for anxiolytic effect using rotarod model of motor coordination and elevated plus maze (EPM) models. The hydroalcoholic extract did not show any

significant effect on motor coordination. The anxiolytic effect was most evident in group received 125 mg/kg of aqueous extract, but the maximal efficacy of the extract is lower than diazepam. According to this study, single administration of the aqueous extract of *E. amoenum* produces a significant but mild-to-moderate anxiolytic effect.<sup>[6,33]</sup>

In another study, it was shown that the extract of *E. amoenum* increased the percentage of time spent and arm entries in the open arms of the EPM and decreased the percentage of time spent in the closed arms of EPM with dose 50 mg/kg. Furthermore, it prolonged the latency to sleep induced by ketamine without significant effect on total sleeping time. The locomotors' activity was affected by extract less than diazepam. Therefore, it seems that *E. amoenum* was lower than effect induced by diazepam.<sup>[34,35]</sup>

The anxiolytic effect of *E. amoenum* was investigated during 15-day and 30-day courses. It was shown that in 30-day treatment course, time spent in open arms was significantly higher than that of 15-day treatment in both diazepam and extract groups, and diazepam group showed the highest effect. Hence, time spent in open arms of plus maze increased depending on the duration of treatment.<sup>[36,37]</sup>

Tolerance to anxiolytic effect of *E. amoenum* was evaluated using light/dark box and EPM model acutely and chronically (7 days). The

results showed that administration of *E. amoenum* significantly increased the time in the illuminated zone, without any tolerance to anxiolytic effect of the extract after 7 days.<sup>[38]</sup>

### Anticonvulsant effect

In this research, effect of methanolic extract of *E. amoenum* against picrotoxin-induced seizure in mice was evaluated. The latency of seizure was increased in groups that pretreated with different doses of extract and this effect was only significant at the dose of 6.25 mg/kg. This dose delayed the death time and decreased the percentage of mortality significantly.<sup>[39]</sup>

### Immunomodulatory properties

In a study by Hosseini and Abolhassani, both aqueous and alcoholic extracts of *E. amoenum* were used for the treatment of *Leishmania major* infection in BALB/C mice. The results showed that both extracts possessed immunomodulatory properties and increased the level of interferon-gamma as well as decreased the parasite burden in the proximal lymph nodes and prevented the necrosis of the foot pad as compared with the untreated infected mice.<sup>[40]</sup>

### Effect on cerebral ischemia

Protective effect of *E. amoenum* total anthocyanin extract (ETAE) on partial/transient cerebral ischemia in the rats was evaluated. The findings of this study revealed that ETAE has protective effects against cerebral ischemia, especially at the higher doses, and improved spontaneous activity and memory induced by cerebral ischemia compared to the control group. Furthermore, brain myeloperoxidase activity was decreased following cerebral ischemia. However, ETAE could not affect the ability to climbing, body proprioception, vibrissae touch, and brain water content.<sup>[41]</sup>

### Effect on blood pressure and heartbeat

Effect of aqueous extracts of *E. amoenum* and *Citrus aurantifolia* (as decoction in different doses) was studied in the regulation of blood pressure and heartbeat in rats. Heartbeat was measured noninvasively by tail-cuff method before and after phenylephrine infusion. The results showed that *E. amoenum* elevated blood pressure, especially in rats that had high blood pressure. Furthermore, combination of decoction of *E. amoenum* and *C. aurantifolia* was suggested for decrease of heart beats.<sup>[42]</sup>

### Effect on wound healing

The ability of *E. amoenum* extract ointment on wound-healing process was investigated in rats. Rats were divided to *E. amoenum* 1.5% ointment, eucerin-vaseline, and control groups and treated with topical ointments daily for 21 days. The findings revealed that wound size of the test groups was reduced early as compared to control and placebo groups and demonstrated that borage extract was capable of promoting wound-healing process.<sup>[43]</sup>

### Antidiabetic effect

Effect of *E. amoenum* on blood glucose, lipid profile, and lipoproteins was evaluated in streptozotocin-induced diabetic rats within 30 days. The findings of this study showed significant decrease in serum glucose, cholesterol, triglyceride, and low-density lipoprotein in effective doses. Furthermore, high-density lipoprotein level was significantly increased compared to diabetic control group.<sup>[44]</sup>

### Analgesic effect

The analgesic effect of the extract of *E. amoenum* was studied using formalin and hot plate test. The findings revealed that dose 10 mg/kg of the extract showed the highest analgesic effect as compared to the control group. Pretreatment of animal with naloxone before extract

decreased the analgesia induced by extract. Hence, the opioids receptor may be involved partly in the analgesic effect of *E. amoenum* extract.<sup>[7]</sup>

### Effect on acute pancreatitis

The protective effect of *E. amoenum* extract on a murine model of pancreatitis was evaluated. The results of the study showed that pretreatment with *E. amoenum* extract reduced the inflammatory response in acute pancreatitis induced by cerulein. This study showed that *E. amoenum* extract decreases the severity of cerulein-induced acute pancreatitis with an anti-inflammatory, immunomodulatory, and antioxidant effect.<sup>[45]</sup>

### Hepatotoxicity

Hepatotoxicity effect of *E. amoenum* extract was studied in rats. Liver functions were assessed by serum biochemistry tests including aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and histopathological assessment of the liver section. Serum levels of AST and ALP were reduced significantly in both 1-week and 2-week treated groups compared to controls. Reduction of ALT was observed only in 2-week treated groups.<sup>[46]</sup>

In another study, rats were administrated by oral gavages of *E. amoenum* decoction for 28 days and serums were collected for liver function tests (ALT, AST, ALP, and total bilirubin). In addition, liver was isolated for histopathological study. There was no significant difference between experimental and control groups in all tests ( $P > 0.05$ ) and the histopathological studies of livers showed no evidence of hepatotoxicity. The results of these studies suggest that *E. amoenum* has no hepatotoxicity.<sup>[47]</sup>

Renal and hepatic effects of *E. amoenum* and *Valeriana officinalis* were investigated in animal model. The results showed significant variation of the levels of AST, ALT, and ALP in comparisons with control groups. ALP was increased significantly after oral administration of two extracts with dose of 100 and 200 mg/kg. ALT was decreased with a dose of 100 mg/kg of *E. amoenum* but increased only with dose of 200 mg/kg.<sup>[48]</sup>

### Effect on cataract

Prevention of sodium selenite-induced cataractogenesis by the extract of *E. amoenum* was evaluated in rats. In this study, protective effect of *E. amoenum* extract on selenite-induced cataract was significantly observed in rats and it may be due to antioxidant activity of *E. amoenum*.<sup>[49]</sup>

### Clinical studies

There are four clinical trials on *E. amoenum* aimed to evaluate the efficacy of this plant in anxiety and depression [Table 2].

The efficacy and tolerability of *E. amoenum* aqueous extract in combination with selective serotonin reuptake inhibitors were examined in patients with generalized anxiety disorders who met the Diagnostic and Statistical Manual of Mental Disorders-IV-TR criteria. The results revealed that *E. amoenum* may have positive effects on the anxiety and the positive effects start from the 2<sup>nd</sup> week. In addition, there are no serious side effects accompanying with *E. amoenum*.<sup>[16,34,35]</sup>

In another clinical trial, antioxidant activity of *E. amoenum* aqueous extract was assessed in healthy subjects. Blood lipid peroxidation level was reduced significantly, and total antioxidant capacity of blood and total thiol molecule were increased after 14 days of consumption. Hence, *E. amoenum* has antioxidative stress potential which may be due to antioxidant components (rosmarinic acid and flavonoids).<sup>[3,17,50]</sup>

Efficacy of *E. amoenum* in the treatment of mild-to-moderate major depression B was evaluated. Patient's assessment was done by Hamilton rating scale for depression and the Hamilton rating scale for



**Table 2:** Clinical studies of *Echium amoenum*

Study	Design	Intervention	Duration	Participants	Outcome	Reference
Mild to moderate major depression	Double blind randomized clinical trial	Oral capsule 375 mg/day	8 week	35 patients	Positive effect	[59]
Obsessive-compulsive disorder	Double blind, parallel-group trial	500 mg/day Oral capsule	6 weeks	44 patient	Positive effect	[40]
General anxiety disorder	Double-blind randomized clinical trial	Oral capsule (500 mg) plus fluoxetine or fluoxetine (20 mg/day) plus placebo	8 weeks	37 patient	Positive effect	[16]
Antioxidant activity	Cross-sectional before/ after clinical trial	Oral capsule (7 mg/kg/day) twice daily	14 days	38 healthy subjects	Positive effect	[3]

anxiety (HAM-A14). *E. amoenum* aqueous extract reduced depressive symptoms significantly compares to placebo in the 4<sup>th</sup> week, but the effect on anxiety was not significant. Some side effects such as headache, somnolence, vomiting, dry mouth, constipation, and blurred vision are reported in *E. amoenum* group.<sup>[51-53]</sup> Another study investigated the efficacy and safety of an aqueous extract of *E. amoenum* in the treatment of obsessive-compulsive disorder. Assessment of patients was done by the Yale-Brown obsessive compulsive and the HAM-A14. The results showed positive effects of extract of *E. amoenum* on obsession and compulsion and generalized anxiety and this effect starts from the 4<sup>th</sup> week. In addition, the results showed that use of *E. amoenum* has no serious side effects.<sup>[37]</sup>

## DISCUSSION

Medicinal herbs were used as complementary medicine for many years, and they were the origins of many drugs for the treatment of diseases.<sup>[54]</sup> *E. amoenum* (*Boraginaceae*) is a wild biennial or perennial herb that grows in Iran. It has been used in Iranian traditional medicine for conditions such as depression and melancholy.<sup>[8]</sup> Due to wide usage of this plant among Iranian people (especially in the form of decoction) and lack of comprehensive review on this plant, in this study, we presented a comprehensive review of chemical composition, pharmacological studies, and clinical evaluations of *E. amoenum*.

Chemical composition of essential oil and extract of *E. amoenum* was studied in different articles.

The main component of volatile oil was sesquiterpenes.<sup>[17]</sup> Some pyrrolizidine alkaloids, phenolic compounds, cyaniding, and anthocyanidin were isolated from the extract of *E. amoenum*.<sup>[20,55]</sup> *In vitro* and *in vivo* studies of *E. amoenum* showed different biological activities such as antimicrobial, antiviral, antioxidant, analgesic, antidiabetic, anticonvulsant, and immunomodulatory activity and also anxiolytic effect of this plant.<sup>[6,7,34,36,39,40,44]</sup> In addition, the extract of *E. amoenum* showed significant effect in acute pancreatitis with no hepatotoxicity effect.

Different chemical compounds of *E. amoenum* can be responsible for biological activities of it. For example, rosmarinic acid has some biological activities such as antioxidative, antiviral, and anti-inflammatory activities. Furthermore, cyanidin glycosides showed antioxidant, anti-inflammatory, and antidiabetic effects.<sup>[45-47,56,57]</sup>

Clinical studies of *E. amoenum* in the form of capsule showed positive effect of this plant on anxiety and mild-to-moderate depression B.<sup>[58]</sup>

The results of this review showed that *E. amoenum* possessed different biological activities. Some of these studies confirmed the traditional therapeutic effects of *E. amoenum* which were mentioned in Iranian traditional texts. According to wide consumption of this plant in Iranian folk medicine and limited clinical trials, it suggested that other therapeutic effects and effective doses of *E. amoenum* were investigated using well-designated clinical studies. Indeed, determination of the

active components of this plant and synthesis of new effective drugs are recommended for future studies.

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## Conflicts of interest

There are no conflicts of interest.

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