

Echium amoenum from viewpoint of Avicenna: a brief review

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Objectives The aim of this study was to compare the effects of *Echium amoenum* (Gol-e-gavzaban) in Iranian traditional medicine (ITM) under the lens of Avicenna and modern medicine.

Results *Echium amoenum* has many therapeutic effects in ITM and modern medicine. *E. amoenum* is traditionally used as herbal tea in Iranian traditional medicine (ITM) for conditions such as common cold, bronchitis, stress and fatigue. It also possesses diaphoretic, diuretic and blood rectifying properties. Some of its effects such as general tonic, cardiogenic, diaphoretic, diuretic, sedative and antitussive has been reported according to recent studies.

Conclusion There are many common characteristics about the pharmacological properties of *E. amoenum* in modern medicine and ITM, but more research is needed to prove the safety and efficacy of the plant.

Keywords *echium amoenum*, iranian traditional medicine, avicenna, cardiogenic

Introduction

Echium amoenum, also named as *Gol-e-gavzaban* in Persian, from Boraginaceae family is one of the most commonly used medicinal plants,¹ is distributed in the Northern region of Iran, as well as Europe and Mediterranean region.² This annual herb has more than 100 genera and 2300 species and has long been used for many different diseases in the Iranian traditional medicine (ITM).

Echium amoenum is traditionally used as herbal tea in Iran for conditions such as common cold, bronchitis, stress and fatigue. It also possesses diaphoretic, diuretic and blood rectifying properties. The dried violet-blue petals of Iranian Borage are used as general tonic, cardiogenic, diaphoretic, diuretic, sedative and antitussive according to the ITM. In addition, *Borago officinalis* in Europe has been used for hyperactive gastrointestinal, respiratory and cardiovascular disorders.³ The similarity in clinical and pharmacological aspects of *E. amoenum* and *B. officinalis* is recognized.⁴

So far, several pharmacological activities of constituents of *E. amoenum* have been thoroughly evaluated which showed anti-anxiety,⁵ anxiolytic,⁶ analgesic and anti-depression,⁷ antiobsessive and compulsive,⁸ anticancer,⁹ anti-inflammatory,¹⁰ antimutagenic and cytotoxic,¹¹ antioxidant and radical scavenging,¹²⁻¹⁴ antiviral,¹⁵ antibacterial,¹⁶ neonatal brain growth,¹⁷ and cardiovascular effects.¹⁸ Nowadays, various metabolites of *E. amoenum*, such as flavonoids, saponins, terpenoids, sterols and low amounts of essential oil, have been identified through phytochemistry studies.¹⁹

Uses of ancient knowledge in ethnopharmacology and related fields have prompted better understanding of progression and development of human plant utilization.²⁰ Although the fields of molecular modeling, combinatorial chemistry, and other synthetic chemistry techniques have attracted a lot of attention by pharmaceutical companies and funding organizations, medicinal plants have remained a source of inspiration for finding new drugs, new drug leads, and new chemical entities.²¹

In spite of notable achievements in drug discovery form medicinal plants, still many challenges await us. Natural product scientists such as pharmacognosists and phytochemists have to

make advancements in the quality and quantity of compounds in the drug development to compete with other drug discovery projects.²²

Herbal therapy in Iran also have an old record and many manuscripts regarding this issue are left by great physicians such as Avicenna and Rhazes.²³ *E. amoenum* is one of the important medicinal plants in the ITM. The profits of *E. amoenum* has been first learnt by Romans 300 B.C. Homer, the well-known Greek poet, assumed that the plant has positive effects on mood.⁸

In this study, we describe the traditional uses of *E. amoenum* and its therapeutic properties as defined by Avicenna in Book II, Canon of Medicine, Ketab Al-Adviah Al-Ghalbiah (heart drugs) or from current scientific studies.

Avicenna (980–1032 AD) was an outstanding Iranian physician who wrote the Canon of Medicine (in 1025 AD). This book was taught as a chief medical reference in Western and Eastern countries until the 17th century.³

Avicenna believed that the drug has rarefying and cardiogenic effect and also useful for stomatitis, restlessness, melanotic disorder, palpitation, cough and roughness of upper respiratory tract.²⁴ Avicenna also said in his other great book 'Al-Adviah Al-Ghalbiah' (heart drugs) that *E. amoenum* is a unique herbal drug for modulating of temperament, strengthening and exhilarating.²⁵

Also Hakim Khorasani, one of the most famous physician of the ITM, has written in his book named Makhzan al Adviah about *E. amoenum*. He believed that this drug is useful for the treatment of cough, sore throat, pneumonia and some of pediatric febrile and eruptive disease.²⁶

In this review article, the uses of *E. amoenum* as explained by Avicenna' books, Canon of Medicine, book of Al-Adviah Al-Ghalbiah, and various databases of the latest scientific studies are discussed and compared.

Methods

To compare the therapeutic effects of *E. amoenum*, an extensive search was performed through various databases such as

PubMed, Scopus, ScienceDirect, and Google Scholar. The keywords for our search were: *E. amoenum*, *Gol-e-gavzaban*, Avicenna and "ibn sina". Then therapeutic and pharmacologic properties of this plant were gathered from 2000 up to 2018. Unrelated citations were removed. We used Canon of Medicine in its original language (Arabic) to detect a true outcome. Only the Arabic versions were used because the English version did not clarify the particular effect obviously.

Results

Comparative Evaluation in the Canon and Modern Medicine

Cardiotonic Effects

Avicenna: "Two characteristics has been folded in this drug, so that no other medication could compete it in strengthening and exhilarating. One is its enhancing vitality properties and the other is its temperament feature" (Fig. 1).²⁵

Avicenna: "It is rarefying and cardiotoxic drug".³⁵

The ITM is a medicinal system based on the humoral theory and it dates back to 10,000 years ago.²⁷

According to the teachings of the Iranian medicine, if humor of sowda (black bile), changes to abnormal form (both in terms of quantity and quality), it can cause other pathological results, among which are sadness, anxiety and concern. This condition, named as melanotic disease, means that the disease is caused by sowda. Avicenna believed that *E. amoenum*, can remove these waste materials from the body and would indirectly lead to fright and happiness in the patient.²⁴

Melancholia has been categorized as a kind of mental disease in the ITM and it forms as a result of an alteration in the quality of brain *mizaj* (temperament) that stops the person from rational thinking so that causes a depressed mood, terror, and mistrust without any clear cause.^{24,29,28}

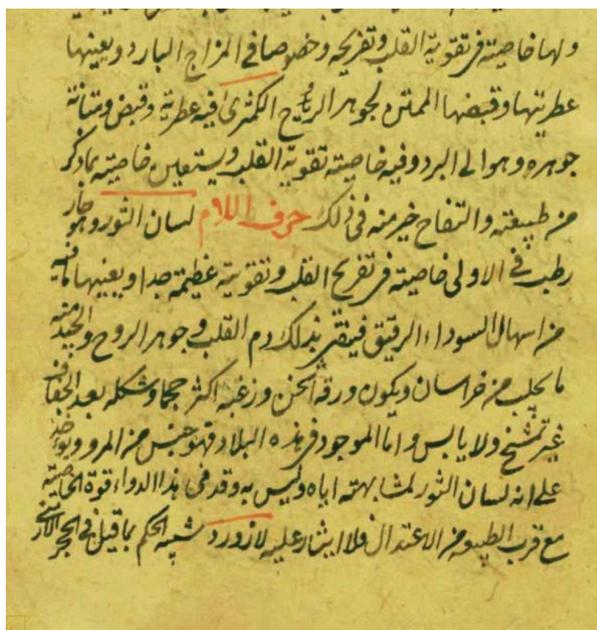


Fig. 1 A screenshot of Avicenna's book Al-Adviah Al-Ghalbiah (courtesy of the Library of the Parliament of Iran).

When we compare melancholia symptoms with major depression according to (DSM-4-TR) criteria, we found that this disorder have been categorized as one of the depression (mood) disorders.²⁹

Nowadays, it is shown that Borage oil is effective on cardiac remodeling after myocardial infarction through an animal study on rats. Based on these results, borage oil reduces development of cardiac remodeling after myocardial infarction and congestive heart failure.³⁰

Furthermore, it is largely acknowledged that emotional elements might impact physical function. This matter is lectured in comprehensive medicine as well as neuroscience. There are handy confirmations for the antagonistic effects of mental disorder on the physical health, for e.g. depressed mood and tension.³¹ Also a positive effect on treatment of major depression of *E. amoenum* is emphasized and it has been suggested for mood elevation.⁸

Avicenna says: "The burnt borage cures stomatitis in children. It relieves burning of the mouth".³⁵

Avicenna believed that *E. amoenum* is useful for aphthous stomatitis of children especially when burnt.²⁴

Anti-inflammatory effects of *E. amoenum* examined in the J774.1A macrophage cell line with preparation of ethyl acetate, dichloromethane and hexane extracts derived from this plant and then probable cytotoxic effects were studied using MTT (a colorimetric assay for assessing cell metabolic activity) *E. amoenum* hexane extract revealed the maximum reduction in macrophage NO secretion compared to other extracts.¹⁰

Avicenna: "It is good for treating restlessness, melanotic disease and palpitation".³⁵

During an 8-week double-blind randomized clinical trial study on 37 patients with general anxiety disorder it was found that the aqueous extract of *E. amoenum* (500 mg/day) together with selective serotonin reuptake inhibitors plus fluoxetine (20 mg/day) or fluoxetine (20 mg/day) plus a placebo had positive anxiolytic effect.³³

Avicenna: "It is also useful in cough and roughness of wind-pipe specially when used in the form of a decoction with honey-water or sugar".³⁵

It may be because of anti-inflammatory and immunomodulatory and radical scavenging effect of *E. amoenum*.^{4,10}

Avicenna: "It is a mild purgative for melanotic humors".³⁵

According to the ITM, repletion of redundant material in human body means "imtila" which can destroy normal function of cells and organs, thus leads to disease.

Purgative drugs can be effective on *imtila* both in prevention and treatment.³⁵

Therapeutic effect of *E. amoenum* as described by Avicenna in Canon of Medicine and Al-Adviah Al-Ghalbiah are listed in Table 1.

Other Therapeutic Effects

Antiviral Activity

It is shown that aqueous extract of *E. amoenum* is effective against herpes simplex virus type I, when it is used with a concentration of 50–1000 µg/ml during 7 days. Significant activity appeared at the concentrations greater than 400 µg/ml by inhibiting virus replication.¹⁵

Table 1. **Therapeutic effect of *E. amoenum* as described by Avicenna in Canon of Medicine and Al-Adviah Al-Ghalbiah. We used closest translation for each word**

Effect or condition noted in Avicenna's two books	Current name of condition
<i>Mofarreh e-ghalb</i> (exhilarating effect for heart)	Cardiotonic
<i>Tawahhosh</i> (useful for)	A disease like panic disorder
<i>Sudawi disease</i> (useful for)	Melancholic disease
<i>Moshele-sowda ye-raghigh</i> (purgative)	Expellant of diluted black bile
<i>Mofarreh</i> (enhancing vitality properties, useful for)	Mood elevator
<i>Ghola</i> (useful for)	Effective on aphtosostomatitis
<i>Lahib –e- fam</i> (useful for)	Oral cavity and tongue inflammation
<i>So –al</i> (useful for)	Cough
<i>Khoshonat-e ghazib</i> (useful for)	Hoarsness

Antiparasitic Activity

The antileishmanial effects of alcoholic and aqueous extracts of *E. amoenum* were demonstrated in a study on BALB/c mice. In this study, the level of IFN- γ were increased and parasite count decreased in the intervention group in comparison with the controls.¹⁵

Antimicrobial Properties

The aqueous extract of *E. amoenum* presented a concentration dependent antimicrobial activity against *Staphylococcus aureus* 8327 which was heat resistant.¹⁶

Antioxidant and Radical Scavenging Activity

An adjacent matching in pharmacological and clinical features of *E. amoenum* and *B. officinalis* (European type) is known.⁴

Immunomodulatory Effects

In one animal study on mice, it was concluded that the hydroalcoholic extract of *E. amoenum* can improve lymphocytic proliferation, but inhibits the proliferation of human antibodies.³⁴

Anticonvulsant Effects

Intraperitoneal administration of the methanol extract of *E. amoenum* at 6.25 mg/kg to mice before the injection of picrotoxin, produced an apparent rising in the latency of seizure and delayed the death time as compared with the control group.¹⁹

Positive Effect on Benign Prostate Hyperplasia

It is shown that the mixed hydroalcoholic solution of *E. amoenum*, *Viola odorata* and *Physalis alkekengi* is effective on benign prostate hyperplasia. Results declared that frequency of urination, intermittency, urgency, weak stream, straining and nocturia significantly decreased in the treatment group in comparison with the control group without any apparent side effect.³⁵

Toxicity and Teratogenicity

The existence of pyrrolizidine alkaloids in *E. amoenum* could be a threat for hepatotoxicity and liver damage. Also, these

kind of alkaloids have been displayed to have teratogenicity in pure situations. In one study with Ames test, it was found that a methanol extract (0.25, 0.5, 0.75, and 1.0 mg/ml) from *E. amoenum* petals could be safe and non-mutagenic. However, during this study it was revealed that this plant has no mutagenic effects in usual daily doses.³⁶ Another rat model study showed that aqueous extract of *E. amoenum* (100, 200, 400, mg/kg/day) had no toxicity on liver during 1 and 2 weeks of treatment.¹⁹

Conclusion

As a common herbal plant, *E. amoenum* is widely used by traditional and conventional healers in Iran and its adjoining countries. Avicenna believed that no other medication could compete it in strengthening and exhilarating. There are many traditional and modern reports that confirm anti-inflammatory effects, antioxidant effects and antianxiolytic properties of this drug. It is probably because of active constituents of the plant, such as flavonoids, saponins, terpenoids, and essential oils. Therefore it may be probably a good option for prevention or treatment of a spectrum of inflammatory disorders specially heart diseases. It is apparent that more pharmacological and toxicological experiments and clinical trials are still required for the use of this herbal drug as a certified medicinal plant in clinical setting.

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Conflict of Interest

There are no conflict of interest. ■

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