INTERNATIONAL JOURNAL OF UNANI AND INTEGRATIVE MEDICINE

E-ISSN: 2616-4558
P-ISSN: 2616-454X
https://www.unanijournal.com
IJUIM 2024; 8(1): 112-118
Impact Factor (RJIF): 6.3
Peer Reviewed Journal
Received: 15-12-2023
Accepted: 23-01-2024

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An Insight into a therapeutically significant herbal drug, Gul-e-Gaozuban (*Borago officinalis* flower), from the treasures of Unani Medicine

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DOI: https://doi.org/10.33545/2616454X.2024.v8.i1b.270

Abstract
Background: The Unani system of medicine is an extensive medical system that deals with various health and disease states. The diagnosis and treatment of patients are based on scientific principles and a holistic approach to health and healing. The holistic approach considers the patient's environment, physical, mental and spiritual state, temperament of disease, diet and drug, which is mostly from plant origin. It believes the entire universe is essentially defined by four primary qualities, i.e. Hot: Cold and Dry: Wet. These qualities are considered in all the basic concepts of the system, such as elements, temperament, humour, etc., which are used for correlating health and disease. This review explores the *Borago officinalis* flower (Gul-e-Gaozuban) according to Unani Medicine, Ethnobotany, Ethnopharmacology, Phytochemicals, and Pharmacological properties, as it is one of the therapeutically significant herbal medicines used in this system.
Method: The classical literature of Unani Medicine, Materia Medica, Herbal encyclopedias, research papers, scientific websites, etc., were used to collect data about the *Borago officinalis* flower.
Result: Classical literature and Materia Medica showed its distribution, description, temperament, doses and pharmacological actions as it has an important activity in brain diseases such as Mania, Melancholia, Depression, Anxiety, Alzheimer's and Parkinson's diseases, etc., and cardiovascular, respiratory and other disorders. Researchers discovered some of the phytochemicals in *B. officinalis* flower and explored preclinical and clinical studies about pharmacological action.
Conclusion: The presence of phytochemicals in plants is the primary reason for its pharmacological properties, which are scientifically validated. This medicinal herb may help manage various disorders and can be an adjuvant therapy for many diseases. However, future experiments are required to evaluate further and apply this drug.

Keywords: Brain diseases, Unani medicine, Phytochemicals, Pharmacological activities, Ethno pharmacology

Introduction
Borago officinalis L. belongs to the Boraginaceae family, a hardy annual plant with beautiful blue flowers (Sharma, 2003) [29]. It originates in the Mediterranean region and has since migrated to Asia, Europe, North Africa and South America (Abu-Qaoud *et al*., 2018) [2]. It is extensively cultivated for its edible leaves, flowers, and seeds and for its medicinal, aesthetic, and cosmetic purposes. Beyond their aesthetic impact, edible flowers are an exciting source of bioactive substances with beneficial health-promoting effects (Moliner *et al*., 2022) [19]. It is highly therapeutically significant in traditional medicine and is widely used in ethnobotany and traditional medicine worldwide (Ramezani *et al*., 2019) [25]. The description of Gul-e-Gaozuban (Flowers of Borage), according to Unani Medicine, was initially described by the Greek physician Dioscórides, from whom Arabs adopted it, and later redescribed by Avicenna (AD 980-1037) under the Arabic name Lissan-us-saur, which has the same meaning as the Persian name Gaozuban, i.e. Cow's tongue, about the leaves being covered by tubercles with tapering points and resembling the enlarged papillae on a cow's tongue and it was imported from Iran (Khan *et al*., 2018; Rafeequddin, 1985; Safiuddin, 1993) [15, 24, 27]. It possesses demulcent, emollient, expectorant, diaphoretic, purgative, tonic, exhilarant, tranquillizer, astringent and various pharmacological effects. *B. officinalis* flower has been used in Unani medicine as a brain tonic, tonic for external receptive and internal perceptive senses, nervine tonic, cardiotonic, used in melancholic diseases, respiratory, hepatobiliary, skin diseases and other illnesses (Gani, 2011) [9].

Other pharmaceutical uses show it is used in skin eruptives, fevers, cough and phlegmasia (Bhattacharjee, 2004) [7].

Taxonomy
Kingdom: Plantae
Phylum: Tracheophytes
Class: Magnoliopsida
Clade: Angiosperms
Clade: Eudicots
Clade: Asterids
Order: Boraginales
Family: Boraginaceae
Genus: Borago
Species: B. officinalis

Habitat and Distribution
It is found in the Mediterranean region, Europe and northern Asia. In most of Europe, including Denmark, France, Germany, the United Kingdom, and Ireland, it grows and self-seeds, remaining in the garden each year. In some regions of Europe, the plant is grown in gardens for culinary purposes since the leaves are edible and used for flavoring claret-cup and as a bee food (Anonymous, 1992; Sharma, 2003) [5, 29]. Additionally, the plant is grown commercially for the borage seed oil derived from its seeds. It grows in hill stations in India (Nadkarni, 1976) [21].

Botanical description
The plant is erect, spreading hispid annual or biennial, growing 30-60 cm in height; root tapering, mucilaginous. It is prickly or hairy all over the stems and leaves. The leaves are simple, alternate, ovate, wavy and toothed. It is 5-15 cm long, lower broadest and stalked.
Flowers are numerous, in terminal drooping bunches are complete, perfect with five narrow, triangular pointed petals, brilliant blue and pink in the bud, corolla 2.5cm, stellate, valves and anthers prominent blackish. Flowers are symmetrical and occur in loose forked cymes at intervals on the stem; cymes arise from the axils of the leaves, each flower having a long pedicel; calyx consists of 5, separate, green, linear-lanceolate sepals, each measures about 7-9 cm long and 2-3 mm maximal width at the base, it exhibits a prominent mid-rib, flat base, acute apex and the surface is covered with prominent hairs; corolla is rotate (star-shaped), and composed of 5 blue petals, they are ovate-lanceolate in shape with an acuminate apex, measure about 1 cm in length and 0.5 cm maximal width, each petal has a separate nectary with a bifurcate apex; androecium is composed of an erect cone of 5 black stamens with introrsely anthers, each 1 cm long and 0.1 cm wide; at the junction of the anther and filament there is a subtended purple flange (forked filament); gynoecium is green, flat and 4-celled; the ovary contains ovules with axile placentation and is surrounded by a short style and flat, terminal stigma (Anonymous, 1987, 1992) [4, 5].

Parts used
Leaves, Flowers and Seeds.

Procedure and time of collection
During the flowering season, the plants are removed. After being separated, the flowers and leaves dried in the shade under sunlight.

Macroscopic
The flowers appear bluish in colour and turn dull brown. The corolla is tubular, funnel-shaped, and vaguely five-lobed with wavy margins. The flower on the opening shows five stamens, which have their filaments adnate on the corolla tube at their basal ends while the filaments are free above. The stamens are attached on different planes and so are of unequal length. In some flowers, the innermost longest one is abortive. The anthers are bound and deflexed on one side to become parallel to the filament. In some flowers, a broken style is also lying between the anthers. The style is quite bifid, each segment linear and bearing capitate stigma. The flowers have a characteristic pleasant odour.

Microscopic
Examination of style shows that the bifid segments are glabrous and bear the capitate stigma, while the rest of the style bears acetate long hairs. The hairs measure 188.4 to 201 Microns in length and 8.79 to 12.56 microns in width at the base. A cross-section of the style shows that it has a central column of thick-walled, compact cells, while vascular strands run on both sides of this column. The rest of the region surrounding this consists of parenchymatous cells of various shapes and sizes. The vascular strand shows 6-8 prominent vessels, while the phloem is not distinguishable from the surrounding tiny, thickened cells. Microscopic examination of the corolla indicates it bears long aseptate hairs, 188.4 to 226.13 microns in length and 25.12 to 31.41 microns in width at the base. It also shows prominent veins and veinlets running along its length. The anthers appear heisted and hairy, while the filament is smooth and glabrous. The pollen grains are oval in shape and soft, measuring 11.82-17.7 microns in width and 19.7-23.64 in length. A cross-section of the corolla through the region where stamens have fused with the surface shows a fragile cellular structure interspersed with vascular strands at regular intervals. A close examination shows 34 prominent vessels surrounded with tiny undifferentiated cellular masses. The cells of the corolla comprise tangentially elongated parenchyma.

Study of the powdered drug
The powder is dull, dark brown, and homogenous. Under the microscope, it shows an abundance of pear-shaped pollen grains and a lot of unicellular hairs, either attached to small fragments of style or lying free. Small pieces of parenchymatous corolla tissue with vascular strands are also visible. (Anonymous, 1992) [5].

Unani description
This plant grows up to 1.5 meters and is located at high altitudes, such as in Kashmir, Nainital, and Darjeeling. All the parts of this plant are hairy and feathery. Leaves are large, rugged, greenish-white and have white spots all over the surface, similar to a cow's tongue; because of this, it is called Gao zoban (Gao=cow, zoban=tongue), in Arabic Lisan-us-saur (Lisan=tongue, saur=cow). In water, it produces mucilage and tastes bland and somewhat bitter. Flowers are small, blue in fresh, and become red in the dry and most delicate part of this plant. The brown seeds have an uneven surface, similar to safflower seeds, but they are small, tasteless, and contain oil. (Gani, 2011; Kabeeruddin, 2014; Lubhaya, 1982; Rafeequddin, 1985; Safiuddin, 1993) [9, 13, 17, 24, 27].

Fig 1 (a): *Borago officinalis* flower

Fig 1 (b): *Borago officinalis* flower powder

Temperament
Fresh: Hot and moist (Gani, 2011; Kabeeruddin, 2014; Rafeequddin, 1985) [9, 13, 24].
Dry: Hot and dry (Gani, 2011; Kabeeruddin, 2014; Rafeequddin, 1985) [9, 13, 24].
Moatadil (Safiuddin, 1993) [27].

Dose (MIQDAR-E-KHURAK)
Flowers: 3 to 5g (Kabeeruddin, 2014; Lubhaya, 1982) [13, 17], 4 g to 1 tola in powder form and 3 Tolas in decoction (Gani, 2011) [9].

Adverse Effects (Muzarrat)
It may cause adverse effects to spleen (Kabeeruddin, 2014) [13] and stomach (Qureshi, 1957) [22].

Correctives (Muslehat)
Sandal safed (*Santalum album*) (Kabeeruddin, 2014) [13]
Murabba Harad (Qureshi, 1957) [22].

Substitute (Badal)
Post Turanj (*Citrus medica*) (Kabeeruddin, 2014) [13]
Abresham (*Bombyx morii*) (Gani, 2011; Qureshi, 1957) [9, 22]
Gul-e-Surkh (*Rosa damascena*) (Gani, 2011; Qureshi, 1957) [9, 22].
Leaves of *B. officinalis* (Kabeeruddin, 2014) [13].

Compound Drug (Murakkabat)
Khamīra Gaozuban Sada, Khamīra Gaozuban Ambari, Khamīra Gaozuban Ambari Jadwar ood Saleeb Wala, Khamīra Abresham Hakeem Arshad Wala, Dawaul Misk Moatadil Jawahar wala (Kabeeruddin, 2014) [13], Khamīra Abresham Shirae Unnab wala, Dawā' al-Misk Mu'tadil, Sharbat Ahmad Shahi, Sharbat Arzani, Sharbat Deenar, Sharbat Sadr (Anonymous, 1992; Lubhaya, 1982) [5, 17]

Pharmacological Actions (Afaal)
Diaphoretic (*Mu'arriq*)-(Vardhna, 2008) [30]
Exhilarant of Heart (*Mufarriḥ Qalb*), Laxative (*Mulayyin*)-(Gani, 2011; Ibn Betar, 2003) [9, 12].
Tonic for Vital organs (*Muqawwī-i-A'ḍā' Ra'īsa*)-(Nabi, N.D.).
Anti-tussive (*Mane sual*)-(IBN Betar, 2003) [12].
Lithotriptic (*Mufattit-i-Ḥaṣāt*), Thirst quenching (*Musakkin-i-Atash*)-(Abdul Hakeem, N.D.).
Astringent (*Qābiḍ*), Ease for expectoration (*Mulaayin-e-sadar*), Cicatrizant (*Mujaffif*)-(Lubhaya, 1982) [17].
Cardiotonic (*Muqawwī-i-Qalb*), Brain Tonic (*Muqawwī-i-Dimāgh*) (Safiuddin, 1993) [27],
Yellow bile purgative (*Mushil-i-Ṣafrā'*), Serous yellow bile purgative (*Mushil-i-Mirra Ṣafrā'*), Black bile purgative (*Mushil-i-Sawdā'*)-(Abdul Hakeem, n.d.; Ibn Betar, 2003) [12].
Burnt humoural purgative (*Mushil Muharriq Akhlat*-(Gani, 2011) [9].
Tonic for external receptive and internal perceptive senses (*Muqawwī-i-Ḥawās Khamsa Ẓāhira wa Bāṭina*), Tonic for innate heat (*Muqawwī-i-Ḥarārat Gharīziyya*)-(Rafeequddin, 1985) [24].

Therapeutic Uses (Istemalat)
Palpitation (*Khafaqān*), Cough (*Su'āl*), Dryness of trachea and chest (*Khushūnat-i-Qaṣaba wa Ṣadr*), Jaundice (*Yarqān*), Excessive Thirst (*Atash*) (Gani, 2011) [9] Asthma (*Dama*), Malencholic diseases like insanity, (*Amrāḍ Sawdāwīyya: Waswās/Wahshat*) (Nabi, n.d.), Mouth ulcers (*Qulā'*), Loosening of Gums (*Istirkhā' al-Litha*), Decreases the heat of mouth, Helps in declining burnt humour (*Khilṭ Muḥtariqa*) (Ibn Betar, 2003) [12], Weakness of senses (*Ḥawās*), Weakness of Heart and brain (Ḍu'f-*i-Qalb wa Dimagh*), (Safiuddin, 1993) [27] Renal and vesicle calculus (*Ḥaṣā al-Kulya wa Mathāna*), Fever (*Huma*), Diaphragmitis (*Barsām*), Meningitis (*Sarsām*), Skin discolouration (*Fasād al-Lawn*) (Gani, 2011) [9], Catarrhal cough (*Surfa Nazlī*) (Rafeequddin, 1985) [24], Pneumonia (*Dhāt al-Ri'a*), and Pleurisy (*Dhāt al-Ri'a*), Arthritis (*Waja' al-Mafāṣil*), Immunoprotective (*Muhafiz-e-Tabiyat*).

In folkore medicine
1. Freshly squeezed juice, in a poultice or as an infusion, is used for sore and inflamed skin.
2. A decoction is used for cough, coryza and catarrh.
3. Flower tea is used for sweating (Vardhna, 2008) [30]
4. It is used as a bee food
5. Flower is used for flavouring claret cup (Sharma, 2003) [29]

Phytochemicals
Organic compounds
Fatty acids
Flowers showed the presence of Caproic acid, Linoleic acid, α-Linolenic acid, γ-Linolenic acid, Caprylic acid, Capric acid, Docosanoic acid, Dodecanoic acid, Heptadecanoic acid, Myristic acid, Pentadecanoic acid.

Oleic acid, Nervonic acid, Myristoleic acid, Erucic acid, Eicosenoic acid, Tricosylic acid, Pentadecanoic acid, Palmitic acid, Stearic acid, Palmitoleic acid, Eicosadienoic acid, Eicosatrienoic acid, Eicosapentaenoic acid. Besides, a previous study showed high amounts of polyunsaturated fatty acid. (Moliner *et al*., 2022) [19].

Phenols

A study showed the presence of these compounds, such as Gallic, chlorogenic, trans-cinnamic, rosmarinic, syringic, sinapic, ferulic, cinnamic, and coumaric acids attributed to phenols in leaf (Abu-Qaoud *et al*., 2018) [2] flower also possess gallic acid, pyrogallol, salicylic acid, caffeic acid. (Karimi *et al*., 2018) [14].

Flavonoids

It was reported the presence of seven flavonoids (catechin-7-O-glucoside, quercetin, isoquercetin, vitexin and isovitexin, naringenin O-hexoside, luteolin 7-O-glucoside) in ethanolic extract of leaf and three flavonoids (naringenin O-hexoside, luteolin 7,30,40-trimethyl ether, and kaempferol 3,7,40-trimethyl ether) in the aqueous extract of leaf (Abu-Qaoud *et al*., 2018) [2]. Flowers also showed the presence of flavonoids such as myricetin, rutin and isoflavonoid daidzein. (Karimi *et al*., 2018) [14].

Tannins and Anthocyanins

Tannins and anthocyanins are in low amounts in leaf extract and aerial parts. (Ramezani *et al*., 2019; Zemmouri *et al*., 2019) [25, 32].

Carbohydrates

Phytochemical analysis showed the presence of carbohydrates in leaves and aerial parts. (Abu-Qaoud *et al*., 2018) [2].

Glycoside, Saponins, Phyto steroids, and alkaloids were reported to be in aerial parts of the plant

Volatile oils

Leaves showed the presence of volatile oils such as Ethanol, 3-Pentanone, a-Pinene, a-Thujene, Hexanal, (E)-2-Hexenal, Octanal, Hexanol, (Z)-3-Hexenol, (E)-2-Hexenol, Benzaldehyde, Camphor, Nonanol, (E)-(E),2-4 Decadienal Nonadecane, Phenol, Carvacrol, and Tetracosane. (Wannes *et al*., 2017) [31].

Inorganic Compounds

Calcium, magnesium, potassium, sodium and iron (Anonymous, 1992) [5].

Pharmacological Studies

Antioxidant activity

Karimi *et al*. 2018 [14] analyzed *Borago officinalis* flowers for their bioactive compounds and antioxidant, antibacterial, anti-inflammatory and anticancer activities using different solvent polarities. The RP-HPLC showed the methanolic extract confirmed the presence of phenols, flavonoids, isoflavonoids and fatty acids. Among the ethanolic, water, and methanolic extracts, the methanolic extract had the most potent antioxidant activities. The antibacterial activity of flower methanolic, ethanolic, and water extracts against ordinary human and foodborne pathogenic bacteria were strong, moderate, and poor, respectively. The flower extracts also showed low anti-inflammatory activity in murine RAW 264.7 macrophage cells and negligible anticancer activity against human hepatocellular, prostate, and colon cancer cells. (Karimi *et al*., 2018) [14].

The methanolic crude extract and its partitions from borage flowers were tested for their antioxidant capacity using a variety of techniques, including ferric ion (Fe3+) reducing power (FRAP), ferrous ion (Fe2+) metal chelating, and DPPH. At the same time, hydrogen peroxide (H_2O_2) was inhibited by peroxidase (POX) and catalase (CAT) activities. Borage extracts' significant antioxidant activity is linked to their potential to prevent peroxidation and scavenge several reactive oxygen species (ROS). These extracts include active components that neutralize free radicals, preventing potential harm in CAT and POX. (Ruaa Mohammed Ibrahim & Dhuha Abdul Saheb Alshammaa, 2023) [26].

Borowy *et al*. 2017 [8] experimented to detect the antioxidant activity of borage flowers and leaves using the FRAP, DPPH, and Folin's methods (measuring the content of polyphenolics). Borage flowers contained more polyphenols and had a more substantial capacity to reduce ferric than the leaves. Furthermore, the flower had a greater concentration of DPPH radicals that had not been eliminated. (Borowy *et al*., 2017) [8].

Bendahou *et al*. 2014 [6] demonstrated the antioxidant activity of essential oil and flavonoid extract of aerial parts of Borage using the ferric reducing and DPPH techniques. This activity appears strong for borage flavonoids and low for essential oils. (Bendahou & Belkaid, 2014) [6].

Neuroprotective activity

Moliner *et al*. 2022 [19] assessed the potential benefits of *B. officinalis* flower extract related to antioxidant, neuroprotective and anti-ageing properties. GC-FID detected the fatty acids, and the antioxidant activity was determined *in vitro* through the DPPH, FRAP and ORAC assays. The Neuro-2a cell line was employed to screen the extract's ability to protect cells from oxidative damage (H_2O_2). Additionally, Caenorhabditis elegans, a model organism, was used to evaluate antioxidant activity, delayed ageing, cytoprotection, and decreased-amyloid toxicity. The MTT test, redox status (ROS production), and activity of antioxidant enzymes showed that cells treated with the extract & H_2O_2 responded to oxidative stress better than the control group (catalase and superoxide dismutase). In the chosen model, B. officinalis flower extract showed encouraging antioxidant activity without producing toxicity. The results of various bioassays involving living organisms that used the antioxidant properties of borage flowers are, therefore, favourable. (Moliner *et al*., 2022) [19].

Improvement of cyclical mastalgia

Premenstrual syndrome's mental and physical symptoms have both been demonstrated to be improved with borago extract (PMS). The Borago extract proved successful and reliable in treating patients with cyclic mastalgia. The greater GLA (gamma-linolenic acid) concentration in the borage extract may be responsible for the beneficial effects that have been documented. This fatty acid's mechanism of action is thought to result in a downregulation of PGE2, which mediates the quick conversion of GLA to DGLA (dihomo-γ-linolenic acid). This conversion raises PGE1 synthesis and intracellular cAMP levels, decreasing phospholipase and lessening arachidonic acid release. (Ruaa

Mohammed Ibrahim & Dhuha Abdul Saheb Alshammaa, 2023) [26].

Analgesic activity

Shahraki *et al*. 2015 [28] evaluated analgesic activity in hydroalcoholic extract *B. officinalis* flowers (Borage), a known sedative in herbal medicine. Seven groups of 56 adult male albino Wistar rats were randomly formed. Control groups A (intact), B (saline), and C (Positive control), as well as test groups D, E, F, and G (n=8). While group G got 25 mg/kg of borage extract and aspirin before the test, groups D, E, and F received 6.25, 12.5, and 25 mg/kg of hydroalcoholic *Borago officinalis* flower extract, respectively. By injecting 1% formalin, a biphasic pain was created. The collected data were examined using the SPSS software version. Statistical differences were considered significant at P<0.05. The findings showed that the test groups D, E, F, and G's acute and chronic pain behaviour scores considerably decreased when compared to groups A and B but that there was no difference between these scores and group C. Group G's chronic pain behaviour score was much lower than all other groups. (Shahraki *et al*., 2015) [28].

Antimicrobial activity

Bendahou *et al*. 2014 [6] assessed the antimicrobial activity of aerial parts of Borage using the agar plating method. It is significant to observe that isolated bacteria that show resistance to various antibiotics were responsive to flavonoid extract and usually also to essential oil. It's intriguing to see that E. coli (resistant), Streptococcus pneumoniae (sensitive to amoxicillin) and Klebsiella pneumoniae (sensitive to Imipeneme) are sensitive to flavonoids. Additionally, unlike flavonoids, which exhibit action against both Gram-positive and Gram-negative bacteria, the essential oils of this species appear to be more potent against gram-negative than gram-positive organisms. Low antibacterial activity was found in the isolated spathulenol from the essential oil extract; this substance is generally believed to be an antifungal agent. (Bendahou & Belkaid, 2014) [6].

Wound healing study

Heersaiy *et al*. 2015 conducted an animal experiment for wound healing using aerial parts of *B. officinalis* hydroethanolic extract ointment. They used forty-four inbred Wistar rats as models, and circular surgical wounds were made using a 7mm biopsy punch on the back. Control, Placebo and Test groups were separated. The animals in the test group were treated with 2% and 4% of *Borago officinalis* ointment for 21 days. Every third, seventh, and fourteenth day, histopathology evaluations were performed. The outcome demonstrated that two treatment groups, exceptionally high concentration, have the most impact on wound healing. These groups resulted in a higher fibroblast, mononuclear cell count, and new vascular development. The excisional wounds may heal more quickly with the *Borago officinalis* extract, especially at higher doses (4%). (Heersaiy1 & Farahpour1, 2015) [11].

Hepatoprotective study

Hamed *et al*. 2021 [10] evaluated the ethanolic crude extract of B. officinalis exhibited hepatoprotective activity against carbon tetrachloride (CCl4)-induced chronic liver damage in rats. This effect may be attributed to the anti-inflammatory and antioxidant properties of the extract, which guard against cellular damage and suppress the production of the CCl4 free radical derivative. GSH was depleted by oral CCl4 treatment, which also induced hepatic lipid peroxidation. Nuclear factor kappa-B (NF-B) and tumour necrosis factor-alpha (TNF-A) protein levels, which are inflammatory indicators, were overproduced after CCl4 administration. Serum liver biomarker levels were also significantly raised. The liver GSH concentration of rats treated with ethanolic extract significantly increased. The administration of ethanolic extract demonstrated liver protection by markedly lowering the increased blood levels of AST, ALT, and lactate dehydrogenase (LDH), indicating that ethanolic extract reduced lipid peroxidation. (Hamed & Wahid, 2021) [10].

Anxiolytic effect

Komaki *et al*. 2015 [16] discovered an Anxiolytic effect in Male Wistar rats. Each rat was put in the elevated plus-maze (EPM) 30 minutes after receiving an intraperitoneal (IP) injection of the Borage extract (50, 100, or 200 mg/kg) or saline. An overhead video camera connected to a monitor and computer in a nearby room captured animal behaviour during the experimental periods. Five minutes' quality of data was logged, including the amount of time spent in the open arms, the percentage of entries into the EPM's open arms, and the number of entries into the closed arms. It showed that injecting rats with Borage extract may have an anxiety-reducing effect. (Komaki *et al*., 2015) [16].

Reducing the withdrawal effects of morphine

Rabiei *et al*. 2016 [23] investigated the effect of hydroalcoholic extract of *B. officinalis* flower on morphine withdrawal syndrome in mice. They demonstrated a substantial decrease in stomach twitching and scratching during opioid withdrawal in animal models induced by naloxone. A considerable reduction in the frequency of blinking, jumping, ptosis, paw trembling, scratching, and bowel movement was seen after co and post-treatment with borage flower extract. The herb's polyphenolic components reduce cholinergic outflow by inhibiting cholinesterase, which leads to feelings of opioid withdrawal. (Rabiei *et al*., 2016) [23].

Anti-Asthmatic study

Mirsadraee *et al*. 2016 [18] conducted a Phase Two Randomized, Double-Blind, Placebo-Controlled Clinical study on patients aged 15-90 years with moderate asthma. In a study, 38 participants with a mean age of 46.88±15.3 years and a mean asthma duration of 71±103 months participated. After receiving treatment, the Borago group experienced considerably less cough, dyspnea, wheezing, nocturnal symptoms, and airway hyper-responsiveness, and their asthma control test (ACT) scores improved significantly (10.8±5.26 before and 15.4±5.12 after the experiment). Both asthma attacks and emergency room visits considerably decreased in the Borago group (from 3.6± to 21.8 asthma attacks per month to 0.62 ± 0.90 for emergency room visits per month, respectively). Sputum cytology did not alter considerably, including eosinophil and neutrophil counts, fractional exhaled nitric oxide (FENO), and other physiological measurements. (Mirsadraee *et al*., 2016) [18].

Studies on Compound formulation of Gul-e-Gaozuban (*B. officinalis* flower) in Unani Medicine

Anxiolytic effect

Discovered the Anxiolytic effect of herbal medicine, Khamira Gaozaban Ambri Jadwar Ood Salib Wala (KGJ), in experimental rat models. Thirty male Sprague Dawley rats were divided into five groups, each with six animals. The groups consisted of a saline group, a control group that received 1 mg/kg of diazepam, and three test groups that received 86, 170, and 360 mg/kg of oral Khamira, respectively. Evaluations of various KGJ dosages in comparison to diazepam were done using the "Elevated Plus Maze," "Light and Dark Activity Box," and "Open Field" paradigms for anxiety. The result showed the anxiolytic potential of KGJ with non-sedative properties.

Antioxidant and hepatoprotective effect

Akhtar *et al*. 2013 [3] conducted a study to evaluate the antioxidant and hepatoprotective effect of Khamira Gaozaban Ambri Jadwar Ood Saleeb Wala (KGA) in ex vivo and *in vivo* studies. Several methods were used to measure the antioxidant activity and compare it to rutin and ascorbic acid standards. Then, the hepatoprotective effect against carbon tetrachloride-induced liver injury was investigated by comparing SGOT, SGPT, ALP, total cholesterol, bilirubin, and total proteins in the serum of treated and untreated rats. It shows that the formulation's potential role in hepatoprotection may remain in its capacity to scavenge free radicals (Akhtar *et al*., 2013) [3].

Discussion

B. officinalis flower has extensive action in the central nervous system, cardiovascular system, respiratory and others, as mentioned in classical literature of Unani Medicine, and it proved some of its activity as shown in the review of its single and compound formulation. Bioactive organic compounds discovered like phenols, flavonoids, isoflavonoids and fatty acids; inorganic *viz* calcium, iron, magnesium, potassium, and sodium. The aerial parts show phytosterols, anthocyanin, glucoside, saponins, mucilages, carbohydrates, tannins and terpenoids with the above constituents. Bioactive compounds in flowers are significant compounds connected to pharmacological actions validated scientifically to have properties such as neuroprotective, antioxidant, anxiolytic, antimicrobial, analgesic, hepatoprotective and anti-asthmatic. These compounds play a prime role in the brain, heart and other organs as they have fatty acids, phenols and flavonoids, essential for protecting vital organs from damage. Further exploration of phytochemicals, particularly in flowers, and the use of *B. officinalis* in brain diseases such as Melancholia, Mania, Anxiety, Alzheimer's, Parkinson's and other neurodegenerative disorders in preclinical and clinical trials may help the patients to benefit from the potential drug.

Conclusion

This paper concludes with an immense review of ethnobotany, ethnopharmacology, phytochemistry and pharmacological properties of *B. officinalis* flowers. This work scientifically validates such compounds and actions for its classical literature. *B. officinalis* flower has potential action in different disorders. Further, it may help the researchers in future experiments with this versatile drug for many other conditions.

Acknowledgement

The authors thank the Chairman of the Department of Ilmul Advia (Unani Pharmacology), AKTC, AMU, Aligarh, for the motivation to work.

Source of Funding

This research received no specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Ethical Approval

No ethical approval is required, and no clinical and *in vivo* study has been conducted.

Conflict of interest

The authors have no conflict of interest to declare.

Author's contribution

NS designed the review and provided research materials. AN conducted the literature review, writing of the paper, all correspondence and revisions were performed by AN under the guidance and supervision of NS. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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How to Cite This Article
Amreen Naz KH and Nazish Siddiqui. An Insight into a therapeutically significant herbal drug, Gul-e-Gaozuban (*Borago officinalis* flower), from the treasures of Unani Medicine. International Journal of Unani and Integrative Medicine 2024; 8(1): 112-118.