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Original Article

"Phytochemical Profile and Pharmacological Potential of *Borago officinalis*: Mechanistic and Therapeutic Insights"

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ABSTRACT

Borago officinalis L. (commonly known as borage or starflower) is an annual plant within the Boraginaceae family, whose long history of application is known for its therapeutic use in inflammatory diseases, respiratory, gastrointestinal and cardiovascular conditions [1]. The diverse composition of phytochemicals and the medicinal properties of this plant have attracted significant scientific interest. Borage seed oil contains high levels of gamma-linolenic acid (GLA), an omega-6 polyunsaturated fatty acid, along with linoleic, oleic, palmitic and other fatty acids. [2]. The bioactive ingredients in different parts of plants include flavonoids, phenols, terpenoids, phytosterols, glycosides and pyrrolizidine alkaloids [3]. This paper summarizes the phytochemical composition, traditional applications, extraction techniques, analytical characterization and pharmacological potential of B. officinalis. Antioxidant, antibacterial, hepatoprotective, hypoglycaemic and antithrombotic properties are among the pharmacological activities that have been reported [4]. Several experimental models have studied the effects of these actions and the constituent fatty acids and phenolics of the plant have been associated with these actions, but further studies are required to establish the exact mechanisms of action and the role of specific substances [5]. To extract borage oil and other phytochemical components, both traditional and sophisticated extraction techniques have been investigated, such as solvent extraction, supercritical fluid extraction, and compressed carbon dioxide extraction [6]. Analytical techniques such as gas chromatography–mass spectrometry (GC–MS) and high-performance liquid chromatography (HPLC) have been used to facilitate identification and characterisation of fatty acids, volatile and phenolic chemicals [7]. Potentially hepatotoxic pyrrolizidine alkaloids like glucosamine, intermedine, amabiline and supinine highlight the importance of quality control and correct processing despite potential therapeutic benefits [8]. In general, B. officinalis is a good source of bioactive natural compounds that may be used in nutraceutical and pharmaceutical studies. However, there is a need for more mechanistic research, standardised phytochemical characterisation, comprehensive toxicological assessment, and carefully designed clinical trials to measure its therapeutic potential, safety, and applications in the development of new drugs. [9].

Keywords: Borago officinalis, Borage, Phytochemicals, Gamma-linolenic acid, Pharmacological activities, Antioxidant, Anti-inflammatory, Hepatoprotective, Extraction techniques, Pyrrolizidine alkaloids

INTRODUCTION

1.1 Botanical Profile and Taxonomy

Taxonomic rank	Classification category
Kingdom	Plantae
Phylum	Streptophyta
Class	Equisetopsida
Subclass	Magnoliidae
Order	Boraginales
Family	Boraginaceae
Genus	*Borago*
Species	*Borago officinalis*

1.2 Botanical Description

Borago officinalis: An annual herbaceous plant with prominent hairs, and with a generally rough or hispid surface (6). The flowers are pentamerous, bisexual and the leaves are simple, alternate. Its distinctive flowers are borne in cymose inflorescences, and are frequently blue (7).

1.3 Geographical Distribution and Habitat

Borago officinalis grows in the western and central Mediterranean region, in Spain, Portugal, France, Italy, Greece, Morocco, Algeria, Tunisia and Libya (8). Since then, it has been imported and naturalised

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

in a number of areas outside of its original range (9). It can grow in disturbed habitats, cultivated areas and other appropriate locations, but it is primarily found in temperate climates (10).

1.4 Common Names and Traditional Importance

It is also referred to as starflower or borage and has been utilized for food and medicine for a long time. Historically, many parts of the plant have been exploited for various purposes, but borage seed oil is particularly interesting because of its relative richness in gamma-linolenic acid (GLA), a fatty acid (11).

Phytochemical Constituents

S. No.	Chemical constituent	Type of chemical constituent	Reported activity
1	Apigenin	Flavone (flavonoid)	Antioxidant potential associated with borage flavonoid extracts; compound-specific activity not detailed.
2	Luteolin	Flavone (flavonoid)	Antioxidant potential associated with borage flavonoid extracts; compound-specific activity not detailed.
3	Cynaroside	Flavone glycoside	Not specifically reported for this individual compound in the review.
4	Cosmosiin	Flavone glycoside	Not specifically reported for this individual compound in the review.
5	Linarin	Flavone glycoside	Not specifically reported for this individual compound in the review.
6	4-Carvomenthenol	Monoterpenoid alcohol	Not specifically reported for this individual compound in the review.
7	Eugenol	Phenylpropanoid (phenolic compound)	Borage extracts show antioxidant/antimicrobial activity; activity is not attributed solely to eugenol.
8	(E)-β-Ocimene	Monoterpene	Not specifically reported for this individual compound in the review.
9	Myrtenol	Monoterpenoid alcohol	Not specifically reported for this individual compound in the review.
10	3,3,6-Trimethylhepta-1,5-dien-4-one	Terpenoid ketone	Not specifically reported for this individual compound in the review.
11	Carveol	Monoterpenoid alcohol	Not specifically reported for this individual compound in the review.
12	Umbellulone	Monoterpenoid ketone	Not specifically reported for this individual compound in the review.
13	Davanone D	Terpenoid	Not specifically reported for this individual compound in the review.
14	2,6-Dimethyloct-7-en-4-one	Aliphatic ketone	Not specifically reported for this individual compound in the review.
15	2,6-Dimethylocta-5,7-dien-4-one	Aliphatic ketone	Not specifically reported for this individual compound in the review.
16	γ-Linolenic acid (GLA)	Polyunsaturated omega-6 fatty acid	Antithrombotic effects reported: suppresses platelet aggregation and reduces thromboxane synthesis; also discussed in relation to inflammatory conditions.
17	Palmitic acid	Saturated fatty acid	Part of borage seed-oil fatty-acid profile; individual pharmacological activity not specified in the review.
18	Oleic acid	Monounsaturated fatty acid	Part of borage seed-oil fatty-acid profile; individual pharmacological activity not specified in the review.
19	Linoleic acid	Polyunsaturated omega-6 fatty acid	Major seed-oil fatty acid; individual pharmacological activity not specified in the review.
20	Tetracosane	Long-chain alkane	Not specifically reported for this individual compound in the review.
21	Heptacosane	Long-chain alkane	Not specifically reported for this individual compound in the review.

S. No.	Chemical constituent	Type of chemical constituent	Reported activity
22	cis-3-Hexen-1-ol	Unsaturated alcohol (volatile)	Not specifically reported for this individual compound in the review.
23	Nonadecane	Long-chain alkane	Reported as a minor volatile component of seed essential oil; no specific activity assigned.
24	1-Hexanol	Aliphatic alcohol	Reported as a minor volatile component of seed essential oil; no specific activity assigned.
25	Thesinine-4′-O-β-D-glucoside	Pyrrolizidine alkaloid-related glycoside	Not specifically reported for this individual compound in the review.
26	Acacetin	Flavone (flavonoid)	Not specifically reported for this individual compound in the review.
27	β-Sitosterol	Phytosterol	Not specifically reported for this individual compound in the review.
28	Sucrose	Disaccharide carbohydrate	No pharmacological activity specifically reported in this review.
29	Zerumbone	Sesquiterpenoid	Not specifically reported for this individual compound in the review.
30	Acteoside	Phenylethanoid glycoside	Not specifically reported for this individual compound in the review.
31	Angoroside A	Phenylethanoid glycoside	Not specifically reported for this individual compound in the review.
32	Crocetin monogentibiosyl ester	Carotenoid derivative	Not specifically reported for this individual compound in the review.
33	13(18)-Oleanen-3-one	Triterpenoid ketone	Not specifically reported for this individual compound in the review.
34	Dihydrobuddledin A	Natural product; exact class not established in the review	Not specifically reported for this individual compound in the review.
35	Echinacoside	Phenylethanoid glycoside	Not specifically reported for this individual compound in the review.
36	Forsythoside B	Phenylethanoid glycoside	Not specifically reported for this individual compound in the review.
37	Songarosaponin A	Saponin	Not specifically reported for this individual compound in the review.
38	Campesterol	Phytosterol	Not specifically reported for this individual compound in the review.
39	24-Methylenecholesterol	Phytosterol	Not specifically reported for this individual compound in the review.
40	Lycopsamine	Pyrrolizidine alkaloid	Potential hepatotoxicity concern; pyrrolizidine alkaloids in borage are discussed as liver-toxic.
41	Thesinine	Saturated pyrrolizidine alkaloid	Described as a non-toxic saturated pyrrolizidine alkaloid in the review.
42	Amabiline	Pyrrolizidine alkaloid	Potential hepatotoxicity concern; pyrrolizidine alkaloids in borage are discussed as liver-toxic.
43	Intermedine	Pyrrolizidine alkaloid	Potential hepatotoxicity concern; pyrrolizidine alkaloids in borage are discussed as liver-toxic.
44	Supinine	Pyrrolizidine alkaloid	Potential hepatotoxicity concern; pyrrolizidine alkaloids in borage are discussed as liver-toxic.
45	Pyrrolizidine alkaloids (unspecified)	Alkaloids (pyrrolizidine type)	Some borage pyrrolizidine alkaloids are hepatotoxic; processing may remove them from seed oil.
46	Ascorbic acid	Water-soluble vitamin (vitamin C)	Not specifically reported for this individual compound in the review.
47	Tannic acid	Hydrolysable tannin (polyphenol)	Not specifically reported for this individual compound in the review.

S. No.	Chemical constituent	Type of chemical constituent	Reported activity
48	Allantoin	Ureide compound	The review associates borage extracts with wound-healing activity, but does not assign this effect specifically to allantoin.
49	Acetyllycopsamine	Acetylated pyrrolizidine alkaloid	Potential hepatotoxicity concern; pyrrolizidine alkaloids in borage are discussed as liver-toxic.
50	Acetylintermedine	Acetylated pyrrolizidine alkaloid	Potential hepatotoxicity concern; pyrrolizidine alkaloids in borage are discussed as liver-toxic.
51	β-Caryophyllene	Sesquiterpene	Detected in essential oil; specific pharmacological activity is not individually established in the review.
52	Undecanal	Aliphatic aldehyde (volatile)	Not specifically reported for this individual compound in the review.
53	Hexanal	Aliphatic aldehyde (volatile)	Not specifically reported for this individual compound in the review.
54	α-Pinene	Monoterpene	Not specifically reported for this individual compound in the review.
55	(1R)-2-methyl-5-propan-2-ylbicyclo[3.1.0]hex-2-ene	Monoterpene	Not specifically reported for this individual compound in the review.
56	Carvacrol	Monoterpenoid phenol	Not specifically reported for this individual compound in the review.
57	Linalool	Monoterpenoid alcohol	Not specifically reported for this individual compound in the review.
58	Geraniol	Monoterpenoid alcohol	Not specifically reported for this individual compound in the review.
59	Methyleugenol	Phenylpropanoid	Not specifically reported for this individual compound in the review.
60	β-Ionone	Norisoprenoid (volatile)	Not specifically reported for this individual compound in the review.
61	Heptanal	Aliphatic aldehyde (volatile)	Not specifically reported for this individual compound in the review.
62	Decanal	Aliphatic aldehyde (volatile)	Not specifically reported for this individual compound in the review.
63	2-Hexenal	Unsaturated aliphatic aldehyde	Not specifically reported for this individual compound in the review.
64	Benzaldehyde	Aromatic aldehyde	Not specifically reported for this individual compound in the review.
65	2-Hexen-1-ol	Unsaturated aliphatic alcohol	Not specifically reported for this individual compound in the review.
66	2,4-Decadienal	Unsaturated aliphatic aldehyde	Not specifically reported for this individual compound in the review.
67	Nonan-1-ol	Aliphatic alcohol	Not specifically reported for this individual compound in the review.
68	p-Cymene-8-ol	Oxygenated monoterpene	Reported as a major volatile component of seed essential oil; no specific activity assigned.

2. Pharmacological activity

2.1 Antioxidant activity

Borago officinalis seedcake extract, made using 50% ethanol at 50°C for 48 hours, has a high phenolic content and a strong antioxidant activity. It is used as a natural ingredient in food, medicine, cosmetics, and agriculture. Antioxidant supplements. The antioxidant impact was assessed with 2,2'-azino-bis (3- 2,2-Diphenyl-1-picrylhydrazyl (ABTS) and ethylbenzothiazoline-6-sulfonic acid (ABTS)(12). Using the ferric reducing and DPPH techniques, borage essential oil (13) and flavonoid extract demonstrated antioxidant properties.. This activity seems to be high for the borage flavonoids and low for the essential oil.

Ferric ion (Fe3+) reducing power (FRAP), ferrous ion (Fe2+) metal chelating, and DPPH were among the methods used to assess the antioxidant capacity of the borage flowers' methanolic crude extract and its partitions. Peroxidase (POX) and catalase (CAT) activities were used to exclude hydrogen peroxide (H2O2). Borage extracts' strong antioxidant potential is ascribed to their capacity to scavenge various reactive oxygen species (ROS) and prevent peroxidation. These extracts have active components that react with free radicals to scavenge potential harm (CAT and POX (13). DPPH, the FRAP assay, and Folin's technique (which measures the concentration of polyphenolics) were used to assess the antioxidant impact of borage leaves and flowers. Borage flowers contained more polyphenols and had a greater capacity to reduce ferric acid than leaves. Furthermore, the flowers had a larger residual unreduced DPPH radical concentration. A comparison of the wild and cultivated borage species' antioxidant capacities showed that the wild species had more activity and a higher polyphenolic concentration. Due to the higher solubility of the phenolics in ethanol, a comparative investigation revealed that using ethanol as a diluent had stronger antioxidant and superoxide scavenging capability than distilled water (14). The strong antioxidant action of this species was described in 2019 when about ten flavonoids were discovered in the extract of borage leaves (15).

2.2 Antimicrobial Act

Because of its strong antibacterial properties, borage may be used to treat infections. The phytochemical analysis of the essential oils and flavonoid extracts reveals that the primary constituent of the essential oils is spathulenol, whilst the flavonoids are rutin and quercetin. Spathulenol's chemical structure. Because both extracts contain antibacterial components, the borage extract's flavonoids have a greater antimicrobial effect than the essential oil. The extracted spathulenol from the essential oil extract has little antibacterial activity; it is more commonly thought of as an antifungal agent. Rutin and quercetin are regarded as antibacterial substances. Unlike flavonoids, which exhibit activity against both types of bacteria, this plant's essential oils exhibit greater activity against Gram-negative than Gram-positive bacteria, and extended activity against resistant respiratory strains (16). In another study, the aqueous extract (AE) from borage leaves showed varying degrees of antibacterial activity against Staphylococci and Enterobacteria. The AE had modest effectiveness against Salmonella enterica but no bacterial inhibition against Listeria monocytogenes (17). Distilled water, ethanol, and methanol were the different solvents used to extract the borage flower metabolites that showed the antibacterial effect. Compared to ethanol and distilled water, the methanol extract has a greater antibacterial ability because it contains more flavonoids. Borage extracts are thought to be a promising source of natural antimicrobials and may help with medication and food preservation. Bacillus cereus was the most susceptible strain of Gram-negative bacteria, whereas Micrococcus luteus was the most resistant (18). Escherichia coli was the most sensitive Gram-negative bacterium, whereas Pseudomonas aeruginosa was the most resistant. Flavonoids, fatty acids, and other polyphenolics were linked to the antibacterial properties of the borage flower extracts. According to other research, borage leaf extracts demonstrated antibacterial efficacy against a number of pathogens, including Bacillus subtilis, Salmonella enterica, Staphylococcus aureus, and Listeria (19). Due to markedly increased mononuclear cell counts at the wound site, Borago officinalis's wound-healing activity can aid in the healing process. These characteristics may be caused by phenolic compounds present in the hydroethanolic extract, and these cellular alterations indicate the beginning of the proliferative phase and the reduction of the inflammatory phase (20).

2.3 Hepatoprotective Activity

In rat liver models, the BSO demonstrated hepatoprotective efficacy against disruptions caused by gamma (γ-) radiation. The lipid profile, serum liver enzyme levels, hepatic and serum malondialdehyde (MDA), and reduced glutathione (GSH) levels were all considerably improved by oral BSO therapy (21). Radiation exposure is linked to the notable drop in hepatic and serum levels of reduced glutathione (GSH) and a rise in hepatic and serum levels of malondialdehyde (MDA). The interaction between polyunsaturated fatty acids and free radicals in the phospholipid section of cellular membranes may be the cause of the increased MDA levels. The oxidative stress caused by ionising radiation may be the cause of the decreased levels of GSH. Hepatic GSH levels

significantly increased, and hepatic MDA significantly decreased in rats exposed to γ-radiation and treated with borage (22). Increased serum enzymatic activity of gamma-glutamyl transferase (GGT), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) following γirradiation exposure may indicate the presence of liver damage. Damage to the liver membrane could be the cause of the rise in liver enzyme levels. Oral borage administration effectively reduced the rising blood biomarker levels of ALT, GGT, and AST when hepatobiliary damage, intrahepatic and extrahepatic bile flow impairment, or erythrocyte destruction triggered by radiation were present. Borage's potential as a strong antioxidant to inhibit hepatic damage by preserving plasma membrane integrity and so preventing the enzymes from leaking into the blood may be the reason for the notable drop in liver enzyme levels following borage intake (23).

2.4 Hypoglycemic Activity

In a rat model of alloxan-induced diabetes, a methanolic extract made by Soxhletting B. officinalis demonstrated hypoglycemic qualities (24). The plant under research is high in GLA, which is used as a medication to treat a variety of conditions, including multiple sclerosis, diabetes, heart disease, arthritis, local eczema, and cyclical mastalgia (25). Anti-inflammatory action: Inflammation is a natural defensive reaction triggered by infection or tissue damage that helps the body fight off intruders (microorganisms and other objects) and eliminate damaged or dead host cells. development of inflammatory diseases is significantly influenced by the overproduction of pro-inflammatory mediators and cytokines, including tumour necrosis factor-α, interleukin-6 (IL-6), IL-1, prostaglandin E2 (PGE2), and nitric oxide (NO). By preventing prostaglandin (PG) synthesis and reducing the activities of cyclooxygenase-1 (Cox1) and Cox 2, anti-inflammatory drugs lessen inflammation and pain. enzyme. The lipopolysaccharide (LPS)/gamma interferon (INF-γ)-induced murine macrophage cell line 264.7 was used to assess the anti-inflammatory effects of aqueous, ethanolic, and methanolic borage extracts (26). The presence of phenolic compounds was linked to the low anti-inflammatory impact of borage flower extracts in murine RAW 264.7 macrophage cells. Similar to nitro-L-arginine methyl ester (L-NAME) as an anti-inflammatory drug, the ethanolic and methanolic extracts may inhibit the synthesis of nitric oxide (27).

2.5 Antithrombotic Activity

GLA demonstrates antithrombotic effects by suppressing platelet clumping and lowering thromboxane synthesis (28). In one study that compared borage oil with evening primrose oil, borage oil was shown to have a stronger impact on suppressing thromboxane B2levels and platelet activation, which points to its greater capacity to ease hypercoagulable conditions (29). This antithrombotic mechanism is vital for averting cardiovascular incidents such as myocardial infarction and stroke, especially in individuals with preexisting metabolic disorders (30).

Extraction

Supercritical fluid extraction

For borage seed extraction, the effects of varying CO2 pressures and the addition of caprylic acid methyl ester as an entrainer were investigated. The extract yield increased from 0.14 to 24.29% (w/w) when the CO2 pressure was raised from 100 to 350 bar, although the extract composition did not significantly change. Pure caprylic acid methyl ester was found to be most soluble in dense CO2 at 100 and 300 bar (about 1 g of ester in 1 g of CO2). The yield of pure extract rose by up to 47.8 times at 100 bar and 2.4 times at 200 and 300 bar when this entrainer was added. Because caprylic acid methyl ester is very soluble at lower pressures (100 bar).

Extraction by compressed CO2

CO2 The extraction of borage seed oil using compressed CO2 was studied on a pilot plant apparatus with the aim of optimising plant performance and collecting data for scale-up purposes. The seeds were pre-treated by flaking them Volume 5, Issue 1, November – December 2010; Article-005 ISSN 0976 – 044X International Journal of Pharmaceutical Sciences Review and Research. 0.3 mm flakes before the extraction experiments to achieve quantitative oil recovery. The effects of temperature (10–55 °C), extraction pressure (200–300 bar), solvent flow rate (7.5–12 kg/h), and bed length (0.25–0.50 m) were investigated (31). Up until 70% of the oil was extracted, oil solubility in CO2 was a significant factor in controlling the extraction rate. After that, the rate at which the residual oil was extracted appeared to have

been determined by intraparticle resistances (32). The experimental data were correlated using a mathematical model based on the fact that the oil is partially exposed to solvent following the pre-treatment of the seed. The calculated and observed oil yields differed by an average of 8%. The solid phase mass transfer coefficient (ks), specific interfacial area (a), and fraction of freely accessible oil (fk) all had best-fitting values of 0.7, 2.8 × 10−7 m/s, and 350 m −1, respectively (33)

Chromatography

GC-MS

When subjected to capillary gas chromatography, picolinyl ester derivatives of fatty acids were shown to have as good chromatographic properties as the corresponding methyl esters. By using a capillary column of medium polarity (Supelcowax 10), excellent resolution with respect to chain length, degree of unsaturation and positional isomers was obtained without any serious problems with a disturbed background due to column bleed in the mass spectrometric interpretation of fatty acids with respect to molecular weight, number of double bonds and positional isomers. The usefulness of the technique for the identification of the fatty acids in borage seed oil (Borago officinalis) was demonstrated. In addition to γ-linolenic acid, the most important fatty acid in borage seed oil from a commercial standpoint, a further fourteen different fatty acids could be positively identified (34). Gas chromatography–mass spectrometry analysis of seed Borago officinalis essential oil (EO) revealed the presence of 16 volatile components. β-Caryophyllene (26%) and p-cymene-8-ol (19.7%) represented the major components, while nonadecane (0.7%) and hexanol (0.7%) were the minor ones (35). The EO composition was characterised by a higher abundance of oxygenated monoterpenes (27.7%), followed by sesquiterpenes (26%)(36). Fatty acid composition showed the predominance of linoleic (35.4%), oleic (24.2%) and γ-linolenic (20.4%) acids (37). Polyphenols were analysed by reversed-phase high-performance liquid chromatography after acid hydrolysis of phenolic acid esters. Six phenolic acids were identified in seed extract, and rosmarinic acid was the predominant one with 1.65 mg/g dry matter weight equivalent to 33% of total phenolic acids. These features allowed a simple one-step procedure for characterising phenolic acids (38).

CONCLUSION

This review examines the hepatoprotective, antispasmodic, bronchodilator, vasodilator, cardio-depressant, anxiolytic, antioxidant, antibacterial, anti-inflammatory, and anticancer properties of Gaozaban (39). This validates its therapeutic use in the Unani system of medicine for various ailments (40). Numerous phytochemicals, including fatty acids, alkaloids, glycosides, saponins, flavonoids, resins, and allantoin, are responsible for the aforementioned pharmacological properties. Further research on Gaozaban's pharmacological properties and mechanism of action is crucial for drug discovery, given its claimed activity (41).

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