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Phytoconstituents and pharmacological activity of Gauzaban (*Borago officinalis* Linn): A review

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Abstract

Borago officinalis L. (Boraginaceae) is commonly known as 'Borage' and 'Gauzaban' locally in Iran. The plant is reputed as hepatoprotective, gastrointestinal, respiratory anxiolytic, antispasmodic, antihypertensive, antipyretic, aphrodisiac, demulcent, diuretic and is also considered useful to treat asthma, bronchitis, cramps, palpitations and kidney ailments. Borage oil has been reported to lower serum cholesterol, phospholipids and triglyceride levels and increases the levels of 6 polyunsaturated fatty acids in the plasma, liver, aorta and renal artery tissues and ω-3 polyunsaturated fatty acids (PUFAs) obtained from *Borago officinalis* L. seed oil are useful for cardiovascular diseases. Borage is a good antioxidant agent to improve the learning impairment and hippocampal tissue damageafter the Amyloid β (Aβ) administration. Dietary use of borage oil exhibited immuno-modulatory, cytotoxic and free radical scavenging activities. Borage has gained importance, due to the occurrence of high levels of g-linolenic acid in its seed oil. Flavonoids and phenolic compounds were the important essential oils in this plant and no have tannin. *Borago officinalis* extracts demonstrated excellent antioxidant properties and these effects were attributed to their phenolic constituents. Few studies examining Iron, Copper, Zinc and Manganese fertility in Borage have been conducted, but they are not specific to the medicinal use of this plant.

Keywords: *Borago officinalis*, Borage, Gauzaban, Boraginaceae

1. Introduction

Borago officinalis is known as borage, burrage, bourrache, and bugloss belongs to the family of Boraginaceae [1-4]. It is native to the Mediterranean region and has naturalized in many other locales. It grows satisfactorily in gardens and remaining in the garden from year to year by self-seeding. The leaves are edible and the plant is grown in gardens for that purpose in some parts of Europe. The plant is also commercially cultivated for borage seed oil extracted from its seeds. *Borago officinalis* is an annual, herbaceous and hairy plant which height changes within 70 to 100 cm [5-6]. Stems are straight, often branched [7], hollow, and covered by tough fibers. Its leaves are alternate and simple. Its leaves are covered with tough fibers [8]. The flowers are blue and rarely appear white or rose colored [9]. Their calycle and corolla are five parts which are divided into some parts and make flowers polypetalous appearance. One of the features of the corolla is that lamina parts lead to a tube which is almost seen in plants in this family, which differentiates it from other various plants. Each flower has five flags with anthers near to each other and there is a vertical appendage in their tube base. The pistil has a superior ovary which is changed to a fruit with 3 to 4 brownish nutlet after growing and there is a dark but no albumin seed inside each. The fruit of borage is a small brownish oval wrinkled nutlet [10]. Ripe nutlets are dark without albumin [9].

1.1 Synonym

Botanical Name: *Borago officinalis* Linn.
Arabic: Lisan-us-Saur
Persian: Gaozaban
English: Borage
Gujarati: Gaozaban
Hindi: Gojiva
Urdu: Gauzaban [11].

Fig1: Borago officinalis

1.2 Identity, Purity & Strength of *Borago officinalis* [11]

Foreign matter: Not more than 2%
Total Ash: Not more than 21%
Acid insoluble Ash: Not more than 6%
Alcohol soluble extractives: Not more than 2%
Water soluble extractives: Not more than 16%

1.3 Phytoconstituents

Many researchers have reported about the fatty acids available in leaves or the whole plant of borage, but there is little information about changes in fatty acids during growth period. A research evaluates the quality and the amount of fatty acids available in borage in different growth stages and reported as follows [12]. The amount of dry matter in all considered growth stages was very low. Chemical compound was closely related to the growth stages of plant and the amount of fiber was increasingly raised. The amount of raw protein decreased and the amount of lignin showed age-related increase. Indigestibility of the organic substance decreased in the beginning of the seed formation stage. This decrease was attributed to interactions of some factors including significant increase in fibers parts, relative increase in lignin during growth stages and changes in the ratio of plant tissues components. The amount of total energy was almost constant in first three stages and then increased a little. Since nutritional value during growth period was constant optimum harvest stage of the borage is in the beginning of seed formation stage when performance of dry matter is minimum. The profile of the fatty acids changes upon growth stages. α-Linolenic acid (ALA) and stearidonic acid (SDA) are the main compounds in germination stage which then decreased later. In the beginning of seed formation stage LA is in highest level and the amounts of GLA and acid oleic increase. The leaves of borage contains following compounds: a few amount of pyrrolizidine alkaloids, licosamin, intermedin, sopinin, sopindian, yezan, colin; fatty acids including ALA (55%) and GLA (more than 4%); silicic acid (1.5%-22.0%); potassium, calcium, nitrate potassium (3%), acetic, lactic and malic acid; δ-bornesitol, cianozhens; fresh leaves also contain mucilage hydrolysable to glucose, galactose, arabinose and alantoein up to 30%; leaves of borage in seeding stage contain 2.5-5.0 mg GLA and 5.7-9.0 mg SDA [13, 14]. The most amount of the gama-linolenic fatty acids are seen in May or June and the most amount of that in upper leaves of the stem in August or September [15]. The amount of gum and mucilage available in leave and stem is 3.8% and in inflorescence is 5.4%. The amounts of potassium and calcium are reported 5.3% and 6.2% respectively [16-18]. Compared to inflorescence, less amounts of potassium, gum and mucilage are present in stem and leave but more calcium is in stem and leave. Inflorescence of borage contains mucilage, tannin, calcium, potassium and ash insoluble in acid and alkaloid but has not saponins, flavonoids and cyanogenic glycosides [4, 6, 18, 19]. The flowers of borage and generally all parts of the plant contain 30% mucilage. Green parts of the plant contain nitrate potassium, resin, malate and a little amount of essence, manganese, phosphoric acid and allantoin [20, 22]. SDA is a precursor for prostaglandin synthesis which is found a little in oil of the borage seed while SDA is second frequent fatty acid in leaves of borage [23]. Since animals have very low ability to synthesize this kind of necessary fatty acids, they must be included in daily diet. This vital compounds bearing therapeutic value could increase animal's health and quality of life [12]. Linolenic acid and palmetic acid are collected from flowers and a high level of ALA is in mature leaves [23]. Boraginaceae family is one of the most known resources of GLA. In a chemotaxonomic study on 45 plant biomasses from Boraginaceae family it was determined that all biomasses contain GLA and the lowest amount (7%) was related to Cerinthe major L. species and the highest amount related to borage species (28%). This fatty acid is available in plant in a few amounts but is very important due to its nutritional and medicinal value [24]. SDA is other fatty acid which is found in plants in a little amount but it is found in Boraginaceae family in amount of 2% [25]. Several studies have been conducted on combination of fatty acid available in seed oil of planted and wild species of Boraginaceae. The amount of linoleic acid, ALA, GLA, SDA and erucic acid are of special importance in chemotaxonomic inside this family. Tocopherols are also natural effective antioxidants and borage species have high amount of δ-tocopherols [26, 27]. Phenolic compounds exist in oil seeds and various studies have proved their antioxidant properties. Borage is important due to high amount of GLA available in its seed oil. In a comprehensive research, antioxidants properties of borage extracts have been reported [28, 29]. These excellent antioxidants properties of borage are attributed to phenolic compounds. It has been determined that rosmarinic acid, synergic acid and synaptic acid are main phenolic compounds available in extract of borage seed. Rosmarinic acid is the main component of rosemary extract which is used extensively in food industries. On the other hand synergic acid and synaptic acid are included in phenol and main antioxidants of rapeseed and canola [30, 31]. There is potential for borage antioxidants to be used in food formulations and in skin health products as compounds which absorb UV. It has been suggested that linoleic acid and palmitic acid are dominant fatty acids available in mature seeds of borage [23]. Borage oil due to high amount of GLA is investigated by food and pharmaceutical research groups [32]. Oils containing GLA is used to treat some diseases resulted from lack of GLA in human [33].

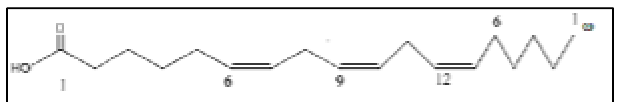

Figure 2: Gamma-Linolenic Acid.

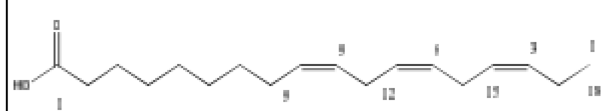

Figure 3: Alpha-Linolenic Acid.

Fig 2: Phytoconstituents of *Borago officinalis*

1.4 Pharmacological Activity

Hepatoprotective Activity

The hepatoprotective effect of *Borago officinalis* L. is aerial ethanolic extract (BAEE) against CCl_4-induced liver damage in comparison to silymarin, a classical antioxidant liver medicine. The hepatoprotective potential of BAEE in rats was evaluated following oral administration of CCl_4, which enhanced hepatic lipid peroxidation and notably depleted reduced glutathione. Moreover, we found that CCl_4 administration caused over expression of the inflammatory markers TNF-α and NFκB protein levels, in addition to a significant increase in the release of liver serum biomarker levels. Administration of BAEE showed hepatic protection by significantly reducing elevated levels of serum enzyme levels. Notably, BAEE significantly reduced expression of the TNF-α and NFκB protein expression levels comparable to wild type and silymarin. These findings were augmented with the histopathological results in which BAEE was able to show an improvement in the liver condition. The results of the current study indicate that BAEE extract has a potential hepatoprophylactic effect against chronic liver injury [34].

1.5 Gastrointestinal, Respiratory and Cardiovascular Activity

The crude leaves extract of *Borago officinalis* were investigated for its antispasmodic, bronchodilator, vasodilator and cardio-depressant activities to rationalize some of the traditional uses. Bo.Cr which was tested positive for flavonoids, coumarins, sterols and tannins produced a concentration-dependent relaxation of spontaneous and K+ (80 mM)-induced contractions in isolated rabbit jejunum preparations, suggestive of Ca++ antagonist effect, which was confirmed when pretreatment of the tissue with Bo.Cr produced a rightward shift in the Ca++ concentration-response curves like that caused by verapamil. In rabbit tracheal preparations, Bo.Cr relaxed the carbachol (1 µM) and K+induced contractions. Verapamil also produced nonspecific inhibitory effect. In rabbit aorta preparations, Bo.Cr exhibited vasodilator effect against phenylephrine and K+-induced contractions similar to verapamil. When tested in guinea-pig atria, Bo.Cr caused inhibition of both atrial force and rate of contractions. These results suggest that the spasmolytic effects of Bo.Cr are mediated possibly through Ca++ antagonist mechanism, which might explain the traditional use of Borage in hyperactive gastrointestinal, respiratory and cardiovascular disorders [35].

1.6 Anti-oxidant Activity

Borage seeds were sampled in Amdoun region (North of Tunisia) during their ripening stage in order to analyse their phenolic compounds and to ascertain their antiradical scavenging activity. The harvesting time effect on some physical properties of borage seed was significant. The increase of dry weight (from 10 to 90%) during ripeness was correlated negatively with that of moisture content (from 90 to 10%). Seed phenolic contents ranged from 2.45 to 10.98 mg GAE/g DW. HPLC analysis permitted to identify nine phenolic acids during seed maturation with the predominance of rosmarinic, syringic and sinapic acids. Total phenolic contents and IC50 values in seed during their maturation, allowed to conclude that antioxidant activity does not depend on the high content of total phenolics but on the phenolic composition [36].

An evaluation of the capacity of a lyophilized water extract of borage leaves to delay the lipid oxidation process in dry fermented sausages enriched with ω-3 PUFAs has been performed. Lyophilized extract (340 ppm) showed an antioxidant capacity equivalent to 200 ppm of a butylhydroxyanisol (BHA) and butylhydroxytoluene (BHT) mixture. Two batches of dry fermented sausages enriched in ω-3 PUFA were developed. One of them was supplemented with a synthetic antioxidants mixture (200 ppm of BHA + BHT) and the other one with natural antioxidants (340 ppm of lyophilized water extract of borage leaves). Furthermore, a traditional formulation of this type of dry fermented sausage (Control) was also manufactured. The natural extract gave rise to lower amount of volatile compounds (including hexanal), than the mixture of synthetic antioxidants (2202 and 2713 ng dodecane/g dry matter, respectively). TBARS and Cholesterol Oxidation Products (COPs) did not show significant differences between products with different antioxidants. The sensorial analysis showed that lyophilized water extracts of borage leaves did not affect the sensorial properties of the products. From the economical and safety standpoints, the use of a byproduct (Borage leaves) and water as extracting solvent are valuable alternatives for obtaining natural antioxidants to be added to dry fermented sausages enriched in ω-3 PUFA [37].

1.7 Anti-inflammatory Activity

The group of 37 patients was tested with all the symptoms of Rheumatoid arthritis (RA), along with inflammation of synovial membrane. During the treatment, borage seed oil containing 1.4 g/d GLA was administered in patients and cottonseed oil as a control. After 24 months, a reduction in symptoms of disease activity ($p<0.05$) has been reported: the decrease of soreness of joints by 36% and reduction of swelling of the joints by 41% as compared with control group as a result of taking borage oil. The results of this study confirm that use of GLA is effective in the treatment of RA. No adverse effects were observed during borage oil intake. Also recent studies conducted on borage seed oil have positive results and may warrant further investigation [43]. Summarizing, there is moderate evidence that oils containing GLA (e.g. borage) can afford some benefit in relieving symptoms of RA [39].

1.8 Seborrheic Dermatological Activity

Seborrheic dermatitis (SD) affects 1–3% of the population and is one of common inflammatory skin diseases. Mostly young people get sick, especially males, but it may also appear in infants. These diseases are difficult to treat due to its recurring nature. The etiology of SD is not known properly, although, it is considered that both internal (genetic predispositions, immunological disorders), and external factors (air pollution, skin irritation, poor hygiene of the body) are involved in its development. However, some patients require usually long-term and cumbersome treatment [40]. The study carried out in Sweden included a group of 48 newborns fully meeting the criteria of SD, in whom borage oil has been used in the treatment of local skin changes [41]. On these children, medically assisted treatment was applied using hydrocortisone, antifungal drugs and moisturizing preparations, without visible effects. In this study, borage oil was applied locally (to 5 ml) on the affected skin twice a day. After 10–12 days from first application the skin became free from the lesions, even in places in which the essential oil was not applied. Discontinuation of the treatment leaded to the relapse of the disease within a week, while the prophylactic use of essential oil 2–3 times a week protected the skin from disease relapse. During the treatment no side effects were observed. The authors of the study confirm that preparations containing GLA in its composition are effective remedies against SD [41].

1.9 Antinociceptive Activity

Borago officinalis flower (Borage) is a known sedative in herbal medicine. The antinociceptive effect of borage was evaluated hydroalcoholic extract in formalin test male rats. Fifty-six adult male albino Wistar rats were randomly divided into seven groups: Control groups of A (intact), B (saline), and C (Positive control) plus test groups of D, E, F, and G (n=8). The groups D, E, and F received 6.25, 12.5, and 25 mg/kg, Borago officinalis flower hydroalcholic extract before the test, respectively but group G received 25 mg/kg borage extract and aspirin before the test. A biphasic pain was induced by injection of formalin 1%. The obtained data were analyzed by SPSS software ver. 17 employing statistical tests of Kruskal Wallis and Mann-Whitney. The results were expressed as mean ±SD. Statistical differences were considered significant at $P<0.05$. The results revealed that the acute and chronic pain behavior score in test groups of D, E, F, and G significantly decreased compared to groups A and B, but this score did not show any difference compared to group C. Moreover, chronic pain behavior score in group G was significantly lower than all other groups. The results indicated that *Borago officinalis* hydroalcoholic extract affects the acute and chronic pain behavior response in formaline test male rats [42].

1.10 Anxiolytic Activity

Medicinal plants with natural antioxidants have been shown to be beneficial in a variety of complications such as anxiety. The elevated plus-maze (EPM) is one of the most widely used models to assess anxiety in small rodents. This study was designed to characterize the anxiolytic-like activity of *Borago officinalis* flowers extract, using an EPM test. Male Wistar rats weighing 220-250 grams were used in the present study. Thirty minutes after an intraperitoneal (IP) injection of the Borage extract (50, 100, 200 mg/kg) or saline, each animal was placed in the EPM. Animal behaviors in the experimental sessions were recorded by a video camera located above the maze, interfaced with a monitor and a computer in an adjacent room. The time spent in the open arms, the percentage of entries into the open arms of the EPM and the numbers of entries into the closed arms were recorded for five minutes. Statistical analysis indicated that acute IP injection of Borage extract before an EPM trial significantly increased the time spent in open arms and percentage of open arms entries. Whereas, the extract had no effect on the number of closed arm entries. Our results demonstrated that injection of Borage extract might have an anxiolytic profile in rats. However, the exact mechanism (s) related to the active compound (s) in Borage extract should be elucidated in future studies [43].

1.11 Mineral Composition

Borage is a plant commonly cultivated for consumption in Spain and other countries. The objective of this study has been to determine the proximate and mineral composition. The edible part of the plant corresponds to the basal leaf petioles. In this part, water was found to be the major constituent with an average value of 94%. Dry matter was mostly constituted by neutral detergent fiber, ash, and protein. Potassium was the major mineral element, reaching an even higher proportion than either fat or starch. Borage had also adequate levels of iron. The values obtained in this study show that borage should be included in the food composition tables within the leafy vegetable group [44].

2. Conclusions

Main sources of borage are from Syria and Asia Minor while this plant is just found in very little amounts. It seems that this plant has originated from west Mediterranean areas, Spain and North Africa and then has naturalized in many other locations. Borage is annual, herbaceous and hairy plants. Stems are straight, often branched, hollow, and covered by tough fibers. Its leaves are alternate and simple. Its leaves are covered with tough fibers. The flowers are blue and rarely appear white or rose colored. The plant reported to contain essential fatty acids, linoleic acid and gamma-linolenic acid. Finally, we conclude that borage has potential hepatoprotective effects against chronic liver injury, which we propose to be due to the antioxidant and anti-inflammatory effects by prevent cellular damage.

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