Sadiya Noorul Basar. *et al.* / *International Journal of Biological & Pharmaceutical Research.* 2013; 4(8): 582-587.

e- ISSN 0976 - 3651
Print ISSN 2229 - 7480

International Journal of Biological & Pharmaceutical Research
Journal homepage: www.ijbpr.com

IJBPR

REVIEW ON BORAGE OFFICINALIS: A WONDER HERB

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ABSTRACT

The plant Borage (*Borago officinalis* L.) family-Boraginaceae, also known as "starflower" bee bread, is a coarse, hairy, erect, annual herb, 30-70 cm high and native to Mediterranean region, North Africa and cultivated in Iran, Turkey, Spain, Asia Minor and India as an ornamental and to repel insects. It is mainly marketed in pharmaceutical sector in health foods and nutritional supplements. It has more than 20% gamma linolenic acid (GLA) in the seed oil. Traditionally borage is used to treat catarrh, rheumatism, some skin diseases, and beneficial effect on the brain, being used to dispel melancholy and to induce euphorbia. The leaves and flowers are galactogogue, diuretic, diaphoretic, expectorant, laxative, nervine and antidepressive. The oleic and palmitic acid of borage may also confer a hypocholesterolemic effect. In Unani system of medicine the plant is very popular as Gaozaban and used in various khamiras for cardioprotection.

KeyWords: Borage, Gaozaban, Gamma linolenic acid, Unani, Cardioprotection.

INTRODUCTION

Borage is a traditional medicinal and culinary herb native to the Mediterranean and first cultivated in Turkish Asia and Syria, and later in Spain by the Moorish Arabs. Today it has spread all over Europe as a weed, even into northern Europe. It is not only a vegetable crop cultivated in many countries but also medicinally important (Montaner C *et al*., 2000). The leaves of borage are reportedly used as diuretic, demulcent, emollient, expectorant, etc (Leung AY and Foster S, 1996). In Iranian traditional medicine, the aerial parts of borage are reportedly used for treatment of a variety of ailments (Farhadi *et al*., 2012). In Unani system of medicine it is used for many ailments like in psychiatric illness, cardiac problems like palpitation, in chest diseases etc (Ghani N; Kabeeruddin HM; Hakeem M, 2002; Kabeeruddin HM, 2007). Naturopathic practitioners use borage for regulation of metabolism and the hormonal system, and consider it to be a good remedy for Pre Menstrual Syndrome and menopause symptoms such as the hot flush (Gupta M, Singh S, 2010). Current interest in this crop is for its seed which contains a high content of gamma-linolenic acid (GLA) (all- cis 6,9,12-octadecatrienoic acid) in the oil. This acid (GLA) is a precursor of the prostaglandin PGE1 in the human body (Murali A, 1995), which is vital in many body functions, such as antithrombotic inhibitory effects on aggregation of platelets, lowering blood pressure, and inhibiting cholesterol formation. Potential medical uses of GLA include treating atopic eczema to decrease disease symptoms (Van gool CJ *et al*., 2003) and reducing side effects of diabetes, such as vascular damage, altered platelet function, and arteriosclerosis. It also has Adrenocorticostimulant, Analgesic, Antiinflammatory, Antipyretic, Antispasmodic, Aperient (Duke JA, 2002). It is called as lisan us saur in arabic, gojiva in hindi, gaozaban in Persian (Govt. of India, 2007).

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ORIGIN AND DISTRIBUTION OF BORAGE OFFICINALIS

The drug consists of dried leaves of *Borago officinalis* Linn. (Boraginaceae). It is an erect, spreading

TAXONOMICAL CLASSIFICATION

Table 1. Taxonomical classification

Kingdom	**Plantae**
Subkingdom	**Tracheobionta** – Vascular plants
Superdivision	**Spermatophyta** – Seed plants
Division	**Magnoliophyta** – Flowering plants
Class	**Magnoliopsida** – Dicotyledons
Subclass	**Asteridae**
Order	**Lamiales**
Family	**Boraginaceae** – Borage family
Genus	**Borago** L. – borage
Species	***Borago officinalis*** L. – common borage

hispid annual biennial plant. The plant found mostly in Mediterranean region, Europe, Northern Asia, it is also report to be planted in Indian gardens. The plant grows during November to January. In India plant is sparsly distributed in Northern eastern Himalayas from Kashmir to Kumaon at altitudes of 3,500-4,500m (Hermann M *et al*., 2002*)*.

BOTANICAL DESCRIPTION

Macroscopic: Leaf is simple, obovate or ovate in shape, with an obtuse apex and crenate margin, the upper leaves are sessile or shortly stalked while the lower ones exhibit a decurrent petiole. The leaves have dark green upper surface with greyish green lower surface due to the prickly hairs (Galle AM *et al*., 2002).

Microscopic: The upper epidermis of lamina is covered with a thin, smooth cuticle and consists of one layer of polygonal cells with almost straight anticlinal walls. Stomata occur fairly frequently and are mainly anisocytic type, some are animocytic. Covering trichomes are numerous, they are unicellular, straight having cellulose walls and tapering apices. The lumen is visible throughout the entire length, the base is somewhat swollen and may contain crystalline inclusions. Glandular trichomes consist of a unicellular stalk and a unicellular, sub-spherical head. The midrib has a typical dicotyledonous structure, the diameter of the central bundle increase from the apex to the base of the leaf. Large trichomes have their base surrounded by several small cells and the walls are sometimes warty. These types of trichomes are not as frequent as those with at the bulbous base. The cortex contains one or two rows of hypodermal collenchymas below the upper epidermis and above lower epidermis (Gareth G *et al*., 1996). The endodermal sheath is consisting of a single layer of cells containing starch grains. In transverse section this layer is horse- shoe shaped. The meristele is sub-spherical in shape and well defined in transverse section. The pericycle consists of a well defined area of collenchymas above the xylem and below the phloem. The transverse section through the petiole is similar to that of the mid-rib with a exception that cells are slightly large due to the increase in size of the total structure. Some trichomes contain crystalline deposit in their basis (Gareth G *et al*., 1996).

PHYTOCHEMICAL STUDIES OF BORAGE OFFICINALIS

Alkaloids Pyrrolizidine-type Lycopsamine, intermedine, acetyllycopsamine, acetylintermedine, amabiline, supinine and thesinine (unsaturated). Concentrations reported as 0.01% and 2-10 ppm for commercial dried samples. Alkaloid concentrations reportedly the same for fresh and dried samples; fresh samples revealed alkaloids as the free base in the roots and mainly as N-oxides in the leaves. Mucilages 11.1%. yielding glucose, galactose and arabinose. Oil Rich in fatty acids, in particular gamolenic acid. Other constituents Acids (acetic, lactic, malic, silicic), cyanogenetic compounds and tannins (up to 3%) are present Pierette PG, 2004; Wretensjo I, Bo K, 2003).

Borage oil is taken orally in nutritional and clinical supplements where impaired or inadequate Δ-6 desaturase activity may be involved in the initiation and progression of several dicades (Senanayake SPJN, Shahidi F, 2008). The impairement may be alleviated by dietary supplementation with γ-linolenic acid. Pyrrolizidine alkaloids (Pierette PG, 2004; Kapoor R et al., 2005), γ-linolenic acid (Lopez-Martinez JC *et al*., 2004), cyanogenetic glycoside dhurrine, rosmarinic acid (Bandoniene D *et al*., 2005) essential oil composed mainly of nonadecane, tetracosane and heptacosane and fatty acids consisting of α- and γ-linolenic, stearidonic and palmitic acids (Badi NH *et al*., 2008; Wretensjo I, 2004) have been reported from the borage leaves.

The analysis with use of gas chromatography connected with mass spectrometry (GC-MS) allowed to mark 16 volatile compounds in the seed oil of *Borago officinalis*, among others: β-caryophyllene (26%), p-cymene-8-ol (19.7%), small amounts of nonadecane (0.7%) and hexanol (0.7%). There are also large amounts of oil monoterpens (17.2%) and sesquiterpenes (26%). In addition, fatty acids have been isolated such as: γ-linolenic acid (10–28%), linoleic acid (35–40%) and α-linolenic acid (4–5%). In the extract from seeds the presence of rosemary

acid in the amount of 1.65 mg/g dry weight has been noted. (Berti MT *et al*., 2010; De Haro A *et al*., 2002; Barn DE, Holub BJ, 1992; Pieszaki M *et al*., 2012).

De Haro *et al.*, have shown that plants of this species blooming blue among all tested genotypes had a lower concentration of γ-linolenic acid compared with plants with white flowers. In the seed oil of *Borago officinalis* (24.2%) oleic acid and erucic acids were also identified. Presence of linoleic acid and γ-linolenic acid (GLA) in borage oil seems to be of a great importance due to the fact that these compounds are classified as higher unsaturated fatty acids (Ω-6). Human beings are not capable to synthesize them, because they do not produce appropriate enzymes. Therefore, supplementation of them is important. The lack of these compounds leads to disorders in the construction and function of nervous system, infections, diseases of cardiovascular system and even cancer. The oil compounds included in borage are involved in the synthesis of eicosanoids, hence they can be used adjunctively in the treatment and prevention of atherosclerosis. In addition, they are also involved in the regulation of metabolism. However, too high concentration of these compounds leads to many disorders, including pro-inflammatory and allergenic reactions and also causes increased blood clotting. Borage herb contains changeable quantities of pyrrolizidine alkaloids (licopsamine, supinidine, amabiline, intermedine) having a toxic effect particularly on liver parenchymal tissue. Their carcinogen activity based on the genotoxic mechanism of action has been shown in the studies carried out in animals (Pieszaki M *et al*., 2012). However, the oil obtained from the ripe seeds of borage by cold pressing is devoid of these toxic compounds that do not pass to this oil during the production process. In the chromatographic studies, Gudej and Tomczyk noticed the presence of many phenolic acids (vanillic acid, p-coumaric acid, p-hydroxybenzoic, gentisic acid, caffeic acid, rosmarinic acid, chlorogenic acid), scopoletin and flavonoids (including quercetin, isorhamnetin, kaempferol) Pieszaki M *et al*., 2012; Khare CP, 2007). In addition, borage herb contains almost 20% mucilages, tannins (3-5%), mineral salts (including soluble silica 1.5–2.2%, calcium and potassium nitrate 3%), organic acids (ascorbic acid, malic, citric, acetic acid, lactic acid), saponins, allantoin (0.5–1%), vitamins, choline, bornesitol, cyanogenic compounds (15 mg HCN/kg) and tocopherols Mhamdi B *et al*., 2009). Leaves of *Borago officinalis* L. contain organic acids, mucilage, carotene, and a small amount of potassium nitrate. However, it should be mentioned that full chemical composition of this plant has not been exactly determined so far.

PHARMACOLOGICAL ACTIONS/ BIOLOGICAL ACTIVITIES

In vitro and animal studies of Borage oil has been reported to attenuate cardiovascular reactivity to stress in rats (Mills DE, 1989).

Antibacterial activity

In an ***in vitro*** study of 25 botanical aqueous extracts, borage was one of the most efficient antibacterial extracts against **Helicobacter pylori**. (O'Mahony R, 2005).

Antihyperlipidemic effects

According to a study of GLA in humans, GLA (source unspecified) decreased plasma triglyceride levels and increased HDL-cholesterol concentration (Guivernau M *et al*., 1994).

Anti-inflammatory effects

Based on recent research, Kast *et al*., hypothesized that borage oil's anti-inflammatory effects may be due to the gamma-linolenic acid component of borage oil, which suppresses tumor necrosis factor-alpha synthesis by increasing prostaglandin E and cAMP levels. The authors continued that if this biochemical path is correct, then "concomitant non-steroidal anti-inflammatory drug use would tend to undermine borage oil effects, and borage oil would be contraindicated in pregnancy as it showed teratogenic and labor inducing effects of PGE agonists (Kast RE, 2001).

Anti platelet effects

According to a review article and a study on GLA (source unspecified), borage seed oil may potentially increase the risk of bleeding or potentiate the effects of warfarin therapy. However, in a study of healthy volunteers, the therapeutic dosage of 3g daily of borage oil supplementation did not affect platelet aggregation (Bard JM *et al*., 1997).

Cardiovascular effects

In a randomized, double-blind study, normotensive subjects ingested 4.5 ml daily for four weeks to assess the effects of dietary safflower (control, N=10), borage (N=9), and fish oil (N=10) on cardiovascular responses to lower-body negative pressure. Borage oil significantly altered plasma norepinephrine and vasoconstrictor responses to 40 mmHg lower-body negative pressure, as well as the reflex vasodilation on its cessation. The authors hypothesize that borage oil may augment arterial baroreflex control of vascular resistance Mills DE *et al*., 1990).

Dermatologic activity

In a study of the influence of nine lipids on normal skin and skin irritated by sodium lauryl sulfate, a single application of borage oil had no effect on irritation (Loden M and Andersson AC, 1996).

Fatty acid activity

Various studies have been conducted to elucidate that borage oil or its primary constituent, gamma-linolenic acid (GLA) has effect on serum and cellular fatty acids. According to studies in humans, ingestion of GLA increases its metabolite di homo-gamma-linolenic acid (DGLA). The increase of DGLA in turn increases the level of its metabolite 15-hydroxyeicosatrienoic acid (15-HETrE) and other chemicals, which are known anti-inflammatories and antiproliferatives (Fan YY and Chapkin RS, 1996). GLA also slightly increases arachidonic acid (AA) levels. However, some researchers hypothesize that GLA should increase arachidonic acid levels much higher, and thus, arachidonic acid may be inhibited by eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA). Nonetheless, this interaction does not seem to be occurring, and GLA has a limited impact on arachidonic acid levels (Demmelmair H, 2001). Interestingly, GLA consumed with alpha-linolenic acid (ALA) significantly, yet negligibly, increased omega 3 and eicosapentaenoic acid in vegan's serum cholesterol. In another human study, a combination of GLA and stearidonic acid also increased the proportion of eicosapentaenoic acid in some lipid fractions Miles EA *et al*., 2004.

Hematological effects

In an *in vitro* study in platelets of men who had consumed borage oil, altered the fatty acid composition of the platelet phospholipids, including a reversible rise in the DGLA and a decrease in n-3 polyunsaturated fatty acids (Barre DE and Holub BJ, 1992).

Immunological effects

In an *in vitro* study, GLA from borage oil dose-dependently reduced tumor necrosis factor-alpha (TNF-alpha) and interleukin (IL)-10 levels to 60% of control levels Dooper MM *et al*., 2003). These effects were not altered by the addition of indomethacin, indicating that DGLA affects TNF-alpha and IL-10 levels independently of COX activation. In addition, ingestion of GLA seems to reduce polymorphonuclear generation of proinflammatory leukotriene B4, although this effect does not appear to be dose-dependent (ziboh VA and Fletcher MP, 1992). In rheumatoid arthritis subjects, GLA suppressed T lymphocyte proliferation, which is related to the propagation of joint tissue injury (Rossetti RG *et al*., 1997). This finding is supported by a more in-depth animal study, in which mice fed borage oil had increased T-helper 1-like responses and decreased T-helper 2-like responses, and possibly enhanced suppressor cell or T-helper 3-like activity (Harbige LS and Fisher BA, 2001).

The results of recent studies show that *Borago officinalis* L. can be successfully used adjunctively in disorders of the respiratory system, urinary tract, in metabolic disorders, gout, arthritis and skin diseases and also relieving menopause discomfort.

Recently, it was reviewed that also the dried flower of borage can be valuable in the treatment of obsessive compulsive disorder (OCD). Results of the study performed in 44 patients with diagnosed OCD in a six-week, placebo-controlled, double blind, parallel-group trial showed the beneficial anxiolytic effect produced a significant reduction of anxiety with a 10 point reduction in the Hamilton Anxiety Rating Scale (6.5 point difference over placebo at endpoint). It can be positive as co morbid, generalized anxiety, common in sufferers from OCD (Sarris J *et al*., 2012).

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