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Review Article

Pharmacological potentials of *Aquilaria agallocha* & *Borago officinalis:* A pragmatic review

Rohima Oraon, Tarique Mahmood Ansari, Arshiya Shamim, Paramdeep Bagga, Farogh Ahsan, Mehtab Alam, Saba parveen and Mohd. Sharique

Faculty of Pharmacy, Integral University, Dasauli, Kursi Road, 226026

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ABSTRACT

Objective: To correlate the pharmacological potentials of *Aquilaria agallocha* & *Borago officinalis*. *Aquilaria agallocha* is an extraordinary plant amongst the most broadly developing types of the family Thymelaeaceae. The present survey compiles critical data with respect to pharmacological effects and restorative properties of *Aquilaria agallocha*. The plant has been accounted for antinociceptive, antimicrobial, diuretic, antioxidant, narcotic, antihyperglycaemic, thrombolytic, antidiabetic, ulcer defensive, anticancer, antidiarrhoeal, hepatoprotective properties. *Borago officinalis* L. (Boraginaceae) is generally known as 'Borage' and 'Gauzaban'. It contains high level content of GLA and the plant is presumed as hepatoprotective, gastrointestinal, anxiolytic, antispasmodic antipyretic& lipid-lowering effect.

Conclusion: The pharmacological potentials of both the plants are quite similar & together they hold a plethora of medicinal potential. If these two plants are used to prepare a fixed-dose combination, it may paw path for a novel herbal formulation that can further be evaluated for future prospects in the prevention of Hypercholesterolemia & associated disorder.

Keywords: Hypercholesterolemia, Polyunsaturated fatty acids, Antihyperlipidemic drugs, Restorative properties

Address for Correspondence: Dr. Tarique Mahmood Ansari, Head & Associate Professor Faculty of Pharmacy, Integral University, Dashauli, Kursi Road, Lucknow-226026, U. P.

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INTRODUCTION

Medicinal plants have been used since prehistoric times for their remedial properties, therapeutic values as well as to impart the flavor of food [1]. Herbal products and dietary supplements or additives are now widely available and considered as complementary approaches for health promotion. They are used to cure and prevent several diseases, such as neurodegenerative disorders, dementia, aging, cancer, diabetes, and cardiovascular disorders. Various substances, screened from plants, are identified as active molecules in modern medicines and many plant extracts work as complex mixtures with synergistic effects [2].

Aquilaria agallocha (Thymelaceceae) is an indigenous evergreen plant of India, China and Tibet. *Aquilaria agallocha* is famous for the resinous wood and it is commonly known as ‘aloe wood' or ‘agarwood', it is a beneficial non-timber aromatic wood [3,4]. Agarwood has been utilized for varied purposes all over the world for many years. It has been reported in Ayurveda and traditional medical practice [5]. Generally, bark, root, leaves, and heartwood of *Aquilaria agallocha*are used for their curative and therapeutic properties. It is reported to have agarol, aquillochin; agarospiranes (sesquiterpines): agarospirol, baimuxinic acid, baimuxinal dihydroxyagarofuran2-(2-phenylethyl)-4H-chromen-4-one derivatives [6,5]. There is a necessity for agarwood and its oil to be standardized according to their chemical study[7]. The most bioactive constituents of agarwood are alkaloids, steroids, saponins, tannins, terpenoids, flavonoids and phenolic compounds[8,9]. *Aquilaria agallocha* have various pharmacological activities and it shows anti-diabetic, anti-bacterial, anti-inflammatory, an effect on cardiovascular disease, antifungal [10-20].

The common name of *Borago officinalis* is Gauzaban. *Borago officinalis* is also known as borage, burrage, bourrache, and bugloss belongs to the family of Boraginaceae native to Europe and North Africa widely distributed in many Mediterranean countries[21].GLA is an omega-6 polyunsaturated fatty acid which can't be produced in the body and though falls in the category of essential fatty acid, it uses as a mediator to dihomo-γ linolenic acid (DGLA) and it helps in reduction of the inflammatory response of Lymphocytes and macrophages and prevention of cardiac failure[22-25]. *Borago officinalis* or borage is a herb which is cultivated for remedial uses, even though it is commercially cultivated for borage seed oil. Borage seeds oil is the huge plant source of the gamma-linolenic acid (GLA) which is used as dietary or food supplements. GLA has constantly prescribed as an anti-inflammatory drug with this belief that it lacks some of the common side effects of other anti-inflammatory drugs [26,27]. GLA, a volatile fatty acid present in the seed is rare to borage with an oddity of very few other plants [28]. Borage is essentially used in different areas along with pharmaceutical and beverage production, for forage, as dietary supplement and salads [29,30]. Borage consists of around 30-40% of oil, of which GLA contains approximately 20-30%. Even though, borage is better in terms of GLA yield, as the quantity of GLA present in borage is about twice than that of evening primrose oil [31,32,29].GLA exhibit antiseizure action, antiasthmatic activity, immunomodulatory property, protective effect [33-38]. Borage oil is known to offer protection in atherosclerosis which is an inflammatory disorder characterized by loss of integrity and function of the arterial endothelium [39]. Borage oil has antimicrobial action & hepatoprotective action in hepatic fatty liver disease [40,41]. Apart from these actions, due to the presence of carvacrol, borage oil is a highly prevalent vector for malaria parasites in Africa [42].

Pharmacological activities reported on *Aquilaria agallocha* & *Borago officinalis*:

S.no.	Plant's name	Pharmacological activities
1.	*Aquilaria agallocha*	• Anti-oxidant Effect (Miles and Grisham et al.,1994, Sharma and Bhat et al.,2009, Miniyar et al.,2008) • Antidiabetic Effect (Omar et al.,2013, Aromdee et al.,2011) • Hepatoprotective Effect (Rahman et al.,2013, J. Alam et al.,2017) • Anti-inflammatory Effect (Chitre et al.,2007, Iyer et al.,1994, Suebsasana et al.,2009, Vakati et al.,2008, Winter and Poster et al.,1957) • Analgesic Effect (Suebsasana et al.,2009, D'Amour and Smith et al.,1941, Khalil et al.,2013, Chitre et al.,2007, Hanskaar and Hole et al.,1987) • Antihistaminic Effect (Kim et al.,1997) • Laxative Effect (Hara et al.,2008)

		• Antibacterial Effect (Rahman et al.,2013, Chen et al.,2011, Wetwitayaklung et al.,2009, Sirilak et al.,2013) • Antimicrobial Effect (Manasi et al.,2008) • Antifungal Effect (Saad S et al.,2015) • Anticancer Effect (Hashim et al.,2014, Dahham et al.,2015, Tabana et al.,2016, Ibrahim et al.,2011, Dahham et al.,2016) • Effect on Central Nervous System (Okugawa et al.,1993, Takemoto et al.,2008, Okugawa et al.,1994, Alla et al.,2007) • Anti-arthritic Effect (Habiburrahman et al.,2016)
2.	*Borago officinalis*	• Hepatoprotective Effect (Ashraf et al.,2015) • Effect on Gastrointestinal, Respiratory and Cardiovascular (Gilani et al.,2007) • Antioxidant Effect (Mhamdi et al.,2010, Ciriano et al.,2009, J. Aliakbarlu et al.,2011) • Anti-inflammatory Effect (Komaki et al.,2015, Cameron M. et al.,2011) • Lipid Lowering Effect (Ahmed et al.,2015) • Seborrheic dermatological Effect (Salomom et al.,2006, Tolleson et al.,1993) • Antinociceptive Effect (Shahraki et al.,2015) • Effect on Central nervous System (Fatemeh et al.,2014, Komaki et al.,2015) • Mineral composition (Medrano et al.,1992)

Activities reported on *Aquilaria agallocha*:

Antioxidant Effect: The antioxidant effect of ethyl acetate extract of the *Aquilaria agallocha* leaves (EAA) tested at the different concentration of test compounds (500µg/ml, 1000 µg/ml, 1500 µg/ml and 2000 µg/ml). It was observed that EAA showed an anti-oxidant effect at a lesser concentration range (500µg/ml) [43].

Free radical scavenging activity of the *Aquilaria agallocha* has been analyzed during 1,1-diphenyl-2- picrylhydrazyl radicals (DPPH). The standard ascorbic acid at the concentration of 0.08-5 g/ml decreased the DPPH oxidation by approximately 30-80%. The anti-oxidative activities of ascorbic acid and *Aquilaria agallocha* extract (AAE) were found to have IC50 values equal to 2.19 g/ml and 47.18 g/ml reciprocally [44].

The anti-oxidant effect of ethyl acetate extract of *Aquilaria agallocha* (EAA) investigated in vitro experiment at the various amount for inhibitory effect on nitrite- activate oxidation of hemoglobin in human blood hemolysate. Result specify a strong antioxidant effect of EAA in a concentration range of 500-3500 µg/ml. Yet the pro-oxidant effect was observed at higher concentrations of these compounds [45].

Anti-diabetic Effect: The effect of methanol and aqueous extracts of agarwood leaves reported in streptozocin-induced diabetic rats with 20% glucose water consumption for 6 weeks, orally administered crude methanolic and aqueous extract which is 250 to 500 mg/kg to the various treatment groups and compared to metformin (0.25 mg/kg). The blood glucose level, body weight, glycosylated hemoglobin, muscle and liver glycogen, lipid profile status were measured and histopathology of the pancreas was performed after 6 weeks of treatment and compared to the normal control. In vitro experiment, the effects of the methanol and aqueous crude extract at a concentration of 100µg/ml to 1000 µg/ml are exposed to α-glucosidase and amylase inhibitory activity. For comparison, Acarbose is used at the same concentration as a standard. This outcome demonstrated that extract of leaves of agarwood represented as potential dietary supplements that may be useful for allowing flexibility in meal planning and automatically reduce the number of diabetic patients in the worldwide population[46].

The anti-diabetic effect of methanol, water and hexane extracts of leaves of *Aquilaria agallocha* tested on hyperglycemia in streptozocin-induced diabetic rats. Only methanol and water extracts at a dose of 1g/kg body weight lowered the fasting blood glucose levels 54 and 40% reciprocally. The results were comparable to 4 U/kg body wt. of insulin (73%). In vitro experiment, the effect of methanol and water extracts of *Aquilaria agallocha* at the concentration of 10µg/ml increased glucose uptake activity on rat adipocytes by 172± 10 and 176±21% of the normal control group respectively. The glucose take-up improvement activity is compared to 1.5 nM insulin (166±16%). The finding shows that agarwood leaves are promising potential anti-diabetic agent [47].

Hepatoprotective Effect: The hepatoprotective effect of ethanolic extract of *Aquilaria agallocha* leaves (EEAA) has been explored, hepatotoxicity induced by CCl4 in the rat model by estimated serum hepatic enzyme levels and histopathological studies of liver tissues of rats. EEAA at dose 200 mg/kg and 400mg/kg body weight administered per oral for 10 days in rats and compared with standard silymarin at a dose (100 mg/kg) orally. The report of the histopathological study of liver tissues exposed to the hepatoprotective activity of EEAA [48].

The hepatoprotective activity of ethanolic extract of *Aquilaria agallocha* (AEE) leaves against paracetamol-induced hepatotoxicity in the rat model by estimated serum hepatic enzyme levels and histopathological study of liver tissues of SD rats. AAE at dose 200mg/kg/day and 400mg/kg/day body weight administered per oral for 7 days in SD rats and compared with standard silymarin at dose 100 mg/kg/day orally. The result specifies the ethanolic extract of *Aquilaria agallocha* leaves possesses hepatoprotective effect as it exhibited protective effect against paracetamol-induced hepatotoxicity in SD rats demonstrated by a significant decrease in AST, ALT, ALP, LDH, cholesterol, bilirubin and increase in ALB, TP concentration, and prevention of paracetamol-induced histopathological changes in liver[49].

Anti-inflammatory Effect: Anti-inflammatory activity from the ethyl acetate extract of heartwood of *Aquilaria agallocha* against acute inflammation in rats' paw was induced by subplantar injection of carrageenan 0.1 ml. Pretreatment with EAA (50mg/kg, 100 mg/kg and 200mg/kg, p.o.) typically reduced edema at 1, 2 and 3 hours after injection of carrageenan. The reduction in edema produced by EAA (800 mg/kg, p.o) is similar to that of standard drug diclofenac (10 mg/kg, p.o.) [50].

The anti-inflammatory activity from the aqueous extract of *Aquilaria agallocha* leaves using carrageenan 0.1 ml injection induced edema in mice. The paw volume of the rat was measured at 1, 2 and 3 hours after carrageenan injection [51] using a plethysmometer [52]. The results specify significant changes in the paw volume from the basal value and reduced edema [51].

Anti-inflammatory action from the extract of *Aquilaria agallocha* bark (AAE) at a dose (800 mg/kg) and aspirin (300 mg/kg) by orally and treated with water (as the control). One hour after treatment, acute inflammation was induced by subcutaneous injection with 0.1 ml of 1% carrageenan in the right paw of the rats. After giving the carrageenan injection, the edema in the paw gradually increased within the 1st hour for the control group, the peak effect was reached over the duration of 3 hours. Animal treated with aspirin at the dose of 300 mg/kg exhibited some enlarged paws, and the paw size was significantly less when compared to the control group after 2 or 3 hours. The result exhibited significant reduce edema and reduce the paw volume [53].

Anti-inflammatory effect of *Aquilaria agallocha* oil (AAO) tested, with the help of carrageenan-induced edema in the animal model and human red blood cell membrane stabilization method using 0.1 ml of carrageenan-injected into subplantar region of left hind paw of rats. The strength of oil was differentiated with standard Diclofenac (10 mg/kg). The paw volume up to the ankle joint was measured at 0, 1, 2, 3 and 4 hours respectively after carrageenan injection using plethysmometer. AAO showed significant inhibition of edema in carrageenan-induced paw edema model maximum at 3 hours for AAO at doses 50 mg/kg, 100 mg/kg, p.o. and Diclofenac 10 mg/kg, orally administered and the percentage decrease in paw volume 58.59%, 62.11% and 68.94% respectably and membrane stabilizing action on human red blood cell membrane at the concentration of 100, 250 and 500 µg/ml shown 39.66%, 62.94% and 78.50% which were comparable with standard drug diclofenac [54].

Anti-inflammatory activity of *Aquilaria agallocha* extracts reported on rats. Sub plantar injection of .01 ml solution of carrageenan-injected to the left hind paw of rats to produce edema. After 1 hour of oral administration of drugs produced edema in rats and right paw served as control group. Pretreatment with EAA (extract of *Aquilaria agallocha*) at the dose 50, 100 and 200 mg/kg) significantly decreased edema at 1, 2 and 3 hour after carrageenan injection. The reduction in edema produced by EAA at the dose (800 mg/kg, p.o.) has resembled that of diclofenac (10 mg/kg, p.o.)[55].

Antipyretic Effect: Antipyretic activity of aqueous extract of agarwood leaves on rats by oral administration. Baker's yeast (135 mg/kg) induced fever in rats. The results found that, after 5 hours of yeast injection, 400 and 800 mg/kg of aqueous extract of agarwood significantly reduced the rectal temperature of rats. Rats were found significantly less sensitive to heat at an oral dose of 800 mg/kg of aqueous extract of agarwood, after 60 and 90 minutes. The result of the investigation state that aqueous extract of agarwood possesses antipyretic activity [2].

Analgesic Effect: Analgesic action on mice for the reaction time by placing them on a hot plate that was thermostatically kept at 50°C with a four-wall plexiglass container, held by the force to the animals on the hot plate. Recorded the reaction time that each mouse spent on the hot plate (until it licked or jumped in response to pain). The cut-off time of the test was stable at 30 s in order to prevent tissue damage. The result of the study state that it possess analgesic activity [53].

After oral administration of extract, vehicle or standard formulation. The tail flick latency was evaluated at 0, 1, 2, and 3 h by an analgesiometer test. The site of application of radiant heat in the tail was measured at 2.5 cm from the bottom of the tail. The cut off time was set on 15 seconds to avoid any tissue damage. The power of the current passed through naked nichrome wire kept constant at 4 amps. The extract of *Aquilaria agallocha* had established a significant analgesic effect [56].

Analgesic activity of ethanolic extract of *Aquilaria agallocha* leaves in mice [57] using acetic acid induced writhing method or technique [58] and it is also reported to treat toothache, colic, rheumatism and pains during pregnancy. It was clearly specified that the ethanolic extract of *Aquilaria agallocha* possesses analgesic activity [57].

Analgesic activity of the ethyl acetate extract of *Aquilaria agallocha* wood in mice using aqueous acetic acid-induced writhing by administering it at the dose of 10 ml/kg intraperitoneally (i.p.) after 1 h of extract's oral administration. The mice located in the observation chambers and after five minutes allowed to elapse. The no. of writhes was counted at five minutes interval for the next 30 min. A remarkable reduction in no. of writhes by treatment as compared to vehicle-treated animals observed indicating positive analgesic response [50].

Analgesic activity of ethyl acetate extract of *Aquilaria agallocha* investigated by formalin induced paw licking in mice. The formalin test control two distinctive phases, which possibly reflecting several types of pain. Mice treated per oral with ethyl acetate extract of *Aquilaria agallocha* (50, 100 or 200 mg/kg) or 2% Tween 80 solution in water or diclofenac solution (10 mg/kg). After 1 hour, 20 µl of 1% formalin was injected subcutaneously under the dorsal surface of hind paw of mice. Mice were placed in the observation chambers. The number of licks was counted or compute till 5 min (early phase) to the next 30 min (later phase) after formalin injection. The early phase had shown neurogenic pain while the later phase represented inflammation in hind paw of mice. After treatment and as compared with the normal control group, animals showed good analgesic property [59,60].

Antihistaminic Effect: The effect of the aqueous extract of *Aquilaria agallocha* leaves tested on the instant hypersensitivity reactions. The extract specifies inhibitory effects on cutaneous anaphylaxis produced by compound 48/80, and histamine secretes from rat peritoneal mast cell (RPMC). The morphological analysis also clearly showed that the extract blocked the degranulation of RPMC in rats. The level of compound 48/80 actuates intracellular cAMP in RPMC, when the extract added actually enhanced about 8-fold. The result of the study states that the aqueous extract of *Aquilaria agallocha* inhibited the immediate hypersensitivity reaction by inhibiting secretion of histamine from mast cell [61].

Anti-arthritic Effect: The anti-arthritic effect of ethanolic extract of *Aquilaria agallocha* (EEAA) leaves and *Aquilaria agallocha* oil (AAO) of heartwood showed a considerable anti-arthritic effect in both in-vivo and in-vitro methods. *Aquilaria agallocha* oil (AAO) of heartwood showed relatively better activity than Ethanolic extract of *Aquilaria agallocha* (EEAA) leaves. The difference in the evaluated action could be due to the existence of sesquiterpenes and phenolic in oil. The mechanism of anti-arthritic activity may be due to blockage of chemical moderators involved in the evolution of arthritis and inhibition of protein denaturation, hematological and radiological study expose their anti-arthritic activity[62].

Laxative Effect: The laxative effect of acetone extract of *Aquilaria agallocha* leaves and the activity had measured by counting the stool frequency and stool weight. An acetone extract of leaves of *Aquilaria agallocha* (at a dose of 1000 mg/kg, p.o.) induced significant increase (up to 2-3 times the control value) in stool repetition and weight. However, a low dose of acetone extract (100 or 300 mg/kg, p.o.) did not produce any remarkable effect but at a higher dose of acetone extract of *Aquilaria agallocha* (1000 mg/kg, p.o.) had a laxative effect on mice [63].

The pharmacological investigation demonstrated that agarwood has a gastrointestinal regulating effect. The studies demonstrated that agarwood ethanol extracts remarkably enhanced intestinal peristalsis, improved gastric clearance, and a decrease in gastric ulcer [64]. The ethanol extract of agarwood leaves increased intestinal propulsion [65]. The Agarwood trees' leaves induced loosening of stool (laxation) via acetylcholine receptors on loperamide-induced constipation in mice [66] The ethanol extract of agarwood leaves had a laxative effect without causing diarrhea in a

rat model of low-fiber diet-induced constipation [67]. Mangiferin and genkwanin 5-O-primeveroside were the two major bioactive constituents [68]. Additionally, benzyl acetone, an active substance from the essential oil, had the effect of increasing appetite [69]. Even though agarwood on abdominal irritation has been widely used for the gastrointestinal regulating effect, especially on a particular disease, is not fully clear.

Anti-bacterial Effect: Antibacterial activity of *Aquilaria agallocha* oil and Citrulluslanatus seed oil by agar well diffusion technique and compared with standard ciprofloxacin (10 mcg/ml). The test organisms used were Escherichiacoli, Enterococcusfaecalis, Staphylococcus aureus, Pseudomonasaeruginosa. From the study, it was specified that both had the antibacterial activity and the Citrullus oil had more antibacterial activity than *Aquilaria agallocha* oil [70,48].

Agarwood essential oil derived from artificial or natural agarwood had inhibitive activities towards Bacillussubtilis and Staphylococcus aureus [71].

Extracts of agarwood (A. crassna), isolated by water distillation process, supercritical fluid carbon dioxide, and supercritical fluid carbon dioxide with ethanol as the co-solvent, explored antimicrobial activities against S. aureus and Candidaalbicans but were not against Escherichia coli [72].

An aqueous extract of Agarwood leaves possessed an in vitro antibacterial action against Staphylococcus epidermidis, causing bacterial cells to swell and distort, inhibiting the biofilm formation, and leading to cell wall rupture [73].

Antimicrobial Effect: The aqueous and methanol extracts of *Aquilaria agallocha* leaves and bark investigated for antimicrobial activity opposite to pathogenic bacteria such as Shigellaflexneri, Bacillusbrevis, dermatophytes and helminthes [74] by a disk-diffusion method [75]. Anti-microbial activity was performed for various varieties of *Aquilaria agallocha* leaves. All the varieties of *Aquilaria agallocha* were investigated to oppose pathogenic microbes Bacillus cereus, Candidaalbicans, Staphylococcus aureus, Pseudomonasaeruginosa, E. coli, and Aspergillusniger. The aqueous extract of the leaves inhibited the growth of Pseudomonasaeruginosa and Staphylococcus aureus [74].

Antifungal Effect: A piece of good evidence reported for β-caryophyllene being an active constituent of Agarwood essential oil. The structure of β-caryophyllene was confirmed by using FT-IR, NMR and MS and the study conclude that in particular, β-caryophyllene have a potential source of selective anti-fungal agents [80].

Anticancer Effect: The agarwood essential oil possesses anticancer activity against MCF-7 breast cancer cells and HCT 116 colorectal carcinoma cells [76-79]. β-Caryophyllene, obtained from the essential oil of Agarwood, expressed selective anti-proliferative effects against colorectal cancer cells IC50 19 μM) and produced apoptosis via nuclear condensation and fragmentation pathways. β-Caryophyllene showed the potential reduction of clonogenicity, migration, invasion and spheroid promotion in colon cancer cells[80].

Effect on the Central Nervous system (CNS): Change of brain monoamines and EEG wave in Alzheimer's disease in rats for ethanolic extract of *Aquilaria agallocha* leaves. Medication with *Aquilaria agallocha*leaves extract restored the monoamine levels of brain regions to near control levels. The constituents agarospiral and Jinkoh-eremol obtained from *Aquilaria agallocha* injected by peritoneal and intracerebroventricular route exerted a beneficial effect on the central nervous system and declined both methamphetamine and apomorphine produced spontaneous locomotion in the mice [81,82]. Activity has been recorded by locomotor [83].

The sedative effect of Agarwood oil using a spontaneous vapor administration system. It was specified to have the sedative effect in mice. The volatile constituents benzyl acetone, α-gurjunene and calarene derived from it were also tested in mice which reproduced the result of the oil or extract. It was specified that the effective dose of the substance was lower than their actual content in the oil and extract(benzyl acetone 0.1%, α-gurjunene 1.5%, calarene 0.17%)[84].

The anxiolytic activity in mice with the EPM (Elevated Plus-Maze Test) for an alcoholic extract of heartwood of *Aquilaria agallocha* (AEAA). At a lower dose of AEAA (30 mg/kg, p.o.) did not indicate any significant effect on the number of entries in both open and closed arms. But at medium and higher doses (100 & 300 mg/kg) of AEAA significantly increased both open arm entries and closed arm entries and time spent in closed arms and open arms. However, AEAA and diazepam did not impinge on the total entries during the test period. The study showed that the AEAA possess anxiolytic activity at a medium dose (100 mg/kg) [85].

Anti-convulsion action of alcoholic extract of *Aquilaria agallocha* (AEAA) using PTZ (Pentylenetetrazole) to induced convulsion. AEAA at lesser dose (30 mg/kg) did not offer any

significant anti-convulsion effect, medium dose (100 mg/kg) had typically altered onset of clonus but not onset of tonic seizures, but higher dose displayed a significant anti-convulsion action by increasing postponement of clonus, beginning of tonic seizures and depreciate mortality of mice, 33% of animals were suffered withAEAA at a dose of (100 mg/kg) and 67% suffered with AEAA at a dose of (300 mg/kg)[85].

Activities reported on *Borago officinalis*:

Hepatoprotective Effect: The hepatoprotective impact of *Borago officinalis* L. is airborne ethanolic extract (BAEE) against CCl4-prompted liver harm in contrast with silymarin, an established cancer prevention agent liver prescription. The hepatoprotective capability of BAEE in rodents was assessed following oral organization ofCCl4, which improved hepatic lipid peroxidation and eminently exhausted diminished glutathione. In addition, we found that CCl4organization caused over-articulation of the fiery markers TNF-α and NFκB protein levels, notwithstanding a critical increment in the arrival of liver serum biomarker levels. Organization of BAEE indicated hepatic insurance by altogether diminishing raised dimensions of serum chemical dimensions. Quite, BAEE altogether decreased articulation of the TNF-α and NFκB protein articulation levels equivalent to the wild kind and silymarin. These discoveries were enlarged with the histopathological results in which BAEE could demonstrate an improvement in the liver condition. The aftereffects of the present examination demonstrate that BAEE separate has a potential hepatoprophylactic impact against liver damage [86].

Effect on Gastrointestinal, Respiratory and Cardiovascular: The crude leaves extract of *Borago officinalis* were reported for its bronchodilator, vasodilator and cardio- depressant activity to justify some of the traditional purposes. crude extract of Borage leaves which was tested specifically for flavonoids, coumarins and tannins produced a concentration-dependent relaxation of spontaneous and K+ (80 mM)-caused constrictions in isolated rabbit jejunum preparations, signification of Ca++ antagonist action, which was proved when pretreatment of the tissue with crude extract of Borage leaves created a rightward shift in the Ca++ concentration-response curves like that created by verapamil. In rabbit tracheal preparations, the crude extract of Borage leaves calmed the carbachol (1 μM) and K+ induced constrictions. Verapamil also produced a nonspecific inhibitory effect. In rabbit aorta preparations, the crude extract of Borage leaves showed a vasodilator effect against phenylephrine and K+ -induced contractions similar to verapamil. When tested in guinea-pig atria, the crude extract of Borage leaves lead reduction of both atrial force and rate of contractions. These results propose that the spasmolytic effects of crude extract of Borage leaves are mediated conceivably through Ca++ antagonist mechanism, which might define the traditional use of Borage in hyperactive gastrointestinal, respiratory and cardiovascular defect [87].

Anti-oxidant Effect: Borage seeds were examined in Amdoun region (North of Tunisia) amid their aging stage so as to break down their phenolic mixes and to determine their antiradical searching action. The gathering time impact on some physical properties of borage seed was critical. The expansion of dry weight (from 10 to 90%) amid readiness was related contrarily with that of dampness content (from 90 to 10%). Seed phenolic substance went from 2.45 to 10.98 mg GAE/g DW. HPLC investigation allowed to recognize nine phenolic acids and seed development with the transcendence of rosmarinic, syringic and sinapic acids. Absolute phenolic substance and IC50 values in seed during their development time, permitted to reason that antioxidant action does not rely upon the high substance of all-out phenolics however on the phenolic synthesis [88].

An assessment of the limit of a lyophilized water concentrate of borage leaves to postpone the lipid oxidation process in dry aged sausages advanced with ω-3 PUFAs has been performed. Lyophilized concentrate (340 ppm) demonstrated a synthetic antioxidant limit proportionate to 200 ppm of a butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) blend. Two clusters of dry aged wieners enhanced in ω-3 PUFA were created. One of them was enhanced with a synthetic antioxidant blend (200 ppm of BHA + BHT) and the other one with regular cell reinforcements (340 ppm of lyophilized water concentrate of borage leaves). Besides, a conventional definition of this sort of dry matured sausages (Control) was additionally made. The common concentrate offered to ascend to bring down the measure of unpredictable mixes (counting hexanal), then the blend of synthetic antioxidant agents (2202 and 2713 ng dodecane/g dry issue, separately). TBARS and Cholesterol Oxidation Products (COPs) did not indicate noteworthy contrasts between items with various cancer prevention agents. The sensorial investigation demonstrated that lyophilized water concentrates of borage leaves did not influence the sensorial properties of the items. From the prudent and security points of view, the utilization of a result (Borage leaves) and water as extracting dissolvable are significant options for getting natural antioxidants agents to be added to dry fermented sausages improved in ω-3 PUFA [89].

The antioxidant activity reported of the extract of Borage (*Borago officinalis*) flowers. The antioxidant activity of the extracts was evaluated utilizing 2,2-diphenyl-1-picrylhydrazyl (DPPH), β-carotene/linoleic acid and reducing power assays. In DPPH assay, the sequence of free radical scavenging activity of the extracts was: methanol extract (ME) > acetone extract (AE) > water extract (WE). In theβ-carotene/linoleic acid assay, the inhibition capacity (%) of WE (95.62%) was in the most elevated amount. When reducing power assay was used, a similar action pattern was seen as given in the DPPH assay. In conclusion, the WE of Borage flower indicated potent antioxidant activity [90].

Anti-inflammatory Effect: The group of 37 patients was tried with all the symptoms of rheumatoid joint inflammation (RA), alongside irritation or pain of the synovial membrane. At the time of treatment, borage seed oil containing 1.4 g/d GLA was controlled in patients and cottonseed oil as a control. Following two years, a decrease in symptoms of disease activity ($p<0.05$) has been accounted for: the decline of soreness of joints by 36% and a decrease of swelling of the joints by 41% as contrasted and control aggregate because of taking borage oil. The aftereffects of this investigation affirm that utilization of GLA is successful in the treatment of RA. No unfavorable impacts were seen during borage oil consumption. Likewise, late examinations led on borage seed oil have positive outcomes and may warrant further examination [91]. Summarizing, there is moderate proof that oils containing GLA (for example borage) can manage some advantage in calming indications of RA [92].

Lipid-lowering Effect: Lipid-lowering effect of aqueous extract of *Borago officinalis* and uranyl acetate on activity in oxidation- antioxidants system was designed to estimate as well as its effect on biochemical parameters. Treatment of the albino male rabbits by uranyl acetate and aqueous extract of Borage resulted in a significant reduction at level ($p\leq0.05$) as compared to uranyl acetate group through the average of the Glucose level, triglycerides (TG), LDL, total cholesterol (TC), VLDL. The increment in average of HDL and GSH, the treatment or medication of the albino males rabbits by aqueous extract only resulted in a significant increment at level ($p\leq0.05$) as compared with positive control group through the average of the Glucose level, TC , TG , LDL,VLDL, and resulted in a significant decrement through the average of HDL and GSH [93].

Seborrheic Dermatological Effect: Seborrheic dermatitis (SD) influences 1– 3% of the populace and is one of the basic incendiary skin disorders. For the most part, youngsters become ill, particularly guys, however, it might likewise show up in newborn children. These sicknesses are tough to treat because of their common nature. It is viewed as that both interior (hereditary inclinations/genetic predisposition, immunological disorders), and outer variables (air contamination, skin irritation, poor cleanliness of the body) are engaged with its improvement [94].

They think about did in Sweden incorporated a group of 48 babies completely meeting the criteria of SD, in whom borage oil has been utilized in the treatment of nearby skin changes. On these youngsters, restoratively helped treatment was connected utilizing hydrocortisone, antifungal medications and saturating arrangements, without unmistakable impacts. In this investigation, borage oil was connected locally (to 5 ml) on the influenced skin two times every day. After 10– 12 days from the first application the skin turned out to be free from the injuries, even in spots in which the basic oil was not connected. Cessation of the treatment led to the backside of the malady inside seven days, while the prophylactic utilization of fundamental oil 2– 3 times each week shielded the skin from ailment backslide. During the treatment, no symptoms were watched. The creators of the examination affirm that preparation containing GLA in its structure are successful cures against SD [95].

Antinociceptive Effect: *Borago officinalis* blossom/flower (Borage) is known as sedative or narcotic in herbal medication. The antinociceptive impact of borage was assessed hydroalcoholic extract in formalin test male rodents. 56 male albino Wistar rodents were randomly separated into seven groups: Control group A (intact), B (saline), and C (control) in addition to experimental groups of D, E, F, and G. The groups D, E, and F receive 6.25, 12.5, and 25 mg/kg, *Borago officinalis* blossom hydroalcoholic separate before the test, individually yet bunch G receive 25 mg/kg borage concentrate and ibuprofen before the test. A biphasic pain was actuated by an infusion of formalin 1%. The received information was broke down by SPSS software ver. 17 utilizing statistical trial of Kruskal Wallis and Mann-Whitney. The outcomes were communicated as mean ±SD. Statistical differences were viewed as huge at $P<0.05$. The outcomes uncovered that the acute and chronic pain behavior score in test groups of D, E, F, and G fundamentally diminished contrasted with gatherings An and B, however this score did not demonstrate any distinction to group C. Additionally, constant agony conduct score in group G was fundamentally lower than every single other group. The outcomes showed that *Borago officinalis* hydroalcoholic extract separate affect the

acute/intense and chronic pain behavior reaction in formalin test male rodents [96].

Effect on Central Nervous System (CNS): The protective effects of *Borago officinalis* extract have been reported on Amyloidβ (Aβ)-Induced memory impairment. Male Wistar rats got intra hippocampal (IHP) injection of the A (25–35) and borage extract throughout incubation (100mg/kg). Learning and memory functions in the rats were analyzed by passive avoidance [97] and the Morris water maze (MWM) tasks [98]. Finally, the antioxidant capacity of the hippocampus was measure during ferric on decreasing antioxidant action assay. The outcomes showed that (25–35) impaired step-through latency and time in the dark compartment in the passive avoidance task. In the MWM, A (25–35) remarkably increased escape latency and traveled distance. Borage administration diminished the Aβ- induced memory impairment, in both passive avoidance and MWM tasks. Aβ induced a notable decrease in antioxidant action of hippocampus and borage prevented the decrease of the hippocampal antioxidant status. The data obtained from the study suggested that borage could improve the learning impairment and oxidative harm in the hippocampal tissue following Aβ treatment and that borage utilization may promote to an improvement of AD-induced cognitive dysfunction [97].

Medicinal plants with normal cell reinforcements have been appeared to be useful in an assortment of confusions, for example, nervousness. The raised in addition to labyrinth (EPM) is a standout amongst the most generally utilized models to evaluate nervousness in little rodents. This investigation was intended to describe the anxiolytic-like action of *Borago officinalis* blooms remove [86], utilizing an EPM test [94]. Male Wistar rodents weighing 220-250 grams were utilized in the present examination. Thirty minutes after an intraperitoneal (IP) infusion of the Borage remove (50, 100, 200 mg/kg) or saline, every creature was put in the EPM. Animal behavior in the test sessions was recorded by a camcorder situated above the maze, interfaced with a screen and a PC in a nearby room. The time spent in the open arms, the level of sections beyond all detectable inhibitions arms of the EPM and the quantities of passages into the shut arms were recorded for five minutes. Statistical examination demonstrated that intense IP infusion of Borage separate before an EPM trial essentially expanded the time spent in open arms and level of open arms passages. Though, the extract had no impact on the number of closed arm sections. The outcomes exhibited that infusion of Borage extract may have an anxiolytic profile in rodents. Be that as it may, the definite instruments identified with the active compounds in Borage extract ought to be clarified in future investigations [99].

Mineral Composition: Borage is a plant regularly developed for utilization in Spain and different nations. The goal of this examination has been to decide the proximate and mineral piece. The consumable piece of the plant relates to the basal leaf petioles. In this part, water was observed to be a significant constituent with a normal estimation of 94%. Dry matter was generally established by neutralized cleanser fiber, ash, and protein. Potassium was the significant mineral component, achieving a considerably higher extent than either fat or starch. Borage had additionally sufficient levels of iron. The qualities acquired in this investigation demonstrate that borage should be incorporated into the nourishment synthesis tables inside the leafy vegetable group [100].

Conclusion

The review summarizes a pragmatic & critical perspective on a surfeit of pharmacological properties hidden in the plants *Aquilaria agallocha*&*Borago officinalis. Aquilaria agallocha* has been reported for antioxidant effect, hepatoprotective effect, analgesic effect, anti-inflammatory effect, antihistaminic effect, antidiabetic effect, anticancer effect, cardioprotective effect. *Aquilaria agallocha* is rich in alkaloids, steroids, saponins, tannins, terpenoids, flavonoids, and phenolic compounds. *Borago officinalis* has been reported for antioxidant effect, analgesic effect, hepatoprotective effect, anti-inflammatory effect, seborrheic dermatological effect, lipid-lowering effect, antinociceptive effect & cardioprotective effect. *Borago officinalis* contains essential fatty acids, linolenic acid, and gamma-linolenic acid. There are some common pharmacological activities in both plants like hepatoprotective activity, antioxidant activity, anti-inflammatory activity, and analgesic activity etc. By all counts and with proven results, we conclude that the pharmacological activities of both plants are about similar.Despite extensive ongoing research on *Borago officinalis* and *Aquilaria agallocha*, there is a lot to be explored. Along with the benefits of both plants, its side-effects are also less which are not serious. Such as if these two plants are combined in a fixed dose combination they can prove a boon for prevention of many diseases & may give a synergistic effect or desired therapeutic effect in the form of a novel herbal formulation in future.

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