JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2025/45169
REVIEW ARTICLE

Exploring the Therapeutic Potential of *Hyssopus officinalis*: A Comprehensive Review on its Pharmacological Benefits

Sweta B. Besh*, Maitri Mahant, Sapana Patil, Kinjal Patel and Rajesh A. Maheshwari

Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Piparia, Vadodara – 391760, Gujarat, India; swetababesh@gmail.com

Abstract

Hyssopus officinalis L., a perennial herbaceous plant belonging to the Lamiaceae family, is grown for its medicinal and culinary properties in the Asian continent, Europe, and the Americas. Research on the therapeutic effects of *H. officinalis* L. has been considerable. *H. officinalis* L., a medicinal herb, has a long and diverse history of usage in several medical systems. The purpose of this review was to consolidate and summarise all the knowledge on the subject. Essential oils of this drug contain considerable levels of β-pinene, isopinocamphone, pinocamphone, and other terpenoids, which are the principal active components. Flavonoids (quercetin, luteolin, apigenin, and their glucosides) and phenolic chemicals (p-hydroxy-benzoic acid, protocatechuic acid, ferulic acid caffeic acid as well as chlorogenic acid) have been identified in *Hyssopus*. It has antioxidant and antibacterial properties that are slightly potent against both Gram -ve and Gram +ve microorganisms. Furthermore, it has antifungal, insecticidal, and antiviral properties when examined under controlled laboratory conditions. A variety of ailments, including the common flu, cough, fungal infection, loss of hunger, and spasmodic diseases, can be relieved by using this plant's species. This plant has demonstrated antiplatelet, myorelaxant, and α glucosidase inhibitory properties in animal model analysis. This plant exhibits remarkable therapeutic values and can effectively alleviate many conditions such as microbiological infections, ulcers, epilepsy, and spasms. The general belief is that this plant is typically considered safe when consumed in typical food quantities. Still, more investigation is required to ascertain its safety features.

Major Findings: *H. officinalis* L. demonstrates significant antimicrobial, antioxidant, antispasmodic, and antidiabetic properties. It shows potential for development into therapeutic agents for infections, spasms, and metabolic disorders.

Keywords: Hyssop, *Hyssopus officinalis,* Terpenoids, Therapeutic Potential, Traditional Use

1. Introduction

The common name for the genus of flowering plants, Ruellia, encompasses 250 species. Indigenous to tropical regions, this plant genus is notable for its various species, with several of them serving as traditional medicinal herbs. Hyssop formulations, made from *H. officinalis* (L.), are increasingly essential in the culinary industry, serving as a popular minty flavouring, condiment, and spice[1].

The perennial herbaceous plant, scientifically referred to as hyssop and classified under the Lamiaceae family, is extensively employed in the development of herbal remedies. *H. officinalis* L., generally known as hyssop, is predominantly distributed throughout Asia and the Eastern Mediterranean region. Two Hyssop (English), *Zufah-yabis* (Hindi), *Jufa* (Sanskrit), and *Zufah* (Urdu) are commonly used terms for the therapeutic plant *H. officinalis* L[3].

The plant is a perennial semi-shrub with branches that can be found in nature or developed on purpose. Traditional medicine has recognized the herb's medicinal potential. Hyssop leaves are used as a condiment in European cuisine and also have decorative

*Author for correspondence

Article Received on: 26.07.2024 Revised on: 10.02.2025 Accepted on: 14.03.2025

applications[4]. They are also utilized as folk medicine. Because of its numerous culinary and medicinal applications, this versatile plant has become one of the most popular herbal treatments on the market[5].

Hyssopus officinalis was once valued for its therapeutic qualities in a variety of civilizations. Notwithstanding its long history of usage, there is an increasing need to thoroughly assess and compile an array of scientific data pertaining to its pharmacological advantages[6]. It has antioxidant, anti-microbial, anti-cancer, anti-inflammatory, anti-fungal, mosquito-larvicidal, anti-Alzheimer's, and anti-diabetic properties, among others. To give a comprehensive picture of *H. officinalis*' therapeutic potential, this paper aims to gather the most recent research findings. This study attempts to shed light on *H. officinalis*' numerous pharmacological qualities by evaluating its botanical characteristics, historical use, and the growing body of data from preclinical and clinical trials[1].

The genus *Hyssopus* contains both wild and cultivated perennial herbs and subshrubs with scented leaves. With four to ten flowered pseudoverticils at the terminal, its inflorescence, which resembles a fake spike, measures 20 to 25 cm high[7]. With stems that can grow up to 0.7 m in height, and either upright or drooping, and multiple woody stem divisions, *H. officinalis* has an extremely branching, multiheaded taproot. Measurements: 2 to 4 cm in length and 0.5 to 1 cm in breadth. The leaves appear in opposite directions, lanceolate or oblong, sparkling dark green, alongside entire-edged. *H. officinalis* is a botanical species that is recognised for its therapeutic and fragrant aromatic properties. It is also a producer of honey. The preponderance of the species is situated in the East Mediterranean to central Asia, with an estimated 10 to 12 species. Moreover, it is listed in the pharmacopoeias of Portugal, Germany, Romania, Sweden, and France[8].

2. *Hyssopus officinalis* Chemical Constituents

Hyssopus officinalis includes a diverse range of chemical components, the composition of which can vary depending on several criteria, including the geographical setting and growth surroundings of the plant. *H. officinalis* contains essential oils, flavonoids, resins, mineral salts, oleanolic and ursolic acids, tannins, and organic acids[9]. An extensive examination of the aerial components of the *H. officinalis* plant grown in Xinjiang uncovered the existence of ten flavonoids and two distinctive glycosides in the extract of ethanol. Among these compounds, nine had already been recognised in prior studies. There are several uses for the essential oils that are extracted from hyssop as food, drink, and cosmetic additions[10]. The primary volatile constituents found within the essential oil of *H. officinalis* in different places are methyl eugenol, limonene, 1,8-cineole, β-pinene, β-phellandrene, pinocamphone, pinocarvone, iso pinocamphone, and germacrene-D[11].

These discoveries not only broaden our understanding of *H. officinalis* chemical constituents but also provide new opportunities for investigating the plant's possible uses in a range of sectors. The discovery of many volatile compounds and flavonoids attests to the plant's importance. This includes the plant's use in both traditional and alternative medicine, as well as the quest for natural alternatives by modern corporations.

2.1 The Therapeutic Properties of *H. officinalis*

This herb has a long history of therapeutic usage, primarily for its antifungal, antispasmodic, stomachic, and cough-inducing effects. The medicinal powers and health advantages of hyssop are primarily derived from mythological beliefs rather than scientific evidence[12]. *In vitro* studies have revealed mild antibacterial, antifungal, and insecticidal effects in hyssop extracts and essential oils. Research employing animal models has suggested that this plant possesses, antiplatelet, myorelaxant and α-glucosidase inhibitory properties. Primarily, the essential oil is utilised for enhancing flavour, prolonging the duration that food remains fresh, and for other medicinal uses derived from plants[13].

Hyssopus officinalis possesses antitussive, antiseptic, and anti-inflammatory properties. It promotes digestive health and eases gastrointestinal tract smooth muscle spasms[14]. Infusions of *Hyssopus* are used medicinally to treat a range of conditions, including upper respiratory tract illnesses, rheumatism, angina pectoris, bronchial asthma, pneumonia, cough, bronchitis, pulmonary TB, and skin conditions like bruises and sores. The herb has a high antiviral impact,

in particular against the herpes virus, and it also possesses antispasmodic, expectorant, decongestant, and tonic properties[15]. Maslova *et al.*[8] have shown that *H. officinalis* possesses fungicidal as well as antimycotic, antibacterial, and antiprotozoal activities (Table 1).

Table 1. Pharmacological activities, mechanisms, and key constituents of *H. officinalis*

Activities	Mechanism of Action	Chemical Constituent	Plant Part	References
Anti-oxidant	Decreases oxidative stress and scavenges free radicals	Flavonoids, Phenolic acids, Tannins	Ethanolic Extract	16-18
Anti-microbial	Possesses antiviral, antifungal, and antibacterial properties by preventing the growth of microorganisms	Pinocarvone, Terpinene-4-ol, Carvacrol, β-Pinene	Essential oil	19-24
Anti-cancer	Enable cancer cells to undergo apoptosis and cytotoxicity	Phenolic Compounds, Essential oils,	Essential oil, Extract	26-30
Anti-inflammatory	Lower phagocytic activity and cytokine levels to lessen inflammation	Flavonoids, Essential oils, Phenolic Compounds	Aerial parts	31-33
Antifungal	Restrict the growth of fungi and the germination of spores	Pinocamphone, β-Pinene, Isopinocamphone	Essential Oil	34-41
Mosquito-larvicidal	Has acute toxicity towards mosquito vectors, inhibits the growth of mosquito larvae, and serves as an insect deterrent	β- Pinene, pinocarvone, cis- pinocamphone	Essential oils	42-46
Anti-ulcer	Inhibits the urease enzyme, lowers oxidative stress, strengthens the integrity of the stomach mucosa, and increases secretion of mucus	Polyphenols, flavonoids, phenolic acids, tannins,	Whole plant	47-49
Mio relaxation	Lowers intestinal smooth muscle tone, interferes with plasma membrane ion channels, and inhibits acetylcholine-induced muscular contraction	β- Pinene, Isopinocamphone, limonene	Essential oil	50-52
Anti-convulsant	Elevate seizure threshold, decrease mortality, enhance memory and learning	Polyphenols, Flavonoids	Whole plant (hydroalcoholic extract)	20,53-55
Anti-Alzheimer's	Suboptimal inhibition of AChE and BuChE, impacting neurotransmitter degradation in Alzheimer's disease	Flavonoids, Phenolic acids,	Whole plant (hexane-methanolic extract)	36
Anti-hemolytic	Safeguards red blood cells against oxidative harm and fortifies cell membranes	Flavonoids, Phenolic compounds,	Flowers, Leaves, Stems	57-59
Anti-diabetic	Inhibits digestive enzymes, hence decreasing blood glucose levels and oxidative stress	Caffeic acid, Tannins, Flavonoids,	Aqueous methanolic extract	60-63
Anti-HIV	Inhibits HIV replication and reverse transcriptase, diminishes antigen expression	Caffeic acid, Polysaccharide	Leaves (Methanolic extract)	64,65
Anti-asthmatics	Regulates immunological responses, diminishes airway inflammation, and reinstates a healthy cytokine equilibrium	essential oils, Flavonoids	Whole plant	66-69
Anti-spasmodic	Alleviates muscular spasms by restricting acetylcholine-induced contractions in the gastrointestinal tract	1,8 – Cineole, Linalool, Limonene	Whole plant	70-73
Insecticidal	Impedes larval growth and development, presumably by neurotoxic or growth regulatory processes	Terpenoids, Phenolic compounds	Leaves (Methanolic extract)	74
Anti-leishmaniasis	Decreases skin ulcers and parasite load, presumably by immunological regulation	Tannins, Flavonoids	Whole plant	75

2.1.1 Anti-oxidant Activity

Hyssopus officinalis, often known as hyssop, includes a wide range of bioactive chemicals that may contribute to its antioxidant capabilities. This herb contains phenolic compounds, which possess antioxidant effects. The evaluation of the antioxidant effectiveness of botanical extracts is often performed by the use of 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) tests[16]. These components include several phenolic acids[3]. In their investigation, Vlase *et al.*[12] reported that the extract made with ethanol of *H. officinalis* showed noteworthy antioxidant activity. The demonstration involved a range of tests, such as the DPPH radical scavenging assay, electron paramagnetic resonance, Trolox comparable antioxidant capacity test, radical detection assay, and test to measure the inhibition of haemoglobin ascorbate peroxidase enzyme activity. In a separate investigation, hyssop extracts from Turkey and Serbia demonstrated IC_{50} values of 16.37 mg/mL and 156.60 mg/mL, respectively. Environmental impacts, regional origin, and genetic factors were identified as the sources of variation in antioxidant capacities[17]. The hyssop essential oil's ability to bind transition metals has been linked to its antioxidant qualities. This antioxidative feature has potential applications in food preservation, such as reducing the growth of harmful microbes in ground beef[18].

2.1.2 Anti-microbial Activity

Hyssopus essential oil comprises antimicrobial substances such as pinocarvone, β-pinene, terpinene-4-ol, iso pinocamphone, pinocamphone, carvacrol, and p-cymene. These substances may be used in the study and creation of innovative medications for the management or prevention of infectious diseases in people[19]. *H. officinalis* has weak antibiotic effects in the lab on both Gram+ve and Gram-ve bacteria, as well as antiviral properties and insecticidal, antifungal, and antioxidant properties. *In vivo*, It exhibits anti-platelet, myorelaxant, and α-glucosidase inhibitory properties[20]. According to *Ozer et al.*s'[21] research findings, the *Angustifolius* L. ssp. of *H. officinalis* essential oil showed strong antibacterial properties against various microorganisms including bacteria, yeast *C. albicans* and the fungi *in vitro*. The Minimum Inhibitory Concentration (MIC) was 15.62 to 250 µl/ml. In contrast, the extract of methanol did not kill these germs. In addition, the extract made from methanol demonstrated a value for the IC_{50} of 117.0 µg/ml in the DPPH assay. At a concentration of 2 g/l, it suppressed 40% of the activity in a linoleic acid system when combined with an inert essential oil.

The essential oils derived from the plant species *H. officinalis* L. var decumbens both showed potent antibacterial action *in vitro*, according to a 1998 study by Mazzanti *et al.*[22] The outcome of the study has shown that both species effectively suppressed the proliferation of all varieties of yeast, consisting of the albicans strain of Candida, and seven strains of *Candida tropicalis*, and *Candida krusei*. Hyssop oil was evaluated, along with two other groups of essential oils, in a separate study to determine their efficacy in inhibiting the proliferation of nine strains of Gram-negative bacteria and six strains of Gram-positive bacteria[23]. Another observation revealed that the 5 µl and 10 µl of *H. officinalis* essential oil, derived from Southeastern Anatolia, Turkey, had noteworthy antibacterial activity against *Staphylococcus aureus*, *Staphylococcus pyogenes*, *E. coli*, as well as *Candida albicans* in a disc diffusion test. Nevertheless, it exhibited no efficacy against *Pseudomonas aeruginosa*[24].

2.1.3 Anti-cancer Activity

Cancer is a significant health issue in modern society. The World Health Organisation received 2.09 million lung cancer reports in 2019, making it the most often occurring kind of cancer in men and women. Lately, there has been increasing attention on *H. officinalis* due to its potential anti-cancer properties. Studies on colon and breast cancer cells have demonstrated their possession of cytotoxic and apoptotic properties[26]. An extensive examination was performed on different Hyssop extracts utilising the MTT test on human cancer cell lines to evaluate their potential as anticancer agents. This test is frequently used to evaluate the viability and proliferation of cells by measuring their metabolic activities. Reduced MTT indicates lower cell viability as a result of cytotoxic effects[27]. The experiment was conducted using cell lines from Human Colon Cancer (HCT116 lines), malignant melanoma (A375) and human breast cancer (MDA-MB 231). Hyssop essential oils and extracts had an inhibitor impact on malignant cell lines that were dependent upon concentration. The documented IC_{50} values for the A375, HCT116

cell lines and MDS-MB 231 were 35.16, 29.91 µg/mL, and 62.66, respectively[28]. In a further investigation, MRC-5, HeLaand MDA-MB231 cancer cell lines were subjected to the anticancer activity of *Hyssopus* essential oil. A comparable slight cytotoxic impact of *H. officinalis* subsp. aristatus is observed on the adenocarcinomic human alveolar basal epithelial cell A549 cell line[29]. In an additional investigation, CIV17-EO demonstrated cytotoxic activity at a 200 µg/mL concentration, in comparison to the negative control, causing a 12% decrease in cell viability ($p<0.01$)[30].

2.1.4 Anti-Inflammatory Activity

The well-known medicinal herb *H. officinalis* L., often known as hyssop, has been used historically for a variety of therapeutic purposes. Scientific validation is crucial for therapeutic applications that depend on traditional techniques. A study was done to assess the features that reduce inflammation of the ethanol-based extract created using *H. officinalis*' aerial parts[31]. This was achieved by performing a comparison analysis between the test subject and diclofenac, using a laboratory rat model to replicate acute inflammation. It consisted of four groups, each consisting of 10 animals. The outcome is displayed. The extract decreased the activity of phagocytes, the nitrite/nitrate levels in the inflammatory group, as well as the Phagocitary Index. An extract of *H. officinalis* L. showed significant anti-inflammatory efficacy in an acute inflammation paradigm, comparable to diclofenac[32].

The Uygur plant *H. officinalis* was shown in a separate scientific study to affect the levels of several cytokines in asthmatic mice, particularly interleukin-4, 6, 17, and interferon-γ. The herb was also assessed for its impact on the immune system's control and the inflammation in mice's chronic asthmatic airways. *H. officinalis* L. ultimately impedes the infiltration of eosinophils, diminishes IgE levels, and regulates the immunological system[33].

2.1.5 Antifungal Activity

Hyssopus officinalis essential oil exhibits potent antifungal properties, namely in inhibiting the growth of fungus species like *Candida krusei*, *Candida tropicalis* and *Candida albicans*[34]. Through several *in vitro* and *in vivo* experiments, the fungal killing and antifungal properties of hyssop (*H. officinalis*) oil and its components have been investigated[1]. To ascertain whether *H. officinalis* L.'s essential oil has antifungal properties contrary to *Mycogone perniciosa* (Mang), a prominent pathogenic disease regarding Serbia's cultivation of the *Agaricus bisporus* (Lange) Imbach mushrooms, Glamoålija *et al.*,[35] performed the study. The study's results showed that it has positioned antifungal action, consisting of a minimum of 15 to 20 µl/ml for fungicidal activity and 5 µl/ml for inhibitory effect. Although relative biological control systems aren't commonly utilised in mushroom farming, research into the antifungal capabilities of medicinal and aromatic plants has taken centre stage[36].

Hyssopus officinalis L. ssp., which is grown in two different locations close to Urbino (Italy, Marche), was the subject of an independent examination. It was determined that the essential oil's main ingredients were identified as isopinocamphone (3.2% and 29%), β-pinene (10.5% and 10.8%) and pinocamphone (18.5% and 34%). Nevertheless, they exhibited noticeable variations in the pinocamphone/isopinocamphone ratio, as well as in the camphor (0.3% and 5.3%) and linalool (0.2% and 7.9%) percentages[37]. The principal components of the two distinct essential oils isolated from *H. officinalis* L. ssp. officinalis were identified by analysis as isopinocamphone (3.2% and 29%), β-pinene (10.5% and 10.8%) and Pinocamphone (34.5% and 18.5%). The concentrations of linalool were 0.2% and 7.9%, while the concentrations of camphor were 0.3% and 5.3%. Additionally, the ratio of pinocamphone to isopinocamphone showed significant variation**.** However, essential oils showed antifungal action against thirteen different types of phytopathogenic fungus; plants grown at an altitude of one thousand metres yielded the best essential oil[38].

In their study, Motiejunaite and Kalediene[39] employed the agar-diffusion technique to assess the antifungal properties of essential oils made from several plants belonging to the Lamiaceae family. Most examples, comprising *H. officinalis* L., showed full suppression of *Aspergillus niger* development at dosages ranging from 0.5 to 1.5% v/v[39]. A separate study investigated the impacts of twelve essential oils extracted from aromatic plants indigenous to the Mediterranean region on four different species of fungi: *Penicillium italicum*, *Rhizopus stolonifer*, *Botrytis cinerea*, and *Phytophthora citrophthora*. The oils were

assessed at different concentrations. The study's findings indicate that hyssop oil exhibited a level of antifungal activity ranging from mild to moderate. However, when combined with these essential oils, hyssop oil could serve as a viable natural food preservative[40].

Hyssop oil, at a concentration of 0.4%, effectively stopped the growth of the plant-derived pathogenic fungus *Pyricularia oryzae* and *Pyrenophora avenae*. The growth of each of these fungi was entirely suppressed by the volatile chemicals emitted by agar plates containing 0.4% hyssop oil. Isolated constituents of hyssop oil, such as isopinocampheol, L-bornyl acetate, and pinocamphone, demonstrated significant inhibitory effects on the growth of *P. avenae* when used individually. Any mixture containing isopinocampheol completely inhibited the growth of fungus when multiple combinations of these ingredients were utilized. The various oil constituents had little effect on *P. oryzae* growth[41].

2.1.6 Mosquito-Larvicidal Activity

Mosquitoes are increasingly becoming a leading cause of mortality in developing and poor nations. Controlling mosquito vectors is a challenging task since it involves taking into account environmental factors and dealing with the development of resistance to pesticides. Consequently, researchers are aggressively pursuing novel plant-derived compounds to tackle illnesses spread by mosquitoes, such as malaria, dengue, Zika virus and chikungunya[42]. In research on the acute toxicity of binary combinations of *Culex quinquefasciatus* vectors, which are recognised carriers of lymphatic filariasis, *H. officinalis* essential oil demonstrated LC50 values over 90 µl/L. This discovery provides evidence that the essential oil of *H. officinalis* is both ecologically benign and economically efficient as a larvicide for mosquitoes[43].

Insect biting deterrent, larvicidal, antibacterial, and antifungal properties of two Lamiaceae plants' essential oils, *H. officinalis* L. as well as *Dracocephalum heterophyllum* Benth, were investigated[44]. In *H. officinalis* oil, β-pinene, cis-pinocamphone and pinocarvone were the main ingredients. We used larval bioassays, as proposed by Pridgeon *et al.*[45] to find out the efficacy of *D. heterophyllum* and *H. officinalis* essential oils in killing Aedes aegypti larvae. A controlled environment at a temperature of 27±2°C and a relative humidity of 60±10% was used to incubate the eggs and keep the larvae in a hatching cup overnight. The LC50 value of 37.3 ppm for *D. heterophyllum* essential oil was lower than the LC50 value of 58.7 ppm for *H. officinalis* essential oil, indicating that the former was more poisonous[46].

2.1.7 Antiulcer Activity

Hyssopus officinalis exhibits anti-ulcer properties. A significant inhibition rate of 92.67% was seen against urease produced from jack bean in the extract of *H. officinalis*, which includes high quantities of polyphenolic components like tannins, flavonoids, and phenolic acids. However, it only demonstrated a modest inhibition rate of 19.6% against α-chymotrypsin. This suggests that the extract could potentially be used as a treatment for ulcers[47]. In a separate experiment, albino rats were given a pre-treatment of *H. officinalis* ethanolic extract at doses of 100 mg/kg and 125 mg/kg body weight. This prior to treatment occurred one hour before the rats were given ethanol[48]. The experimental results demonstrated that the extract of *H. officinalis* had potent antioxidant and antiulcer characteristics. This was evidenced by a decrease in nitric oxide levels, a decrease in the generation of Reactive Oxygen Species (ROS), an improvement in the integrity of the stomach, and an improvement in mucus secretion. These findings encourage the traditional application of *H. officinalis* in folk remedies[49].

2.1.8 Miorelaxation Activity

Lu *et al.*,[50] conducted a study to investigate the myorelaxant effects of the essential oil of *H. officinalis* on guinea pig and rabbit intestinal muscle samples. To find out how the essential oil worked, scientists set out to conduct this investigation. The oil's myorelaxing effects were caused by an essential oil component called isopinocamphone. IC_{50} values of 48:3 and 70.4 µg/mL for BaCl2 indicated that it had a role in myocontraction in the ileum. On the other hand, isopinocamphone exhibited myorelaxation by inhibiting the effects of acetylcholine on the muscles of the ileum (IC_{50} values of 42.4 and 61.9 µg/mL). Isolated rabbit jejunum also showed a decrease in basal tone and an amplitude of spontaneous activity after injection with essential oil[51].

Limonene and β-pinene, which were present in *H. officinalis* oil, did not affect muscular contraction. We are unable to rule out the possibility that these

components' synergistic effect contributed, though. The study's authors postulated that hyssop oil's ability to interact with the plasma membrane and alter ion channels could cause muscles to relax. Chemical structure, lipophilic nature, and subcomponents, like the interplay between β-pinene and limonene, impact the cumulative effect of essential oil components[52].

2.1.9 Anticonvulsant Activity

The botanical species *H. officinalis* L. plays an important role in ancient medicine, particularly in the treatment of seizures. In a particular investigation, they evaluated the impact of *H. officinalis* hydroalcoholic extract on seizures caused by Pentylenetetrazol (PTZ) in rats. Using dosages of 25, 50, and 100 mg/kg, the anti-seizure efficacy of the extract was evaluated. The extract from *H. officinalis* raised the threshold for tonic seizures and reduced mortality caused by PTZ.[20] Extract administration treatment led to an outcome in a considerable improvement in memory and learning abilities in kindling rats. Additionally, it raised the brain's antioxidant capacity while reducing levels of brain MDA and NO. In addition, compared to the negative control group, the previously treated groups indicated an increase in GABA receptor gene expression. Because of its effects on the GABAergic system, the extract of *H. officinalis* may have antiepileptic capabilities. In addition to improving memory and learning capacities in rats, the extract of *H. officinalis* has a positive effect in preventing damage to neurons in the hippocampus[53].

Recent research on the effects of *H. officinalis* extract upon rat hippocampus area iNOS mRNA levels and pentylenetetrazole-induced convulsions suggests that hyssop extract, at a dosage of 100 mg/kg, may possess anticonvulsant characteristics. However, it's possible that these anticonvulsant effects are not due to iNOS gene activation[54].

GABAA receptor antagonists (IC_{50}: 35-64 mM) and tonic/clonic convulsions in mice (LD50: 175 mg/kg to >250 mg/kg i.p.) were observed as a consequence of the inhibition of 40-ethynyl-4-n-[2,3-3H2] propylbicycloorthobenzoate ([3H] EBOB) binding in mouse brain membranes by trans-3-pinanones, cis-3-pinanones, and *H. officinalis* oil. Another study found this. Both 2-hydroxy-cis-3-pinanone and 2,10-dehydro-3-pinanone, metabolites of cis-3-pinanone, inhibited [3H] EBOB binding and were less hazardous[55].

2.1.10 Anti-Alzheimer's Effects

Ellman's colorimetric technique was utilised to study the symptomatic management of Alzheimer's disease using 12 botanical extracts in hexane and methanol, including *H. officinalis*, a European medication treatment for central nervous system disorders. The study examined how plant extracts influenced AChE and BuChE inhibitors, the standard approach to treating early and moderate Alzheimer's disease. No substantial inhibitory effect was seen in *H. officinalis*. At 100 mg/ml-1, the Hexane-methanolic extracts inhibited AChE by 5.2 ± 8.2 and 29.6 ± 2.3%, and BuChE by 11.5 ± 0.5 and 23.2 ± 2.0%, respectively[56].

2.1.11 Anti-Hemolytic Activity

Hyssopus officinalis extracts exhibited remarkable antihemolytic action against H_2O_2-induced hemolysis in rat erythrocytes, with the flowers exhibiting a concentration of 48.51 ± 2.27 µg/ml, the leaves exhibiting a concentration of 19.47 ± 0.73 µg/ml, and the stems exhibiting an IC_{50} value of 63.1 ± 2.65 µg/ml[57]. The extracts were evaluated for their antihemolytic activity in accordance with the methodology outlined by Nabavi *et al.*[58]. After conducting tests to determine the effects of extracts, It was shown that they did not cause any harmful effects on red blood cells. Compared to other extracts, leaf extract had superior antihemolytic efficacy. There is a high prevalence of olyphenolic chemicals, such as flavonoids, in food products that are produced from plant sources. These substances are shown to have strong antihemolytic effects[59].

2.1.12 Anti-Diabetic Activity

In both living organisms and laboratory conditions, the *H. officinalis* herb studies have demonstrated its anti-diabetic capabilities. In both *in vitro* and *in vivo* applications, it has been demonstrated that the *H. officinalis* plant holds anti-diabetic qualities[60]. A 100 mg/kg and 300 mg/kg body weight dose of an aqueous methanolic extract of dried *H. officinalis* leaves were used by the researcher in order to determine the activity. The outcome demonstrated that the extract had an α-glucosidase inhibitory action in mice, as determined by Miyazaki *et al.*[60], according to Matsuura *et al.*[61]. In addition, another research suggests that it has the potential to reduce blood sugar levels; nevertheless, it should not be administered to people who have

liver diseases[62]. There is yet another discovery that demonstrates the anti-diabetic action of plant extract. Examination of physicochemical and phytochemical properties, quantification using high-performance thin-layer chromatography, and *in vitro* testing of antidiabetic and antioxidant activity were carried out. The starch-iodine test was used to make some minor adjustments to the alpha-amylase inhibition assay, which served as the basis for the antidiabetic assay that was being carried out. The *in vitro* DPPH radical scavenging experiment yielded an IC_{50} value of 0.50 µg/ml, whereas the *in vitro* anti-diabetic assay yielded an IC_{50} value of 0.8366 mg/ml. One way to find out if *H. officinalis* extract can slow down diabetes progression is to see if it can decrease the biochemical activity of the alpha-amylase enzyme[63].

2.1.13 Anti-HIV Activity

The methanolic extracts obtained from dried leaves of *H. officinalis*, after undergoing chloroform, ether and chloroform-ethanol extractions, exhibited potent anti-HIV activity. This was established by evaluating the effect on syncytia formation, p17 and p24 antigen expression, and HIV reverse transcriptase inhibition. The observed activity is likely attributed to caffeic acid. These findings suggest that *H. officinalis* extracts could be beneficial in the management of those diagnosed with Acquired Immunodeficiency Syndrome (AIDS)[64]. Gollapudi *et al.*[65] conducted their research into the efficacy of a particular polysaccharide (MAR-10) obtained from the watery extract of *H. officinalis* against the SF strain of HIV-1. To conduct the study, the polysaccharide was tested on two cell lines: the HUT78 T cell line and beginning cultures of peripheral blood mononuclear cells. An efficient suppression of HIV-1 replication was demonstrated by the researchers to be dependent on the concentration of the MAR-10 chemical. Importantly, the MAR-10 compound did not cause significant harm to cells or have any negative impact on the activities of lymphocytes or the counts of CD4+ and CD8+ T cells.

2.1.14 Anti-Asthmatic Activity

The plant has been used as a seasoning in Central Europe. Hyssop, an herb known for its cleansing properties, alleviates catarrh and decreases the production of mucus. It also helps regulate blood pressure, whether it is high or low, and can clear the chest and promote a sense of calmness in the nerves. This plant is beneficial for managing patients with fever as it induces sweating[66].

Extensive research has shown that the Uygur plant *H. offcinalis* L. can influence the concentration of particular cytokines in asthmatic mice, such as IL-4, IL-6, IL-17, and IFN- γ. Through observing morphological changes and detecting MMP-9 and TIMP-1 expressions, the researchers hope to deduce how the Uygur plant *H. officinalis* L. contributes to airway remodelling. The airway remodelling group showed higher levels of MMP-9 and TIMP-1. Nonetheless, there was a decrease in the MMP-9 to TIMP-1 ratio. However, dexamethasone and *H. offcinalis* L. therapy resulted in decreased levels of MMP-9 and TIMP-1. Pathological changes like mucus production, collagen deposition, and smooth muscle proliferation improved alongside this decrease. *H. offcinalis* L., a herb native to Uygur, may inhibit airway remodelling by restoring a healthy ratio of MMP-9 to TIMP-1[67].

Presently, there is no existing information on the utilization of *Hyssopus cuspidatus* Boriss' Volatile Oil (HVO) for the management of respiratory conditions. *H. cuspidatus* Boriss is a traditional Uyghur remedy employed for treating respiratory ailments, including colds, asthma, Bronchitis and pneumonia[68].

By conducting network pharmaceutical analysis and validating the results through experiments conducted both *in vivo* and *in vitro*, it has been conclusively demonstrated that HVO effectively reduces airway inflammation in mice with OVA-induced asthma. By maintaining the integrity of the airway barrier and inhibiting the PI3K/Akt/JNK/P38 signalling cascade, HVO has a healing effect. The result suggests a unique idea for both the discovery of targets for therapy for allergic asthma and the development of new drugs[69].

2.1.15 Antispasmodic Activity

Hyssopus officinalis L. is utilised as a carminative and antispasmodic stomachic in the ancient medical practices of Iran and India[70]. Recent investigations indicate that the essential oil extracted from the above-ground sections of the plant exhibits antimicrobial properties in laboratory conditions[71]. This activity is mostly attributed to linalool, a component of the oil's chemical constituents. Some essential oils, such as those

derived from certain Lamiaceae plants (*Mentha piperita* L., *Salvia officinalis* L., and *Rosmarinus officinalis* L.), have a spasmolytic effect. This is why they are used to alleviate gastrointestinal spasms[72].

Essential oil of *H. officinalis* L. var. decumbens was shown by Mazzanti *et al.*[73] to alleviate muscular spasms. In isolated guinea pig ileum, the essential oil and its principal components—limonene, linalool, and 1,8-cineole—effectively inhibited the contractions induced by acetylcholine and $BaCl_2$. The essential oil, limonene, linalool, and 1,8-cineole each had IC_{50} values of 37, 60, 10, and 51 µg/ml, respectively. Myorelaxant activity is a desirable quality in antispasmodic medicines, and hyssop oil may have it.

2.1.16 Insecticidal Activity

Using third-instar Egyptian cottonworm (*Spodoptera littoralis*) larvae as test subjects, an investigator examined the insecticidal effects of eight medicinal plants, one of which was *H. officinalis*. Significant effects on the growth indices were seen in the larvae when exposed to the 10% (w/v) methanolic extract of *H. officinalis*, suggesting a certain degree of toxicity. With a 95% confidence interval spanning 1.66 to 1.82, the LC50 value was found to be 1.78[74].

2.1.17 Anti-Leishmaniasis Activity

A study has indicated that the use of *H. officinalis* extracts in the form of ointment for a period of 20 days, every day twice, significantly decreased the size of skin ulcers and the presence of Leishmania parasites in the spleen of specific BALB/C mice, when compared to the use of glucantime[75].

Several natural substances have demonstrated efficacy in inhibiting bone loss and enhancing bone density. The rising interest in herbal medicines, especially medicinal plants for conditions such as osteoporosis and rheumatoid arthritis, indicates an escalating need for plant-based therapeutics[76,77].

Hyssopus officinalis has a wide range of pharmacological actions, including antioxidant, anti-inflammatory, neuroprotective, antibacterial, and metabolic effects, due to its varied phytochemical makeup. The plant's importance is shown by the finding of various volatile chemicals and flavonoids, which support its usage in traditional and alternative medicine. The rising desire for natural alternatives in modern therapies also shows its potential for more pharmacological uses. More research is needed to explore its clinical efficacy, safety profile, and mechanisms of action, despite considerable research validating many of its bioactivities.

3. Conclusion

The *Hyssopus* genus has a large distribution in the Mongolian, East Mediterranean, and Central Asian regions. Among its six primary species, *H. officinalis* is most known for its medicinal uses; another is its widespread use as a flavouring and condiment in the food sector. There are a total of six species: H. macranthus, *H. seravschanicus*, *H. cuspidatus*, *H. latilabiatus* and *H. ambiguus*. Key components found in its essential oils include pinocamphone, β-pinene, other terpenoids and isopinocamphone. In addition to the glucosides of flavonoids like luteolin, quercetin, and apigenin, and phenolic compounds like protocatechuic acid, ferulic, chlorogenic acid, p-hydroxy-benzoic acid, and caffeic acid, the *Hyssopus* genus also contains various secondary metabolites. *Hyssopus* essential oils are often obtained by conventional techniques, such as hydrodistillation. The genus *Hyssopus* contains vital constituents that have diverse functions. In addition to their potent antibacterial properties, the essential oil components have curative effects against fungal infections, spasmodic conditions, coughs, and lack of appetite. Other responses observed in living organisms include sedative effects, relaxing of the plasma membrane, and cytotoxic activity. The biological activities and scent of essential oil indicate its potential application as an antioxidant dietary additive and in the development of medicinal medications. It has a range of pharmacological and biological effects, including antifungal, antioxidant, anticonvulsant, antibacterial, anti-ulcer, antihemolytic, and antispasmodic actions. *H. officinalis* L. is a highly valuable medicinal plant with numerous pharmacological compounds that have substantial therapeutic potential for treating various ailments, including ulcers, microbial infections, epilepsy, and spasms. Traditional uses of the herb *H. officinalis* L. in medicine date back to many different traditions, including *Ayurveda* and *Unani*, and this study compiles and summarises the most relevant

research on the subject. Additional research into this plant's phytochemistry, pharmacology, and traditional applications could lead to the development of novel herbal medicines; this review covers all of these subjects.

Acknowledgment:

The author would like to express sincere gratitude to all those who have supported and contributed to the successful completion of this review article. Special thanks are extended to mentors, colleagues, and institutions whose guidance and encouragement were invaluable throughout the work.

Author Contribution:

All authors contributed to the conception and design of the review. Ms. Sweta Besh performed the literature survey, critically analyzed the relevant studies, and drafted the manuscript. All authors have read and approved the final version of the manuscript.

4. References

1. Fathiazad F, Hamedeyazdan S. A review on *H. officinalis* L.: Composition and biological activities. Afr J Pharmacy Pharmacol. 2011; 5(17):1959-1966. https://doi.org/10.5897/AJPP11.527
2. Dragland S, Senoo H, Wake K, Holte K, Blomhoff R. Several culinary and medicinal herbs are important sources of dietary antioxidants. The Journal of nutrition. 2003 May 1;133(5):1286-90. https://doi.org/10.1093/jn/133.5.1286 PMid:12730411
3. Fathiazad F, Mazandarani M, Hamedeyazdan S. Phytochemical analysis and antioxidant activity of *H. officinalis* L. from Iran. Adv Pharm Bull. 2011; 1(2):63. https://doi.org/10.5681%2Fapb.2011.009
4. Jankovský M, Landa T. *Genus Hyssopus* L. - Recent knowledge. Hort Sci (Prague). 2002; 29(3):119-123. https://doi.org/10.17221/4474-HORTSCI
5. Dzhumaev KH. Essential oil from leaves of *Hyssopus seravschanicus* from Southern Uzbekistan. Chim Prir Soedin. 1990; 1:123-125. https://doi.org/10.1007/BF00605221
6. Lugasi A, Hovari J, Hagymasi K, Jakoczi I, Blazovics A. Antioxidant properties of a mixture of Lamiaceae plants intended to use as a food additive. Acta Aliment. 2006; 35(1):85-97. https://doi.org/10.1556/aalim.35.2006.1.10
7. Mijani S, Nasrabadi SE, Zarghani H, Abadi MG. Seed germination and early growth responses of hyssop, sweet basil and oregano to temperature levels. Not Sci Biol. 2013; 5(4):462-467. https://doi.org/10.15835/nsb549164
8. Maslova E, Gulya N, Perelugina T, Semykina V, Kalashnikova E. Introduction of *H. officinalis* L. into *in vitro* culture to optimize the conditions for obtaining callus tissues and microclonal propagation as a promising method of innovative agrobiotechnologies. BIO Web of Conferences (Vol. 30); 2021. p. 05006. https://doi.org/10.1051/bioconf/20213005006
9. Kizil S, Haşimi N, Tolan V, Kilinc E, Karataş H. Chemical composition, antimicrobial and antioxidant activities of hyssop (*H. officinalis* L.) essential oil. Notulae Botanicae Horti Agrobotanici Cluj-Napoca. 2010; 38(3):99-103. https://doi.org/10.15835/nbha3834788
10. Murakami Y, Omoto T, Asai I, Shimomura K, Yoshihira K, Ishimaru K. Rosmarinic acid and related phenolics in transformed root cultures of *H. officinalis.* Plant Cell Tissue Organ Cult. 1998; 53:75-78. https://doi.org/10.1023/A:1006007707722
11. Garg SN, Naqvi AA, Singh A, Ram G, Kumar S. Composition of essential oil from an annual crop of *H. officinalis* grown in Indian plains. Flavour Fragr. 1999; 14(3):170-172. https://doi.org/10.1002/(SICI)1099-1026(199905/06)14:3<170::AID-FFJ808>3.0.CO;2-Q
12. Vlase L, Benedec D, Hanganu D, Damian G, Csillag I, Sevastre B, *et al.,* Evaluation of antioxidant and antimicrobial activities and phenolic profile for *H. officinalis*, *Ocimum basilicum* and *Teucrium chamaedrys*. Molecules. 2014; 19(5):5490-5507. https://doi.org/10.3390/molecules19055490 PMid:24786688 PMCid:PMC6270679
13. Benedec D, Parvu M, Popescu H, Tiperciuc B. *In vitro* effect of *H. officinalis* extract on pathogenic fungi on ornamental plants. Farmacia-Bucuresti. 2003; 51(4):67-72.
14. Soleimani H, Barzegar M, Sahari MA, Naghdi Badi H. An investigation on the antioxidant activities of *H. officinalis* L. and *Echinacea purpurea* L. plant extracts in oil model system. J Med Plant. 2011; 10(37):61-72. http://dorl.net/dor/20.1001.1.2717204.2011.10.37.8.9
15. Myadelets MA, Domrachev DV, Cheremushkina VA. A study of the chemical composition of essential oils of some species from the *Lamiaceae* L. family cultivated in the Western Siberian Region. Russ J Bioorganic Chem. 2013; 39:733-738. https://doi.org/10.1134/S1068162013070091
16. Venditti A, Bianco A, Frezza C, Conti F, Bini LM, Giuliani C, *et al.,* Essential oil composition, polar compounds, glandular trichomes and biological activity of *H. officinalis* subsp. aristatus (Godr.) Nyman from central Italy. Indust Crop Prod. 2015; 77:353-363. https://doi.org/10.1016/j.indcrop.2015.09.002

17. Benea A, Ciobanu C, Ciobanu N, Pompuş I, Cojocaru-Toma M. Polyphenolic content and antioxidant activity of *H. officinalis* L. from the Republic of Moldova. Moldovan Med J. 2022; 65(2):41-46. https://doi.org/10.52418/moldovan-med-j.65-2.22.06
18. Džamić AM, Soković MD, Novaković M, Jadranin M, Ristić MS, Tešević V, *et al.,* Composition, antifungal and antioxidant properties of *H. officinalis* L. subsp. pilifer (Pant.) Murb. essential oil and deodorized extracts. Indust Crops Prod. 2013; 51:401-407. https://doi.org/10.1016/j.indcrop.2013.09.038
19. Darzi MT, Sadeghi Nekoo B, Haj Seyed Hadi MR. Effects of organic fertilizers on essential oil composition and yield in sustainable cultivation of Hyssop (*H. officinalis* L.). J Agroecol. 2022; 14(1):53-68. https://doi.org/10.22067/agry.2021.20242.0
20. Tahir M, Khushtar M, Fahad M, Rahman MA. Phytochemistry and pharmacological profile of traditionally used medicinal plant Hyssop (*H. officinalis* L.). J Appl Pharm Sci. 2018; 8(7):132-140. https://doi.org/10.7324/JAPS.2018.8721
21. Özer H, Sökmen M, Güllüce M, Adigüzel A, Kilic H, Şahin F, *et al. In vitro* antimicrobial and antioxidant activities of the essential oils and methanol extracts of *H. officinalis* L. ssp. angustifolius. Ital J Food Sci. 2006; 18(1).
22. Mazzanti G, Battinelli L, Salvatore G. Antimicrobial properties of the linalol-rich essential oil of *H. officinalis* L. var decumbens (Lamiaceae). Flav Frag J. 1998; 13(5):289-294. https://doi.org/10.1002/(SICI)1099-1026(1998090)13:5<289::AID-FFJ750>3.0.CO;2-A
23. Marino M, Bersani C, Comi G. Impedance measurements to study the antimicrobial activity of essential oils from Lamiaceae and Compositae. Int J Food Microbiol. 2001; 67(3):187-195. https://doi.org/10.1016/S0168-1605(01)00447-0 PMid:11518428
24. Oalđe M, Kolarević S, Živković J, Aradski AA, Marić JJ, Kolarević MK, *et al.,* A comprehensive assessment of the chemical composition, antioxidant, genoprotective and antigenotoxic activities of Lamiaceae species using different experimental models *in vitro*. Food Funct. 2021; 12(7):3233-3245. https://doi.org/10.1039/D1FO00447F PMid:33877247
25. de Groot PM, Wu CC, Carter BW, Munden RF. The epidemiology of lung cancer. Translational lung cancer research. 2018 Jun;7(3):220. 7(3):220. https://doi.org/10.21037%2Ftlcr.2018.05.06 PMid:30050761 PMCid:PMC6037963
26. Kumar V, Kaur N, Kaur A, Wadhwa P. Phytochemistry and pharmacology of Indian traditional plant Hyssop (*H. officinalis* L.): A review. Nat Prod J. 2023; 13(4):11-41. https://doi.org/10.2174/2210315512666220811153919
27. Guevara E, Paulina M. *H. officinalis* L. subsp. aristatus (Godr.) Nyman (Italy) and *Ocimum campechianum* Willd. (Ecuador): Botanical identification, chemical and biological characterization; 2020.
28. Mićović T, Topalović D, Živković L, Spremo-Potparević B, Jakovljević V, Matić S *et al.,* Antioxidant, antigenotoxic and cytotoxic activity of essential oils and methanol extracts of *H. officinalis* L. subsp. aristatus (Godr.) Nyman (Lamiaceae). Plants. 2021; 10(4):711. https://doi.org/10.3390/plants10040711 PMid:33916934 PMCid:PMC8067569
29. Guerrini A, Sacchetti G, Echeverria Guevara MP, Paganetto G, Grandini A, Maresca I *et al.,* Wild Italian *H. officinalis* subsp. aristatus (Godr.) Nyman: from morphological and phytochemical evidences to biological activities. Plants. 2021; 10(4):631. https://doi.org/10.3390/plants10040631 PMid:33810509 PMCid:PMC8065824
30. Sharifi-Rad J, Quispe C, Kumar M, Akram M, Amin M, Iqbal M, Koirala *et al., Hyssopus* essential oil: An update of its phytochemistry, biological activities, and safety profile. Oxidat Med Cell Long. 2022; 2022(1):8442734 PMid:35069979 PMCid:PMC8776447
31. Hanganu D, Pârvu A, Mărculescu A, Oniga I, Tiperciuc B, Benedec D. *H. officinalis* L. (fam. Lamiaceae) a potential plant food supplements with anti-inflammatory effect. https://doi.org/10.1155/2022/8442734 PMid:35069979 PMCid:PMC8776447
32. Ghasempour M, Hosseini M, Soltani-Zangbar MS, Motavalli R, Aghebati-Maleki L, Dolati S, Mehdizadeh A *et al.,* The impact of Hyssop (*H. officinalis*) extract on activation of endosomal toll like receptors and their downstream signaling pathways. BMC Res Notes. 2022; 15(1):366. https://doi.org/10.1186/s13104-022-06253-3 PMid:36503515 PMCid:PMC9742021
33. Ma X, Ma X, Ma Z, Wang J, Sun Z, Yu W, *et al.* Effect of *H. officinalis* L. on inhibiting airway inflammation and immune regulation in a chronic asthmatic mouse model. Exp Ther Med. 2014; 8(5):1371-1374. https://doi.org/10.3892/etm.2014.1978 PMid:25289025 PMCid:PMC4186396
34. Proškovcová M, Čonková E, Váczi P, Harčárová M, Malinovská Z. Antibiofilm activity of selected plant essential oils from the Lamiaceae family against Candida albicans clinical isolates. Annals Agri Environ Med. 2021; 28(2):260-266. https://doi.org/10.26444/aaem/135892 PMid:34184508
35. Glamočlija JM, Soković MD, Vukojević JB, Milenković IM, Brkić DD, Van GL. Antifungal activity of essential oil *H. officinalis* L. against micopathogen *Mycogone perniciosa* (Mang). Zbornik Matice srpske za prirodne nauke. 2005; (109):123-128. https://doi.org/10.2298/ZMSPN0519123G
36. Ghfir BL, Fonvieille JL, Koulali Y, Ecalle R, Dargent R. Effect of essential oil of *H. officinalis* on the lipid composition of *Aspergillus fumigatus*. Mycopathologia. 1994; 126:163-167. https://doi.org/10.1007/BF01103770 PMid:7935731
37. Fraternale D, Ricci D, Epifano F, Curini M. Composition and antifungal activity of two essential oils of hyssop (*H.*

officinalis L.). J Essent Oil Res. 2004; 16(6):617-622. https://doi.org/10.1080/10412905.2004.9698810
38. Raila A, Lugauskas A, Kemzuraite A, Zvicevicius E, Ragazinskiene O, Railiene M. Different drying technologies and alternation of mycobiots in the raw material of *H. officinalis* L. Ann Agric Environ Med. 2009; 16:93-101.
39. Motiejunaite O, Kalediene L. Antimicrobial activity of Lamiaceae plant essential oils on *Aspergillus niger* growth. Biol Sci. 2003; 51:237-242.
40. Camele I, De Feo V, Altieri L, Mancini E, De Martino L, Luigi Rana G. An attempt of postharvest orange fruit rot control using essential oils from mediterranean plants. J Med Food. 2010; 13:1515-1523. https://doi.org/10.1089/jmf.2009.0285 PMid:20874226
41. Letessier MP, Svoboda KP, Walters DR. Antifungal activity of the essential oil of hyssop (*H. officinalis*). J Phytopathol. 2001; 149(11-12):673-678. https://doi.org/10.1046/j.1439-0434.2001.00692.x
42. Dahmana H, Mediannikov O. Mosquito-borne diseases emergence/resurgence and how to effectively control it biologically. Pathogens. 2020; 9(4):310. https://doi.org/10.3390/pathogens9040310 PMid:32340230 PMCid:PMC7238209
43. Benelli G, Pavela R, Canale A, Cianfaglione K, Ciaschetti G, Conti F *et al.,* Acute larvicidal toxicity of five essential oils (*Pinus nigra*, *H. officinalis, Satureja montana*, *Aloysia citrodora* and *Pelargonium graveolens*) against the filariasis vector *Culex quinquefasciatus*: Synergistic and antagonistic effects. Parasitol Int. 2017; 66(2):166-171. https://doi.org/10.1016/j.parint.2017.01.012 PMid:28110082
44. Stappen I, Wanner J, Tabanca N, Wedge DE, Ali A, Kaul VK, Lal B *et al.,* Chemical composition and biological activity of essential oils of *Dracocephalum heterophyllum* and *H. officinalis* from Western Himalaya. Nat Prod Comm. 2015; 10(1):1934578X1501000131.
45. Pridgeon JW, Becnel JJ, Clark GG, Linthicum KJ. A high-throughput screening method to identify potential pesticides for mosquito control. J Med Entomol. 2009; 46(2):335-341. PMid:19351085
46. Abbott WS. A method of computing the effectiveness of an insecticide. J Econ Entomol. 1925; 18(2):265-267. https://doi.org/10.3109/13880209.2012.674950 PMid:22889050
47. Saini ASA, Sharma RSR. To explore the ulceroprotective and antioxidant potential of *H. officinalis* in ethanol-induced gastric ulcers in rats. J Pharm Res Int. 2012; 2(3):197-214. https://doi.org/10.9734/BJPR/2012/1930
48. Paun G, Litescu SC, Neagu E, Tache A, Lucian Radu G. Evaluation of Geranium spp., *Helleborus* spp. and *Hyssopus* spp. polyphenolic extracts inhibitory activity against urease and α-chymotrypsin. J Enz Inhib Med Chem. 2014; 29(1):28-34. https://doi.org/10.3109/14756366.2012.749399 PMid:23317419
49. Saini A, Sharma R. To Explore the ulceroprotective and antioxidant potential of *H. officinalis* in ethanol-induced gastric ulcers in rats. Brit J Pharm Res. 2012; 2(3):197-214. https://doi.org/10.9734/BJPR/2012/1930
50. Lu M, Battinelli L, Daniele C, Melchioni C, Salvatore G, Mazzanti G. Muscle relaxing activity of *H. officinalis* essential oil on isolated intestinal preparations. Plant Med. 2002; 68(03):213-216. https://doi.org/10.1055/s-2002-23139 PMid:11914956
51. Aihaiti K, Li J, Yaermaimaiti S, Liu L, Xin X, Aisa HA. Non-volatile compounds of *Hyssopus cuspidatus* Boriss and their antioxidant and antimicrobial activities. Food Chem. 2022; 374:131638. https://doi.org/10.1016/j.foodchem.2021.131638 PMid:34839965
52. Atazhanova G, Ishmuratova M, Levaya Y, Smagulov M, Lakomkina Y. The Genus *Hyssopus*: Traditional use, phytochemicals and pharmacological properties. Plants. 2024; 13(12):1683. https://doi.org/10.3390/plants13121683 PMid:38931115 PMCid:PMC11207324
53. Fatahinezhad N, Lorigooini Z, Arabi M, Rabiei Z, Sheykhshabani SK, Rafieian-Kopaei M. Effects of *H. officinalis* hydroalcoholic extract on pentylenetetrazol-induced convulsive seizures in rat. Neurochem Res. 2022; 47(12):3792-3804. https://doi.org/10.1007/s11064-022-03759-x PMid:36287300
54. Gholami M, Jafari F, Baradaran Z, Amri J, Azhdari-Zarmehri H, Sadegh M. Effects of aqueous extract of *H. officinalis* on seizures induced by pentylenetetrazole and hippocampus mRNA level of iNOS in rats. Avicenna J Phytomed. 2020; 10(3):213.
55. Höld KM, Sirisoma NS, Sparks SE, Casida JE. Metabolism and mode of action of cis-and trans-3-pinanones (the active ingredients of hyssop oil). Xenobiotica. 2002; 32(4):251-265. https://doi.org/10.1080/00498250110095745 PMid:12028660
56. Wszelaki N, Kuciun A, Kiss A. Screening of traditional European herbal medicines for acetylcholinesterase and butyrylcholinesterase inhibitory activity. Acta Pharm. 2010; 60(1):119-128. https://doi.org/10.2478/v10007-010-0006-y PMid:20228046
57. Alinezhad H, Azimi R, Zare M, Ebrahimzadeh MA, Eslami S, Nabavi SF, Nabavi SM. Antioxidant and antihemolytic activities of ethanolic extract of flowers, leaves, and stems of *H. officinalis* L. Var. angustifolius. Int J Food Prop. 2013; 16(5):1169-1178. https://doi.org/10.1080/10942912.2011.578319
58. Nabavi SF, Ebrahimzadeh MA, Nabavi SM, Eslami B. Antioxidant activity of flower, stem and leaf extracts of Ferula gummosa Boiss. Grasas y aceites. 2010; 61(3):244-50. https://doi.org/10.3989/gya.110809
59. Ebrahimzadeh MA, Nabavi SF, Nabavi SM, Eslami B. Antihemolytic and antioxidant activities of *Allium paradoxum*. Cent Eur J Biol. 2010; 5:338-345. https://doi.org/10.2478/s11535-010-0013-5

60. Miyazaki H, Matsuura H, Yanagiya C, Mizutani J, Tsuji M, Ishihara C. Inhibitory effects of Hyssop (*Hyssopus* of ficinalis) extracts on intestinal α-glncosidase activity and postprandial hyperglycemia. J Nutrit Science Vitaminol. 2003; 49(5):346-349. https://doi.org/10.3177/jnsv.49.346 PMid:14703310
61. Matsuura H, Miyazaki H, Asakawa C, Amano M, Yoshihara T, Mizutani J. Isolation of α-glusosidase inhibitors from hyssop (*H. officinalis*). Phytochem. 2004; 65(1):91-97. https://doi.org/10.1016/j.phytochem.2003.10.009 PMid:14697274
62. Akram M. Diabetes mellitus type II: Treatment strategies and options: a review. J Diabetes Metab. 2013; 4(9):304. https://doi.org/10.4172/2155-6156.1000304
63. Srivastava A, Awasthi K, Kumar B, Misra A, Srivastava S. Pharmacognostic and pharmacological evaluation of *H. officinalis* L. (Lamiaceae) collected from Kashmir Himalayas, India. Pharmacog J. 2018; 10(4). http://dx.doi.org/10.5530/pj.2018.4.114
64. Kreis W, Kaplan MH, Freeman J, Sun DK, Sarin PS. Inhibition of HIV replication by *Hyssop officinalis* extracts. Antiviral Res. 1990; 14(6):323-337. https://doi.org/10.1016/0166-3542(90)90051-8 PMid:1708226
65. Gollapudi S, Sharma HA, Aggarwal S, Byers LD, Ensley HE, Gupta S. Isolation of a previously unidentified polysaccharide (MAR-10) from *Hyssop officinalis* that exhibits strong activity against human immunodeficiency virus type 1. Biochem Biophy Res Commun. 1995; 210(1):145-151. https://doi.org/10.1006/bbrc.1995.1639 PMid:7741735
66. Akbar S, Akbar S. *H. officinalis* L. (Lamiaceae) (Syns.: H. altissimus Mill.; H. angustifolius M. Bieb.; H. hirsutus Hill; H. torresii Sennen; H. vulgaris Bubani). Handbook of 200 medicinal plants: A comprehensive review of their traditional medical uses and scientific justifications; 2020. p. 1029-1034. https://doi.org/10.1007/978-3-030-16807-0_110
67. Ma X, Ma X, Ma Z, Sun Z, Yu W, Wang J The effects of uygur herb *Hyssopus officinalis* L. on the process of airway remodeling in asthmatic mice. Evid Based Complement Alternat Med. 2014; 2014(1):710870. https://doi.org/10.1155/2014/710870 PMid:25383084 PMCid:PMC4212596
68. Xie C, Gul A, Yu H, Huang X, Deng L, Pan Y *et al.,* Integrated systems pharmacology and transcriptomics to dissect the mechanisms of Loki Zupa decoction in the treatment of murine allergic asthma. J Ethnopharmacol. 2022; 294:115351. https://doi.org/10.1016/j.jep.2022.115351 PMid:35533913
69. Zhang YL, Peng HM, Li JJ, Chen J, Zhang MR, Wang X *et al.,* The volatile oil of *Hyssopus cuspidatus* Boriss (HVO) ameliorates OVA-induced allergic asthma via inhibiting PI3K/Akt/JNK/P38 signaling pathway and maintaining airway barrier integrity. J Ethnopharmacol. 2024; 334:118568. https://doi.org/10.1016/j.jep.2024.118568 PMid:38996949
70. Tahir M, Rahman MA, Khushtar M. Gastroprotective effect of *H. officinalis* L. leaves via reduction of oxidative stress in indomethacin-induced gastric ulcer in experimental rats. Drug Chem Toxicol. 2022; 45(1):291-300. https://doi.org/10.1080/01480545.2019.1685537 PMid:31694395
71. Cabo J, Crespo ME, Jimenez J, Zarzuelo A. The spasmolytic activity of various aromatic plants from the province of Granada. I. The activity of the major components of their essential oils.1986.
72. Rees WD, Evans BK, Rhodes J. Treating irritable bowel syndrome with peppermint oil. Brit Med J. 1979; 2(6194):835. https://doi.org/10.1136%2Fbmj.2.6194.835 PMid:389344 PMCid:PMC1596628
73. Mazzanti G, Lu M, Salvatore G. Spasmolytic action of the essential oil from *H. officinalis* L. var. decumbens and its major components. Phytother Res. 1998; 12(S1):S92-S94. https://doi.org/10.1002/(SICI)1099-1573(1998)12:1+%3CS92::AID-PTR261%3E3.0.CO;2-9
74. Pavela R. Insecticidal activity of certain medicinal plants. Fitoterapia. 2004; 75(7-8):745-749. https://doi.org/10.1016/j.fitote.2004.08.005 PMid:15567255
75. Akhlaghi L, Yeganeh M, Maleki F, Golestani M, Noori M, Ghelman M *et al.,* Antileishmanial activity of *Hyssopus officinalis*, *Tussilage farfara*, *Carum copticum* extracts in mice infected with Leishmania major. Int J Herb Med. 2014; 2(2):142-145.
76. Mahant M, Besh SB, Kanojiya D, Sajan C, Rajput H, Maheshwari RA. Herbal remedies for osteoporosis. J Nat Remed. 2023: 1373-1383. https://doi.org/10.18311/jnr/2023/34056
77. Besh SB, Mahant M, Kanojiya D, Patil S, Maheshwari RA. Plants used in the treatment of rheumatoid arthritis. J Nat Remed. 2023; 23(4):1269-1286. https://doi.org/10.18311/jnr/2023/34055