

Star Anise: A Purported Antiviral Herb with Numerous Associated Health Benefits

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Abstract

Star anise belongs to the Schisandraceae family. About 166 varieties exist, and 42 species are grown in the tropics of East Asia and Southeast Asia. Many beneficial effects of star anise have been established, including ameliorating the symptoms of rheumatism and joint pain, warding off insects (insect repellent), lessening cold and flu symptoms, and potentially acting as an antioxidant against reactive oxygen species (ROS), reducing oxidative stress, inhibiting apoptosis, preventing DNA damage, and expressing a DPPHH radical scavenging effect.

Following the onset of the COVID-19 pandemic, star anise has been used as a natural immune-booster and antiviral in teas and aerosol sprays. (Star anise oil is used for fragrance in soap, cosmetics, and perfume manufacturing.) However, more in-depth and extensive research needs to be conducted, investigating the efficacy of star anise's purported beneficial properties. This review discusses the distinctions between the varieties of anise, indications and beneficial effects, modes of application and administration, and contraindications and precautions.

Keywords: Antifungal; Antiviral; Carcinopreventive; Herbal Remedy; Herpes Simplex; Immune Response; Prophylaxis

Abbreviations

ATWE: Ambient Temperature Water Extract; BWE: Boiling Water Extract; CNS: Central Nervous System; MFC: Minimum Fungicidal Concentration; NDEA: Nitrosodiethylamine; OSP: Oseltamivir Phosphate; ROS: Reactive Oxygen Species; SAWRE: Star Anise Waste Residue Extract

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Introduction

Star anise (*Illicium verum*) is an evergreen tree that bears star-shaped fruits. It is distributed widely throughout Southwestern Asia. Apart from being an important spice, it is well-known for its potent antiviral effects. It is the source of shikimic acid, the substrate for the chemical synthesis of the drug oseltamivir phosphate (OSP), known as Tamiflu [1]. In addition to being an effective antiviral, it is recognized as having antioxidant, antimicrobial, antifungal, anthelmintic, insecticidal, antinociceptive, gastroprotective, sedative, estrogenic, expectorant, secretolytic, and spasmolytic properties [1].

The spice was introduced in Europe by English navigator Sir Thomas Cavendish in 1578 CE. The plant is native to South China and Vietnam. The history of star anise dates back to about 100 BCE. It is used in soups, stews, broths, and baking. The taste is licoricey and is an integral part of Chinese and Malay cuisines; also, it is a significant constituent of pho—a Vietnamese noodle soup. Star anise forms an essential part of the quintessential garam masala of Indian households. It is also used as a scent in cleansers, beauty care products, and toothpaste [2,3].

Anise varieties

Star anise belongs to the Schisandraceae family. About 166 varieties exist, and 42 species are grown in East and Southeast Asia [4]. Species include *Illicium Mexicana* (Mexican anise), *I. anisatum*, *I. floridanum*, *I. parviflorum*, and *I. lance datum* [5]. The name *Illicium* comes from the Latin word “alluring,” meaning fragrance. It is grown in various topographical regions, such as China, Japan, Laos, the Philippines, Indonesia, Vietnam, and Jamaica. *Illicium verum* is a well-known source of carbohydrates, vitamin A, ascorbic acid, and a rich source of minerals (sodium, calcium, zinc, magnesium, potassium, iron, and copper). The commercial production of star anise is restricted to China and Vietnam. The optimal conditions for growth are woodlands with sunny edges with variegated shade, soil-rich humus, and a neutral pH. Even though star anise can grow under diverse climatic conditions, it should be protected from low temperature, supplied with ample water, and provided with acidic soil to proliferate well [6].

The varieties of anise include common anise, star anise, Japanese star anise, and other similar plants with corresponding names. Available information on the varieties, regions cultivated, and uses are given in Table 1.

Variety	Regions cultivated	Uses and indications
Common anise– <i>Pimpinella anisum</i>	Eastern Mediterranean region	Gastric ulcer, constipation, hot flashes, cough and catarrh, muscle cramps, hot flashes, candidiasis, viral flu, epilepsy [7]
Star anise– <i>Illicium verum</i>	East and Southeast Asia	Asthma, bronchitis, breath freshener, rheumatism, colic pain [8]

Table 1: Uses and indications of different varieties of anise.

Star anise applications and beneficial effects

Star anise has multiple uses, from being a culinary spice to a wide array of pharmacological applications.

Star anise antiviral effects

In a study by Astani A., et al. (2011), the essential oil of star anise was found to have antiviral effects against the herpes simplex virus *in vitro*, reducing the viral infectivity by more than 99% [9]. The plant oil acts on the herpes simplex virus by directly inactivating free virus particles in viral suspension assays. The presence of phytoconstituent anethole in abundance is responsible for positive viral inhibi-

tion. On pretreatment with star anise oil, it was observed that the viral infectivity was reduced by more than 99%. The active ingredients directly inactivate the virus by opposing the virion envelope physicality or masking the structures necessary for entry adsorption. The efficacy of star anise oil as a mixture and a solitary contributor with its high SI has been well established in treating viral conditions through topical application and as an essential oil for inhalation [9].

In vitro evaluation of antiviral activity is generally carried out using a viral yield reduction assay, cytopathic effect reduction assay, and plaque reduction assay. The viral activity is assessed through IC₅₀ values, and antiviral SI essential oils obtained from star anise have demonstrated high anti-herpes simplex type-1 activities *in vitro*. The essential oil of star anise is the most potent with an IC₅₀ value of 1µg/mL and an SI value of 160 among the tested extracts for antiviral effect. Star anise oil exhibited the most potent activity within an IC₅₀ value and selectivity index (SI) value of 36 [9].

An antiviral acts by blocking some stage of the viral replication cycle [10]. The possible mechanism of antiviral action includes inactivation of extracellular virus particles, prevention of attachment and entry of the virus into the host cell, prevention of replication of the viral genomic sequence, aversion of the synthesis of viral protein, and obstruction of the assembly or release of new infectious virions, thereby reducing the viral infectivity [11]. The viral diseases that respond to star anise are listed in Table 2.

Condition	Bioactive compound and effective concentration
Herpes simplex virus-1	IC ₅₀ of 1 µg/ml and SI of 160, intracellular
Herpes simplex virus-2	IC ₅₀ of 1 µg/ml and SI of 160, intracellular
Swine flu	Shikimic acid <i>in vitro</i>
Dengue	Shikimic acid <i>in vitro</i>
Influenza	Sesquiterpene CC ₅₀ -160 ± 30.7, EC ₅₀ -1 ± 0.1

Table 2: Viral diseases that respond to star anise [12,13].

Star anise prophylactic applications

In a study undertaken by Yadav and Bhatnagar (2007), star anise was assessed for its potential to act as an anticarcinogen. The study was conducted by inducing carcinogenesis with a single dose of nitrosodiethylamine (NDEA) for approximately 14 weeks. NDEA was found to increase liver weight while star anise reduced the bulkiness and liver weight. Also, star anise significantly reduced nodule incidence and multiplicity at 20 weeks. Furthermore, it restored hepatic erythrocyte superoxide dismutase levels, decreased tumor burden and oxidative stress, and increased phase-II enzymes. The anti-cancerous effect was attributed to anethole, and the effects were demonstrated on breast cancer and cervical fibrosarcoma [14].

Elmasry, *et al.* (2018) conducted a rat study exploring probable prophylactic effects of star anise extracts on the alterations of sexual hormones, sperm abnormalities, the toxicity of testes, sperm count, and testicular damage caused by equigan. When administered with equigan, star anise extracts improved electrolyte imbalances, DNA damage, sperm count, and sexual toxicity [15].

Illicium verum has antimicrobial, antifungal, anthelmintic, and insecticidal properties. The trans-anethole present in *Illicium verum* is responsible for these properties. *Illicium verum* is an effective antifungal agent against plant pathogenic fungi, such as *Pythium aphanidermatum* and *Botryodiplodia theobromae*. The essential oil from *Illicium verum* demonstrates a broad spectrum of inhibitory activities attributed to its high trans-anethole content [16].

The phytochemical analysis of the essential oil identified 13 active ingredients, including trans-anethole, caryophyllene, and limonene. The total flavonoid content amounted to 65.9 ± 0.9. Flavonoids are potent antioxidants that inhibit lipid peroxidation and exhibit

anti-hypertensive and anti-arthritic activity due to the hydroxyl group that mediates redox reactions and scavenges free radicals, thereby contributing to its antioxidant activity [17]. (*Illicium verum* is an ingredient in a traditional “five-spice powder”—a mixture of star anise, clove, cinnamon, pepper, and fennel [18]).

Free radicals determine the extent of DNA damage and are precursors to carcinogenesis. Studies showed that both ambient temperature water extract (ATWE) and boiling water extract (BWE) of star anise extracts are rich in carbohydrates and polyphenols. Aqueous extracts are antioxidants at a dosage of 25 µg and protect DNA against peroxide, mainly due to the high content of polyphenols and carbohydrates, along with the combined effect of all phytochemicals. Dinesha R., *et al.* (2019). indicated that star anise extracts reduced the mean nodular volume and the development of nodules in the liver of rats with induced carcinogenesis [19].

Star anise in combating multidrug resistance

The increasing incidence of multidrug resistance has led to the need for the development of immune modulators. Star anise waste residue extract (SAWRE) was tested against numerous isolates belonging to two gram-positive and four gram-negative organisms. The gram-positive organisms included *Staphylococcus aureus* and *Streptococcus pneumonia*. The gram-negative organisms included *Klebsiella pneumonia*, *Escherichia coli*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*. Each was tested against specific drugs such as chloramphenicol, tetracycline, and amoxicillin. The SAWRE contained higher phenolic compounds that combat multidrug resistance [20].

Health benefits and conditions that respond to star anise

Illicium verum, apart from being antiviral, effectively mitigates many illnesses, some of which are listed below (Table 3) [21–29].

Health benefit	Condition
Antibacterial	MRSA skin lesions and urinary tract infections [21]
Antifungal	Candidiasis [22]
Carminative	Cough [23]
Anti-inflammatory	Bronchitis [24]
Anti-aging	Signs of premature skin aging [25]
Antioxidant	Stress-induced metabolic disorders [26]
Chemopreventive	Cancer prevention and oxidative stress [27]
Galactagogue	Lactating women with decreased milk [28]
Sleep aid	Insomnia [29]

Table 3: Certain health benefits and other conditions that respond to star anise.

Common conditions treated with star anise

The property of star anise as a stomachic is used to treat loss of appetite. It is also used as an expectorant and has anti-spasmodic activity in the gastrointestinal tract, thereby playing a role in relaxing smooth muscles. The high anethole content of about 75.76% is credited with healing properties in respiratory infections, such as bronchitis. It is helpful as an antiseptic, stimulant, antidiabetic and hypotensive. The seeds are a rich source of B complex vitamins, vitamin C, and vitamin A. The spice acts as a breath freshener, and it is an effective anti-diarrheal [30].

Star anise COVID-19 research

Following the onset of COVID-19, the public has resorted to supplementing social distancing norms with herbal decoctions. Star anise has been infused in many homes as an antiviral agent, and ingested as tea to boost and maintain immunity. As a neuraminidase inhibitor, oseltamivir (Tamiflu), a compound from *Illicium verum*, prevents the release of newly formed viruses from the surface of host cells, thus preventing their spread to other cells. Star anise contains the precursor molecule for shikimic acid, used in the manufacture of Tamiflu [31].

Star anise modes of application

The different modes of application through which star anise is beneficial include ingestion as a tea or an extract, dermal application as an oil, and inhalation. It is used in cooking and baking, added to soups, broths, and stews to enhance the flavor and add a licorice-peppery taste. When used in diffusers and inhalers, the carminative and muscle relaxant properties help relieve cold and flu symptoms. The oil is used for fragrance in soap, cosmetics, and perfume manufacturing [32].

Externally, the dermal application is used to relieve rheumatism and joint pain [33]. The essential oil is 80% more effective than other insect repellents—the anethole-rich odor repels insects [34]. The oil extract minimizes the appearance of wrinkles, increases collagen content, and covers blemishes, keeping the skin looking vibrant [35].

The spice is an effective remedy that induces sleep and relaxation [36]. The use of star anise essential oil boosts the immune system against various pathogenic infections caused by specific bacteria, viruses, and fungi [37].

Illicium verum acts as an astringent due to the presence of tannins and polyphenols [38]. It improves liver function, stimulates bile production, and aids in fat metabolism [39]. When paired with a suitable carrier, such as citrus oils, star anise oil is an effective antioxidant and anti-inflammatory agent.

An extensive quantitative and qualitative analysis of the essential oils of *Illicium verum* by Huang, *et al.* (2017), led to the identification of 22 compounds. Among the identified compounds, trans-anethole was found to be 94% of the vital bioactive compound, showing significant inhibitory activity against fungi with inhibitory concentration (IC_{50}) values between 0.07 milligram per ml to 0.25 milligram per ml. The significant components elicited broad-spectrum properties, such as insecticidal, larvicidal, and antimicrobial [40].

The antifungal activity was examined by a vapor contact assay method. The results revealed a 94% decrease in mycelia owing to the presence of trans-anethole [40]. The volatile oil obtained from the fruits of star anise is used as an antimicrobial and fragrance in soaps, cosmetics, perfumes, and toothpaste. The oil is also effective in treating dyspepsia, productive cough, painful periods, and anorexia.

In a study by Vermaak I, *et al.* (2019), the antifungal activity of star anise was measured against two strains, such as *Aspergillus fumigatus* and *Aspergillus niger*, using the agar-disk-diffusion-test method. The minimum inhibitory concentration (MIC) and the minimum fungicidal concentration (MFC) were determined. The absolute methanol showed MIC and MFC values of about 31.2 and the highest inhibitory effect ($p < 0.05$, 71%) against *A. fumigatus* at all concentrations [41].

According to Madhu CS, *et al.* (2014), the antioxidant activity of star anise is due to the presence of its high polyphenol content. Carbohydrates and other phytochemicals, such as alkaloids, steroids, proteins, flavonoids, tannins, and phenolic compounds, are also found in abundance [42].

Star anise dosage

The suggested dosage guidelines for star anise consumption are as follows:

- As a tea: 1 cup consumed orally, 4 times a day, the tea is prepared by boiling 0.5 to 1 gm of seeds in 150 ml of water for about 120 minutes and then strained.
- Star anise powder: 3g per day consumed orally.
- In inhalation: 5 to 10% of star anise essential oil is used for inhalation [43].

Star anise is considered safe due to its low veranisatin content; however, it may cause neurotoxicity when administered in higher concentrations, causing neurological symptoms—such as seizures, irritability, hyperexcitability, emesis, vertical nystagmus, and myoclonic movements [44].

Star anise contraindications

Star anise is contraindicated in liver diseases, alcoholism, ulcerative colitis, Crohn's disease, estrogen sensitivity disorders, ovarian cancer, uterine fibroids, and when taking oral contraceptives [45].

In a study conducted by Ize-Ludlow, *et al.* (2004), Chinese star anise increased adverse neurological reactions in seven infants after ingestion. The infants who ingested more than the prescribed dose reported malaise, nausea, and vomiting about two to four hours after taking star anise [46].

Star anise toxicity

Toxicity studies in mice showed lethal effects at a dose of 3 mg/kg in mice. *Illicium verum* possesses potent central nervous system (CNS) depressant action and causes neurotoxicity as it contains neurotoxic sesquiterpenes veranisatins A, B, and C [47].

Chinese star anise has been generally regarded as being nontoxic and safe. However, Japanese star anise has been well documented to cause both neurologic and gastrointestinal toxicity. There are numerous cases of Chinese anise being adulterated with Japanese anise, and there are several concerns regarding the toxicity of Japanese star anise as it contains anisatum, which is highly toxic to humans [48].

Star anise drug interactions

Illicium verum may interact with antiepileptic medications due to the presence of the neurotoxin anisatin (*I. anisatum*—a Japanese variety). The Chinese variety also contains veranisatins A, B, and C, which may interfere with regular CNS activity and cause seizures, loss of motor coordination, and fainting [49].

Star anise research studies

Fritz, *et al.* (2008) described the anatomical differences between *Illicium verum* and *Illicium anisatum* and established their relevance to ensure non-contamination during ingestion [50]. Yan, *et al.* (2002) performed a component analysis of volatile oil derived from *Illicium verum* fruit from which 14 hydrocarbon, 22 oxygenated hydrocarbon derivatives, and a small number of nitrogenous compounds were derived [51]. Sy and Brown (1998) reported the extraction of a new compound seco-cycloartane derived from a dichloromethane extract of leaves *Illicium verum* leaves [52]. Shukla, *et al.* (2009) reported the toxicity of essential oils obtained from *Illicium verum* against flour beetle *Tribolium castaneum* Herbst [53]. Chang and Ahn (2002) described fumigant activity of (E)-anethole identified in the *Illicium verum* fruit against *Blattella germanica* [54].

Star anise sources (where to buy star anise)

Star anise is readily available in typical grocery markets. However, it is crucial to buy the Chinese variety with eight segments—with each segment having a shiny seed. Fresh star anise releases a viscous fluid when broken. Star anise is available in tablet form (1000 mg)

and as an essential oil. Brands manufactured by FDA-approved facilities, gluten-free, GMP-certified, and vegan are preferred choices. Japanese star anise is highly toxic due to anisatin, a neurotoxin (GABA antagonist). Ingestion may lead to seizures, respiratory distress, and death [55].

The future of the antiviral effects of star anise

Many of the beneficial effects of star anise have been established. However, more in-depth and extensive research needs to be conducted, using star anise as a solitary or an adjuvant antiviral. The chemopreventive property needs to be analyzed on a large-scale basis to gain conclusive evidence about developing an antioxidant formulation that will combat reactive oxygen species, reduce oxidative stress, inhibit apoptosis, and prevent DNA damage owing to its DPPHH radical scavenging effects [56].

There is a broad scope for research on star anises, such as polysaccharide extraction, the development of antifungal molecules as a solitary source, or in combinations. Such studies may provide a wide array of prospective bio-actives to be isolated and add to the emerging potency of *Illicium verum*, an antiviral, antifungal, chemoprotective, hepatoprotective, stomachic, and analgesic agent. The results from such vast studies may provide more data for further drug development and the reliability of star anise and its utilization [56].

Conclusion

Star anise (*Illicium verum*) is an evergreen tree that bears star-shaped fruits. It is recognized for its potent antiviral effects and is a source of shikimic acid, the substrate needed for the chemical synthesis of the drug oseltamivir phosphate (OSP), known as Tamiflu. Star anise is known to have antioxidant, antimicrobial, antifungal, anthelmintic, insecticidal, antinociceptive, gastroprotective, sedative, estrogenic, expectorant, secretolytic, and spasmolytic properties. Also, it has been evaluated for its potential as an anticarcinogen. The property of star anise as a stomachic is applied to treat loss of appetite. It is also used as an expectorant and has anti-spasmodic activity in the gastrointestinal tract, thereby performing a role in relaxing smooth muscles. Regarding COVID-19, star anise has been infused in many homes and ingested as tea in the form of a supplement to boost and maintain immunity—as a neuraminidase inhibitor.

Although star anise is readily available, consumers should take heed of the geographical sources where it is grown, the manufacturing practices, and if it is produced in an FDA-approved facility or not. It is consequential to note that Japanese star anise is highly toxic due to anisatin, a neurotoxin (antagonist). Ingestion may result in seizures, respiratory distress, and death.

Many beneficial effects of star anise have been established. However, more in-depth and extensive research needs to be conducted using star anise as a solitary or an adjuvant antiviral. Its chemopreventive properties need to be analyzed on a large-scale basis to gain conclusive evidence about developing an antioxidant formulation that will combat reactive oxygen species, reduce oxidative stress, inhibit apoptosis, and prevent DNA damage due to its DPPHH radical scavenging effect.

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