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Pharmacological Insights Into Star Anise: Comprehensive Review Of Therapeutic Potential And Mechanism

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Abstract :

Star anise (*illium verum*) is a spice widely recognised for it's distinctive flavour and diverse applications in culinary , medicinal and industrial fields. This review provides comprehessive analysis of star anise , fowing on it's totonical charecteristics, chemical composition , culinary uses and medicinal properties . Key bioactive compounds such as anethole , sequiterpenes , phenylpropanoids , lignons flavanoids and shikimic acid are highlighted for their pharmacological significance , particularly in antiviral treatments and as precursors in the synthesis of the antiviral drug oseltamivir (TAMIFLU) . It is the chief source of anticancer agent (shikimic acid). Role in the production of the antiviral drug oseltamevir (tamifler) . Ileum verum (Chinese star anise) and ileum anisatum (Japanese star anise , which is toxic) . The review also differentiate between *illicium verum* , and toxic illicium Anisatum , emphasing the improper of proper identification and safety additionally, the economic and trade aspects of star anise are examined along with innovative applications in various industries . Despite extensive research , gaps remain in understanding the full potential of star anise necessitating further studies . The review aims to consolidate current knowledge and inspire future research to explore and harness the benefits of this multifaceted spice.

Keywords : *Oseltamivir , shikimic acid , ileum verum , ileum anisatum.*

INTRODUCTION

Plant-based Chinese medicine is a generic term for Chinese medicines derived from plant resources, which are processed from natural plants or parts of naturally occurring flora under the guidance of the Traditional Chinese Medicine (TCM) doctrine. The medicinal parts of plants for Chinese medicines include roots, rhizomes, stems, leaves, flowers, fruits, seeds, skins and whole herbs Before the rapid development of medicinal chemistry in the 20th century, human beings fought diseases with plants and other natural medicines. Even in the rapidly developing 21st century, the use of herbal remedies for various diseases is a very common practice around the world. In addition, many plant-based Chinese medicines have been found to be used both as medicines to treat illnesses and as food in culinary dishes, and star anise is one of them.

Star anise is mainly found in East and Southeast Asia and southern North America. In East Asia, China is the main production area of star anise, followed by Vietnam, Cambodia, Myanmar, Sumatra in Indonesia, Kalimantan in the Philippines and other regions and countries. In North America, star anise is found mainly in Mexico, Haiti and Florida. In China, star anise oil, also known as “HuiYou” and “BaJiaoYou” is chemically diverse and has a wide range of uses. It is produced in China but is very popular in Malaysia, Vietnam, Indonesia and other regions (customs.gov.cn, accessed on 20 November 2022) [1]. Shikimic acid is the key synthetic precursor of Tamiflu (Roche Group, Basel, Switzerland) and is the only specific drug recommended by the International Health Organization to use against the H5N1 subtype. Star anise has a wide variety of pharmacological effects, including antioxidant, antibacterial, anti-inflammatory, insecticidal and antiviral properties. It is very similar to many plants, and confusing it with others has led to poisoning incidents.

The chemical composition of star anise is diverse, and the most important and widely studied components are SAO and shikimic acid [2]. SAO is volatile oil that is extracted from star anise fruit. It has a unique anise flavor and is widely used in the food and pharmaceutical industries because of its antimicrobial and antioxidant properties. In addition to SAO, the other important compound in star anise, shikimic acid, is the main component of Tamiflu, which was developed by the Swiss Roche Group. Tamiflu is the only specific drug recommended by the International Health Organization to be used to treat the highly pathogenic avian influenza of the H5N1 subtype. Currently, the main industrial use of shikimic acid is for the synthesis of Tamiflu, and this has attracted widespread attention towards organic acids. Before 2000, shikimic acid was generally used as a chemical raw material to be converted into other chemicals and chemical reagents.

So far, a total of 201 chemical components have been isolated from star anise, including hydrocarbons, alcohols and esters, as well as natural products such as star anise oil, flavonoids, phenylpropanoids, organic acids phenols, terpenoids and others. These ingredients have been verified to have a variety of biological

activities, and various extraction methods including steam distillation have been established for their extraction. This article reviews the general characteristics, chemical properties and biological activities of the constituents obtained from star anise, focusing particularly on SAO and shikimic acid. The outlook is that the research prospects of star anise are very broad and worthy of further research.

In light of star anise's rich ethnobotanical heritage, diverse phytochemical profile, and expanding pharmacological footprint, a critical synthesis of the scattered literature is both timely and necessary. Therefore, the present review consolidates current evidence on Illicium verum—from cultivation and constituent chemistry to mechanisms of action and emerging industrial applications—while spotlighting methodological advances and unresolved questions that will shape the next decade of discovery and development.

BOTANICAL CHARACTERISTICS

Illicium verum Hook. F. is the English name of star anise, alias Illicium san-ki. It is a 10–15 m tall arbor plant. The leaves are either alternate or in 3–6 clusters of branches in a whirl at the top and are leathery or thick leathery, obovate-elliptical, oblique lance-shaped or oval, measuring approximately 50–150 mm long and 1–1.5 mm wide. The apex is short and acuminated or slightly obtuse-rounded, the upper midrib is slightly depressed or flat when fresh and the base is cuneate, with 4–6 pairs of lateral veins and 8–20 mm petioles. The flowers are pink to crimson, solitary in leaf axils or subterminal with a 15–40 mm long pedicel. The tepals number 7–12 and often exhibit inconspicuous translucent glandular dots. The largest tepal is broadly elliptical to broadly ovoid, 9–12 mm long and 8–12 mm wide. Its aggregated fruits tend to spread and are 35–40 mm in diameter, whereas the fruit stalks are 20–56 mm long. The seed pods number 7–8 and are 14–20 mm long with an apical rostrum and are obtusely rounded without apices. The seeds are brown and are 7–10 mm long. The star anise tree blooms twice a year, once in March–May with high yields and ripe fruits and again in August–October. According to the Flora of China, the type specimen of star anise was originally obtained from Kew Gardens, England, grown and propagated in Beihai, Guangxi Province, China The medicinal part of star anise is its fruit, which is picked in autumn and winter when the fruit turns from green to yellow. Star anise is classified in the kingdom Plantae, phylum Angiospermae, class Magnoliopsida, order Austrobaileyales, family Magnoliaceae and genus Illicium. The fruit of star anise is cogwheel shaped and consists of an average of eight pods, and therefore it is generally called star anise. The "Huixiang" herbs include fennel, red fennel, star anise and cumin. As mentioned earlier, the genus name Illicium comes from the Latin word "illicere", which can be translated as "to seduce and attract", indicating that the fruits and branches of the plant have a seductive fragrance [3].In summary, the botanical characteristics of *Illicium verum* reveal it as an evergreen, star-shaped fruit-bearing tree with distinct morphological features such as lanceolate leaves, aromatic properties, and star-shaped schizocarp fruits. These traits not only aid in accurate identification and classification but also contribute to its therapeutic and commercial significance. Understanding these botanical features lays a vital foundation for further pharmacognostical, phytochemical, and pharmacological investigations [4]

PHARMACOLOGY

Antimicrobial:

The antimicrobial effect of star anise is one of the important focuses of modern pharmacological research. SAO has a wide inhibitory spectrum of activities against plant pathogenic fungi [5].Additionally, some studies have shown that extracts from different parts such as the roots, branches, peels and leaves of star anise have certain antibacterial and antifungal activities. For four tested fungi (Helminthosporiummaydis, Rhizoctonia cerealis, Helminthosporiurn carposaprum, Verticillium dahlia), the antifungal rates of the seedpod and leaf extracts of I. verum were greater than 50%, and those for the root and branch extracts were lower than 50%. The antimicrobial activity of SAO (minimum inhibitory concentration, MIC = 0.5 μL/mL) for Bacillus subtilis was stronger than that of common preservatives, such as paraben [6].

For some fungi such as Aspergillus flavus, Fusarium tricinctum and Candida albicans, star anise also exhibits fungicidal characteristics, with MIC and MFC (minimum fungicidal concentration) values of 2.5–25 µL/mL [7] .Huang et al. determined the IC50 values for 11 plant pathogens (including Alternaria solani, Bipolaris maydis and Botryodiplodia theobromae) using a direct contact assay, and the IC50 values of SAO against mycelar growth ranged from 0.06 to 0.25 mg/mL. Pythium aphanidermatum and Botryodiplodia theobromae were selected to evaluate the antifungal activity of the vapor components the SAO from I. verum as well as that of trans-anethole by using the vapor contact assay. There was also a strong inhibition of Magnaporthe oryzae spore germination when using an inhibition assay, and the IC50 value of the oil was determined to be 0.32 mg/mL. At all concentrations in medium, trans-anethole displayed a very similar inhibitory rate to that of SAO against the test fungi, which suggested again that this was the main active component among the volatiles in the oil [8] .In accordance with these studies, Singh et al. used an inverted petri-plate technique, and they found that the volatile oil exhibited 100% zone inhibition for Fusarium moniliforme. It was also found to be highly effective in controlling the growth of Penicillium citrium, Aspergillus flavus and Penicillium viridicatum by exhibiting more than 75% mycelial zone inhibition, as well as 50% inhibition for Aspergillus niger.

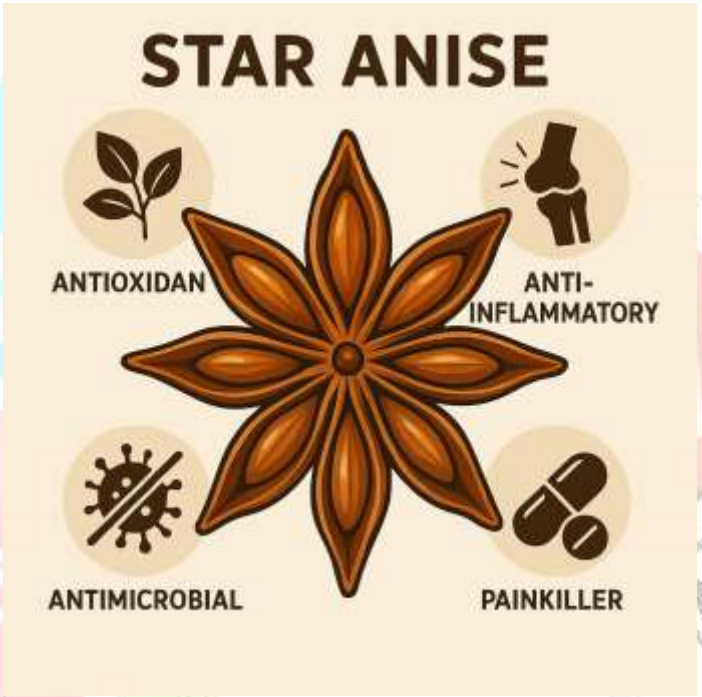
Antioxidant:

The fruits of star anise are commonly used as spices, and these are an alternate source of antioxidants that has been used for a long time. The fine powder and extracts of star anise prepared using water and ethanol under normal or under supercritical CO2 conditions as well as SAO have all be found to have antioxidant properties. The antioxidant activity of star anise and its extracts were verified by adopting linoleic acid peroxidation, the β-carotene-linoleic acid system and DPPH (1,1-diphenyl-2-picryhydrazyl) radical-scavenging methods in different studies [(9)].The addition of star anise fine powder to lemongrass oil enhances its oxidative stability, and together they form a natural antioxidant. The scavenging ability of the star anise antioxidant was evaluated by using the DPPH assay at various concentrations (500, 1000 and 1500 ppm) and was found to be 80.67, 81.38 and 81.73%, respectively [10] . The antioxidant activity of star anise against H2O2-induced DNA damage and human peripheral lymphocyte death was evaluated by assessing lipid peroxide inhibitory, hydroxyl-radical-scavenging, DPPH and superoxide free-radical-scavenging activities. The results showed that the water extracts of star anise had the most effective antioxidant activity. It was also shown that the aqueous extract of star anise acted as an antioxidant at a dose of 25 µg, and this amount provided protection to DNA against peroxides [11].

The DPPH-radical-scavenging method was also used by Yang et al. [12],who showed that the ethyl acetate extracts of star anise possess superior free-radical-scavenging abilities and reducing power compared to many other preparations. The strong correlation between its DPPH and TEAC values and those obtained from the reducing power assay implied that the antioxidants in the extracts were capable of scavenging free radicals and reducing different oxidants. Qualitative DPPH assays were performed on 25 essential oil products on TLC for 1–9 h at a temperature range of 30–70 °C. Two different areas of antioxidant activity with different polarities appeared on all the TLC plates. In addition, the highest antioxidant activity was observed for SAO when the sample was extracted at 60 °C for 1 day (EC50 value = 0.089 ± 0.05 mg/mL). According to numerous reports in the literature, the antioxidant activities of star anise and its extracts could be mainly due to the high polyphenol, carbohydrate, flavonoid and trans-anethole concentrations, along with a combined effect of all the phytochemicals [13]. At present, there is a search for new plant compounds that possess antioxidant activities, and this is a vital area of research in plant medicines. In general plant products are safe and are obtainable at relatively low cost [14].

Anti-Inflammatory:

It is well documented that I. verum has anti-inflammatory properties. The anti-inflammatory effects of star anise aqueous extracts were investigated on xylene-induced auricle edemas in mice. The inhibition rate indicated that star anise significantly improved auricle edemas caused by xylene. In another study, subjects in group A used a star aniseed-based mouthwash, and subjects in group B used a placebo (color-tinted water). This confirmed the effective anti-inflammatory properties of I. verum by recording gingival conditions before and after the intervention [15]. The anti-inflammatory activity of I. verum extract was also studied for its ability to inhibit protein denaturation, and the results were read spectrophotometrically. It was found to be effective at inhibiting heat-induced albumin denaturation at different concentrations of 100–500 µg/mL. Five groups of six mice each were treated with distilled water (10 mL/kg), indomethacin (10 mg/kg) or methanolic, ethanolic or aqueous extracts (150, 250 and 350 mg/kg) of I. verum. Edema was induced in the lower metatarsals of the right hind paws of each animal, and the edema-associated paw thickness was measured after 1, 2, 3, 4 and 5 h by using a plethysmometer. The inflammation of paw volume in rats was



significantly reduced in the methanol and ethanol I. verum extract test groups when compared to that in the control group. At present, star anise has a good therapeutic effect on acute inflammation such as that associated with the ear canal, oral cavity and airway surfaces, but whether it has an effect on other types of inflammation needs to be further researched

Other Activities:

I. verum extracts affected the spontaneous activity as well as the sound and touch pain responses in mice at a dose of 200 mg/kg and produced moderate or slight depression This effect was produced by inhibiting the nociceptors, and this inhibition did not interfere with motor coordination . Star anise processed products have the effects of warming Yang, dispersing cold and relieving pain .I. verum extracts could increase exhaustive swimming and pole-climbing time periods as well as post exercise hepatic glycogen content in mice. They also raised lactate dehydrogenase activity and decreased lactate and serum urea nitrogen levels. These findings demonstrated that I. verum extracts have noticeable anti-fatigue effects on mice [16]. Good inhibition of aluminum corrosion in concentrated hydrochloric acid solution can be caused by

I. verum extracts.A mixture of chamomile and star anise has anti-motility effects and can decrease induced diarrhea in mice ·Furthermore, the results of a new study indicate that synthesized magnetite Fe3O4, spinel (2:1) and (4:1) NiFe2O4 using an extract of star anise as a green reducing agent showed high biomedical activities against liver carcinoma cells and non-small lung adenocarcinoma cell

Chemical compounds

- Star anise is a rich source of essential oils, phenolic compounds, flavonoids, and organic acids.
- Its major phytoconstituents contribute to its distinct aroma, taste, and pharmacological activity.
- The essential oil content of dried star anise fruit ranges from 5–8%, depending on origin and processing.
- The most abundant compound in star anise oil is trans-anethole.

I. Essential Oil Components:

- **Anethole (trans-anethole):**

Accounts for 80–90% of star anise essential oil.

Gives the characteristic licorice-like aroma.

Has antibacterial, antifungal, and estrogenic properties.

Used in perfumery, flavoring, and traditional medicine

- **Estragole (methyl chavicol):**

Structurally similar to anethole.

Present in minor quantities.

Known for mild antimicrobial effects.

Potential genotoxicity at high doses; thus, regulated in foods.

- **Limonene:**

A terpene with citrusy scent.

Exhibits antioxidant and anti-inflammatory activities.

Common in many citrus fruits and aromatic herbs.

- **Linalool:**

Found in smaller amounts.

Has mild sedative and antimicrobial properties.

Widely used in cosmetics and aromatherapy.

❖ **α-Terpineol:**

Contributes to the pleasant fragrance.

Shows antioxidant, antiviral, and anticancer potential in studies.

❖ **Safrole (in very trace amounts in some species):**

Potentially toxic and carcinogenic.

Strictly monitored due to safety concerns.

II. Shikimic Acid:

- A key compound found abundantly in star anise.
- Used as the precursor in the synthesis of oseltamivir phosphate (Tamiflu), an antiviral drug.
- Plays a critical role in the biosynthesis of aromatic amino acids in plants and microorganisms.
- Star anise is the primary commercial source of shikimic acid.
- Extracted through aqueous or enzymatic extraction methods.

III. Phenolic Compounds and Flavonoids:

❖ **Quercetin:**

A powerful antioxidant flavonoid.

Offers anti-inflammatory, antiviral, and antihistamine properties.

❖ **Kaempferol:**

Another flavonoid with anticancer and cardioprotective potential.

Acts by inhibiting angiogenesis and oxidative stress.

❖ **Rutin:**

Strengthens capillaries and helps in vascular health.

Also known for anti-inflammatory activity.

❖ **Gallic acid:**

A phenolic acid with strong antioxidant and antimicrobial properties.

Present in free and bound forms.

- **Caffeic acid:**

Helps reduce oxidative damage and offers neuroprotective effects.

Found in both fruit and leaves of the plant.

Other Bioactive Compounds:

- **Coumarins:**

Mildly aromatic compounds with blood-thinning and anti-inflammatory effects.

- **Tannins:**

Present in small amounts.

Contribute to astringency and antioxidant power.

- **Fatty acids:**

Include palmitic, oleic, linoleic, and stearic acids.

Present in the seed oil portion.

- **Sterols:**

Such as β-sitosterol, with cholesterol-lowering properties.

- **Polysaccharides:**

Extracted from fruit pulp or pericarp.

Show immune-enhancing and antitumor activities in experimental models.

V. Nutritional Elements:

Contains carbohydrates, fibers, and proteins in small quantities.

Also includes trace minerals like iron, magnesium, calcium, and phosphorus.

VI. Summary of Major Compounds and Their Activities:

Compound	Type	Major Activity
Trans-Anethole	Essential oil	Flavor, antimicrobial, estrogenic
Shikimic Acid	Organic acid	Antiviral precursor (Tamiflu)
Limonene	Terpene	Anti-inflammatory, antioxidant
Linalool	Alcohol	Sedative, antimicrobial
Quercetin	Flavonoid	Antioxidant, antiviral
Gallic acid	Phenolic acid	Antioxidant, anti-inflammatory
Kaempferol	Flavonoid	Anticancer, cardio-protective
Caffeic acid	Phenolic acid	Neuroprotective, anti-inflammatory
β-Sitosterol	Sterol	Cholesterol-lowering, anti-inflammatory

Other Constituents:

Some alcohols (177–180), phenols (181, 182), aldehydes (183–185), esters (186–193), phenolic glycosides (194, 195) and other compounds (196–201) with irregular chemical structures have also been isolated from star anise. The other constituents isolated from Illicium verum

Traditional and Modern Uses:

Star anise has a long history of use in traditional medicine systems, particularly in Chinese and Ayurvedic practices. It has been employed to treat various ailments, including digestive issues, respiratory infections, and even as a galactagogue to enhance milk production in breastfeeding mothers. In contemporary applications, star anise is increasingly recognized for its potential in food preservation due to its antimicrobial properties, extending the shelf life of products and enhancing food safety.

Furthermore, star anise is finding its way into modern herbal supplements and functional foods. As consumers become more health-conscious, the demand for natural ingredients that offer both flavor and

health benefits has surged. Star anise is being incorporated into teas, dietary supplements, and various culinary products, showcasing its versatility and appealing flavor profile.

Safety and Side effects:

Star anise (*Illicium verum*) is widely used in traditional medicine and culinary applications for its aromatic and therapeutic properties. While the spice is generally recognized as safe when used in small quantities for flavoring, concerns have been raised about its safety when used medicinally or in high doses. One of the major safety concerns is the potential adulteration or confusion with the toxic Japanese star anise (*Illicium anisatum*), which closely resembles *Illicium verum* in appearance but contains potent neurotoxins such as anisatin, neoanisatin, and pseudoanisatin. These compounds can cause severe neurological effects including seizures, hallucinations, and even death, particularly in infants or immunocompromised individuals.

Clinical reports have documented several cases of adverse neurological reactions linked to star anise consumption, primarily due to accidental use of contaminated or adulterated star anise products. Infants are particularly vulnerable, as star anise tea is sometimes given as a home remedy for colic or indigestion. In such cases, seizures, irritability, and vomiting have been reported. Therefore, it is highly recommended to avoid administering star anise preparations to infants and small children, unless clearly verified for purity and safety.

Another safety consideration involves allergic reactions. Though rare, some individuals may develop hypersensitivity reactions such as skin rashes or gastrointestinal discomfort. The essential oil of star anise, which contains a high percentage of trans-anethole, can be toxic in high concentrations. It is known to act as a convulsant at high doses and may interfere with certain medications, including anticoagulants and hormone therapies, due to its estrogenic-like activity.

The safety of star anise during pregnancy and lactation has not been thoroughly established. Therefore, pregnant or breastfeeding women are advised to limit or avoid its use unless under professional supervision. Furthermore, long-term safety data for medicinal use is lacking. Like many herbal remedies, the lack of standardization in herbal product preparation poses a risk of variable dosage and unintended exposure to harmful compounds.

Proper identification and authentication of star anise are crucial. Analytical techniques such as microscopic examination, gas chromatography–mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and DNA barcoding can help ensure the authenticity of *Illicium verum* and detect adulteration. Regulatory bodies in some countries have issued warnings or restrictions on the use of star anise tea, especially in pediatric populations, highlighting the need for stricter quality control.

CONCLUSION

Star anise, scientifically known as Illicium verum, is a plant of immense pharmacological, nutritional, and industrial significance. This review has highlighted its unique chemical composition, traditional uses, and broad-spectrum biological activities, which collectively establish its value in both modern and traditional medicine systems.

The characteristic aroma and flavor of star anise are primarily due to the presence of trans-anethole, which makes it a popular spice and flavoring agent across various culinary traditions worldwide. Beyond its culinary role, the plant's essential oil and extracts exhibit noteworthy therapeutic potentials including antimicrobial, antifungal, antioxidant, antiviral, and anti-inflammatory effects.

Among its many medicinal uses, the most prominent is its role in the synthesis of shikimic acid—a crucial precursor in the production of the antiviral drug oseltamivir (Tamiflu). This function has propelled the plant into global prominence, especially during pandemics such as the avian flu.

Furthermore, the presence of a wide range of phytochemicals like flavonoids, tannins, and phenolic acids contributes to its therapeutic capabilities. Star anise has been found effective against various bacterial strains, fungi, and even cancer cells in experimental studies, making it a candidate for future drug development.

Traditional systems of medicine, especially Chinese and Indian systems, have long utilized star anise for treating ailments such as digestive disturbances, colds, and coughs. Modern research has only begun to validate these uses through evidence-based studies, demonstrating the scientific basis of ancient practices.

Its antioxidant properties make star anise a promising natural preservative and a health-enhancing dietary component. The demand for plant-based bioactive compounds is growing, and star anise stands as a sustainable and effective source.

However, it's crucial to differentiate *Illicium verum* from *Illicium anisatum*, the Japanese star anise, which is toxic and unsuitable for consumption. Proper identification and quality control are essential in commercial and medicinal use.

Pharmacokinetic studies and in vivo trials are still limited, and further research is needed to fully understand its mechanisms of action, dosage optimization, and potential side effects in humans. This includes long-term toxicity evaluations and clinical trials.

In conclusion, *Illicium verum* remains a potent natural product with vast potential in food, pharmaceutical, and cosmetic industries. Continued interdisciplinary research will help unlock its full therapeutic spectrum and facilitate its integration into mainstream healthcare. As interest in natural remedies continues to grow, star anise offers a promising, multifaceted option that bridges tradition and modern science.

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