

Review

Chinese star anise and anise, magic herbs in traditional Chinese medicine and modern pharmaceutical science

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Abstract: Star anise (*Illicium verum* Hook. f.) is an important herb in traditional Chinese medicine as well as traditional Asian medicine. The fruit is aromatic and has a strong, pungent and mildly sweet taste. Star anise is one of the many species that contain bioactive compounds as well as a number of phenolic and flavonoid compounds, having antioxidant, preservative and antimicrobial properties. All relevant papers in the English language from researchers of different countries were collected. The keywords of Chinese star anise, anise, traditional Chinese medicine and modern pharmaceutical science were searched in Google Scholar, Scopus, Research Gate and PubMed. Its seeds are good source of minerals like calcium, iron, copper, potassium, manganese, zinc, and magnesium. The essential oil of Chinese star anise contains anethole which has shown several functional properties including antimicrobial, antioxidant, hypoglycemic, hypolipidemic and oestrogenic properties. Due to all positive characteristics, such as antidiabetic, hypolipidemic, antioxidant activities, anticancer and antimicrobial properties, both seeds and essential oils of anise is promising for safe use as super food supplements and raw constituents in the both pharmaceutical and food industries. Anise seed oil contains anethol, estragole, eugenol, pseudisoeugenol, methyl chavicol and anisaldehyde, coumarins, scopoletin, umbelliferon, estrols, terpene hydrocarbons, and polyacetylenes as the major compounds. The plant oil has both pharmacological and clinical effects. The pharmacological effects consist of antimicrobial, hepatoprotective, anticonvulsant, anti-inflammatory, antispasmodic, bronchodilator, estrogenic, expectorant and insecticidal effects, and clinical effects such as nausea, constipation, menopausal period, virus, diabetes, obesity and sedative action. Combined with a nutritious diet, other traditional Chinese and Asian medicine, Chinese star anise and anise seed may improve various aspects of health. More clinical studies are necessary to uncover the numerous substances and their effects in ginseng that contribute to public health.

Keywords: Chinese star anise; Anise, traditional Chinese medicine; modern pharmaceutical science

1. Introduction

The ancient Chinese have identified 11,146 medicinal species from 383 families, and more than 400 of which widely used through the world, which means that China is the native home to a greater diversity of the world's herbal plants than any other regions in the world. The herbal apothecary in China grew from hundred herbs recorded in the oldest version of Shen Nong Ben Cao Jing by Tao Hongjing to almost 1,900 substances in Li Shizhen's monumental encyclopedic research, the Bencao Gangmu published a few years after his death in the late Ming dynasty, 1596 AD. TCM which is one of the most important part of the health care system in most Asian countries, relies on natural products and had been playing a very significant role in health protecting and disease control for many years. Traditional Chinese medicine plays an important role in sustainable agriculture and food systems, it also offers a holistic approach to prevent diseases while making appropriate use of organic and herbal products especially growth by small-scale family farmers. The aim of this review is survey on two

important crop in traditional Chinese medicine, namely Chinese star anise and anise and their potential health benefits and pharmacological usages of them.

2. Chinese star anise

2.1. Botany and plant description of Chinese star anise

Traditional Chinese medicines consider as both medicine and food item, because most of Chinese medicine are used as pigments and flavors in the preparation of Chinese food items (Yang *et al.*, 2010; Soleymani and Shahrajabian, 2012; Ogbaji *et al.*, 2018; Shahrajabian *et al.*, 2018; Soleymani *et al.*, 2018; Shahrajabian *et al.*, 2019a,b,c,d,e,f). Star anise (*I. verum* Hook. f.) is a medium-sized evergreen tree which is native to southwest of China; and also widely cultivated in the subtropical and tropical areas of Asia (De *et al.*, 2001; Chouksey *et al.*, 2010; Benmalek *et al.*, 2013; Li *et al.*, 2013; Elmasry *et al.*, 2018). Common name of *I. verum* has many synonyms in different areas: Chinese star anise or Bajiaohuixiang in China; Anis de la Chine, Anise etoile or Badiane in France; Dai-uikyo or Hakkaku-uikyo in Japan; Sternanis in Germany; Anice stellato in Italy; Sonf or Anasphal in India; Anis estrellado in Spain; Bunga lawing in Indonesia and Malaysia (Wang *et al.*, 2011). De *et al.* (2001) reported that star anise is extensively cultivated in a limited area with particular ecological factors in Kwangsi in South East China and Tonkin in Indo-China. Chinese star anise is considered as one of the flavors used in China five spices (Thuat and Ngoc, 2010; Ibrahim *et al.*, 2016; Acimovic *et al.*, 2017). In traditional Chinese medicine, it is called as warming yang and dispelling cold, and regulating the flow of Qi to relieve pain or common cold (Wang *et al.*, 2011). It has been also reported that its crude fruits and its powders were used in traditional teas to treat nervousness and sleeplessness and also as a sedative (Wang *et al.*, 2011). Dried ripe, star anise fruit and seed are used as important spice in Asian cooking especially in Chinese, Vietnamese and Indian cuisines. Vietnam produces more than 5000 t of star anise seeds per annum; and it is estimated that the combined production of China and Vietnam is more than 25,000 t per annum. Moreover, 200-250 t of essential oil are shipped to France and the Czech Republic. In China, which is the largest supplier of star anise to the world market, Vietnamese star anise is blended and then exported to France. In France, it is used as a raw material in the production of alcoholic beverages (FAO, 1993). Wang *et al.* (2011) found that star anise (*Illiciaceae*, *Illicium verum* Hook. f.) has long been used in traditional Chinese medicine and the food industry with the effects of dispelling cold, regulating the flow of Qi, and relieving pain. Chinese star anise together with the morphological similar Japanese star anise together with the morphologically similar Japanese star anise (*Illicium anisatum*), is also used for decoration purposes (Shen *et al.*, 2012). *Illicium verum* Hook. f. mainly grows in the provinces of Guangxi, Guangdong and Yunnan, covered nearly 80% in the world (Yan *et al.*, 2002). This plant also has been reported to possess anti-bacterial, anti-cancer and of course anti-inflammatory characteristics (De *et al.*, 2002; Itoigawa *et al.*, 2004; Yang *et al.*, 2010). Kang *et al.* (2013) noted that Chinese anise star can alleviate inflammatory responses and is a common flavor in medicinal tea, cough mixtures and pastilles. Star anise is classified in the division Magnoliophyta, class Magnoliopsida, sub-class Magnoliidae, order Austrobaileyales, family Illiciaceae. De *et al.* (2001) mentioned that among all *Illicium* species present throughout the world, such as *Illicium dunnianum*, *Illicium griffithii*, *Illicium verum* and *Illicium anisatum*, just *Illicium verum* Hooker *anisatum* is non-poisonous and has been used in culinary preparation and also as famous traditional medicine. Vermaak *et al.* (2013) mentioned that dried fruit of Chinese star anise is used as a remedy to treat infant colic. Japanese star anise, *Illicium anisatum* (Schisandraceae) is an evergreen broad-leaved tree or shrub that exhibits ballochory (Romanov *et al.*, 2013). The plant is widely distributed in the central and southern parts of the Japanese archipelago (Yoshikawa *et al.*, 2018). Japanese star anise looks very similar to Chinese star anise in its dried form but that is where the similarity ends. The Japanese star anise is extremely toxic and is not edible in any form (Vermaak *et al.*, 2013; Yoshikawa *et al.*, 2018). Recently concern has been raised regarding adulteration of Chinese star anise with Japanese star anise (Shen *et al.*, 2012; Scharge *et al.*, 2013). Only Japanese star anise fruits contain the neurotoxic anisatin, which is a strong non-competitive antagonist of the GABA_A-receptor (Kudo *et al.*, 1981). Nakazawa *et al.* (1959) also found that the fruit is also most toxic, followed by the seed, root, leaf and bark. It is very difficult to detect fragments of Japanese star anise fruit in powdered Chinese Star Anise fruit (Tehen *et al.*, 2009). Various methods have been used to identify and distinguish between them, such as morphological, chemical analysis by fluorescent microscopy, gas chromatography and an HPLC/ESI-MS/MS method (Joshi *et al.*, 2005; Lederer *et al.*, 2006). Howes *et al.* (2009) explained that the volatiles desorbed from the pericarps of the toxic *I. anisatum* (Japanese star anise) were characterized by the presence of asaricin, methoxyeugenol, and two other eugenol derivatives, and none of which were detected in any other species examined. Star anise is a medium sized tree, 8-15 m tall and 30 cm depth, with the bark which is white to bright grey. Furthermore, its leaves are 6-12 cm long, alternate, simple, leathery, entire, glabrous, shining, usually crowded in bundles at the end of the branches; it also has large

flower, bisexual, 1-1.5 cm in diameter, white pink to red or greenish yellow, axillary and solitary (Vecchio *et al.*, 2016). Fruit is capsule like, aggregate is star shapes; each arm is seed pod. In China, star anise is frequently used as spice in Chinese cuisine. Its fruit has an agreeable, aromatic, sweet taste and a pleasant fragrance resembling anise (De *et al.*, 2001). Guangxi followed by Guangdong, Yunnan, and Fujian are the original and main production regions of star anise in China, accounting for more than 85% of the total average of star anise in China (Ma *et al.*, 2011). Prajapati *et al.*, (2007) and Fritz *et al.* (2008) reported that fruits are picked before they ripe and dried, and seeds are shiny brown or reddish with high oil content. Vecchio *et al.* (2016) also noted that flowers bloom from March to May, and the fruits ripe from September to October. Anethole of star anise has been utilized in folk medicine industry because of its soothing and antispasmodic properties (Ludlow *et al.*, 2004). Estragole (4-allyl anisole, 1-methoxy-4-enylbenzene) is a naturally occurring compound which can be extracted from Anise, and Chinese star anise; flavors and fragrances containing estragole are used in food products, perfumes, soaps and detergents (Ismail *et al.*, 2016). Verghese (1998) also claimed that, traditionally, the oil of star anise used topically for rheumatism and otalgia and also as an antiseptic. Star anise oil is a pale yellowish liquid (De *et al.*, 2001). A genuine sample of the oil derived exclusively from the fruit displays properties like, the specific gravity at 25°C is 0.984, the refractive index at 25°C is 1.5572, optical rotation $-/+ 0.12$, soluble in 1.5 volumes and more of 90% ethanol, moreover, its oil is stimulant, eupeptic, carminative, mildly expectorant and diuretic (Verghese, 1998). It has been reported that (E)-Anethole, limonene, linalool, and α -pinene are major components of the essential oil of *I. verum* (De *et al.*, 2002; National Committee for Clinical Laboratory Standards, 2002). Star anise is socially accepted in occasions and is traditionally being used in high altitude regions of Arunachal Pradesh where dried seedless fruits are used as incense, flavouring tea, preparation of butter salted tea or sugar tea for sweet fragrance and to increase and improve the potency and strength of alcohol (Mukhia, 2006). Also, used as medicine to cure cough, toothache and sinusitis, used as an anti-fungal agent and food preservative (Angami *et al.*, 2017). Leaves in combination with juniper/thuja/pine leaves are burnt for making smoke which is believed to be scared and help in purifying surrounding air (Paul *et al.*, 2013). De *et al.* (2001) found that its oil is useful in flatulence, spasmodic pains and dysentery, it also relieves colic and is a common ingredient of cough lozenges. Moreover, its oil is used as an applicant in rheumatism and also applicant as an antiseptic. Besides, it is also useful against body lice, bedbugs and is an ingredient of cattle sprays. Other usages of star anise oil is in fevers, scabies, constipation and insomnia. Vecchio *et al.* (2016) noted that *Pimpinella anisum* (anised or green anise) and *Illicium verum* (Chinese star anise or star anise) are both under the name of anise, but each one presents different functional and botanical characteristics. Both Chinese star anise and anise have been widely used in Iranian traditional medicine for antimicrobial effects (Yazdani *et al.*, 2009). It has not only studied for its advantages in food and medicinal science (Ohira *et al.*, 2009), but also it has been studied for its essential oil which is biologically active for both fumigating and repelling *S. zeamais*, *Blattella germanica*, *Lasioderma serricornis*, *Sarocladium oryzae*, *Callosobruchus chinensis*, and *Aedes aegypti* (Ho *et al.*, 1995; Chang and Ahn, 2002; Kim *et al.*, 2003; Dana and Wej, 2006). Gholivand *et al.* (2009) reported that the dried star anise fruit is almost composed of 49 compounds which may included trans-anethole (81.40%), limonene (6.50%), chavicol (2.10%), and also anisaldehyde (1.81%). Li *et al.* (2013) also stated that the dried star anise fruit is composed of nearly 8-12% essential oil. Star anise primarily contains anethole and fatty oil. It is primarily located in the woody shell, to a lesser extent in the seed. Anethole is only slightly soluble in water but exhibits high solubility in ethanol. Besides, it is distinctly sweet, measuring 13 times sweeter than sugar. The essential oil (*anisi aetheroleum*) extracted from steam distillation of ripe ob both *I. verum* and *P. anisum* contain trans-anethole from 80%-95% or more, which is responsible for its characteristics taste and smell, and of course medical properties (Ooi *et al.*, 1994; DerMarderosian and Beutler, 2002), followed by chavicol methyl ether (estragole), anisaldehyde and cis-anethole (Hansel *et al.*, 1999). Ismail (2018) mentioned that star anise is one of the most effective oils against *T. confusum*. In traditional Chinese medicine, *I. verum* has long been used with the actions of dispelling cold and relieving pain (Wang *et al.*, 2011). Parsa *et al.*, (2012) reported that Chinese star anise is used extensively in the both Indian diet and medicine because it does not have any adverse influence and also easily absorbs. They have also found that the oil of star anise is stimulant, stomachic, carminative, mildly expectorant and diuretic. It has been also reported that the fruit of the plant has been used in traditional medicine for treatment of stomach aches, vomiting, rheumatic pain, insomnia and skin inflammation (Sung *et al.*, 2012; Wang *et al.*, 2011; Estevao-Silva *et al.*, 2014; Park *et al.*, 2015). Aly *et al.* (2014) mentioned that its fruit is an important traditional Chinese medicine as well as a commonly used spice. Mathon *et al.* (2013) high levels of anisatin in *Illicium lanceolatum*, *I majus*, and *I anisatum* may cause health concerns if they are misidentified or mixed with edible *Illicium verum*. It is able to increase production of milk new mother (Ibrahim *et al.*, 2016). The use to facilitate birth and to increase the libido, as well as to relieve menopausal discomforts; and its oil is applicant in

rheumatism as recommended by some folk remedies. Zhang *et al.* (2005) showed that trans-anethole, p-anisaldehyde, farnesol, and estragole are main aroma compounds of Chinese star anise. They have also shown that 47 compounds accounted for more than 90% in total Chinese star anise aroma molecules, including trans-anethole (75.76%), p-anisaldehyde (8.65%), estragole (4.70%), farnesol (3.26%), limonene (1.01%), linalool (1.44%), caryophyllene (1.03%) and 4'-methoxypropiofenone (0.72%). Sripongpun (2008) stated that the crude extract of Chinese star anise can be applied as an optional control of house fly at breeding sites. Classification of Chinese star anise is shown in Table 1. Various pharmacological effects of anethole which is the main ingredient in star anise oil is presented in Table 2. Figure 1 is shown Chinese star anise.



Figure 1. Chinese star anise.

Table 1. Classification of Chinese star anise.

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Austrobaileyales
Family	<i>Illiciaceae</i>
Genus	<i>Illicium</i>
Species	<i>Verum</i>

Table 2. Various pharmacological effects of anethole which is the main ingredient in star anise oil.

1-	Increasing the white blood cellular activity. Some agents such as Shengbaining and Shengzuening, whose main active ingredients were extracted from the star anise, can promote mature white blood cells in the bone marrow to spread into the surrounding blood. Due to the body's own feedback, mature and release speed of bone marrow cells were accelerated. It can also keep bone marrow cells' activity, enhancing the white blood cells (especially granulocytes).
2-	Bacteriostatic effect. Star anise oil shows antibacterial effects in a variety of strains (Fu and Li, 2011) including <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>theria bacillus</i> , and <i>Salmonella typhi</i> . The results laid a theoretical foundation for the development and utilization of novel plant-derived antifungal propenylbenzene derivatives.
3-	Antiviral effects (Koch <i>et al.</i> , 2008). Star anise oil can act on different acyclovir-susceptible and acyclovir-resistant herpes simplex virus type 1 (HSV-1) strains.
4-	Other effects. Anethole can improve the activity of anticholinesterase (Bhadra <i>et al.</i> , 2011). It shows significant inhibitory effect against acetylcholinesterase and butyrylcholinesterase, and the IC ₅₀ value was 39.89 ±0.32 µg/mL and 75.35±1.47 µg/mL, which the value for star anise oil was 36.00±0.44 µg/mL and 70.65±0.96 µg/mL, respectively. It has also been reported that anethole has an antioxidant effect.

Evidence indicate that anethole is natural bioactive compound with multiple beneficial effects in human health such as anti-inflammatory, anticancer, chemopreventive, neuroprotective, spasmolytic, hypotensive, antithrombotic, immunomodulatory, and antidiabetic. It has offer a safe approach in treatment of several chronic diseases, especially in skin and lung inflammatory disorders, cancer, type 2 diabetes and neurological diseases. Domiciano *et al.* (2013) found that the anethole maybe effective in controlling some nonimmune acute inflammation-related disease, probably by an inhibitory action on production or release of PGE₂ and NO. Wei *et*

al. (2014) suggested that *I. verum* fruit extracts and trans-anethole can potentially be developed as a grain protectant to control stored-product insect pests. Li *et al.* (2013) also found that *I. verum* which is one of the most important Chinese herb, has possess insecticidal activity against *S. zeamais* and *Cryptolestes pusillus Schnoherr*. Other studies have indicated that the essential oil of *I. verum* has repellent and fumigant actions on *S. Zeamais*, *Blattella germanica* (Change and Ahn 2001), *Lasioderma serricorne*, *Sitophilus oryzae*, *Callosobruchus chinensis* (Kim *et al.* 2003), and *Aedes aegypti* (Dana and Wej, 2006). Parasa *et al.* (2012) observed that minimum inhibitory concentration (MIC) values (mg/ml) for *Illicium verum* Hook fruit against *Aeromonas hydrophila*, *Aeromonas salmonicida* and *Edwardsiella tarda* were 0.15625, 0.078125, and 0.15625. Zhou *et al.* (2016) suggested that *I. verum* extracts have potential as an eco-friendly biopesticide in integrated pest management against *M. persicae*. Wei *et al.* (2014) also indicated that *I. verum* fruit extracts and trans-anethole can potentially be developed as a grain protectant to control stored-product insect pests. Liu *et al.* (2011) found that essential oils of *I. verum* showed strong attractiveness to the German cockroaches at a concentration of 1 pp.

2.2. Modern medicinal usage of star anise

An estimated 66% of China's star anise harvest is used to make Tamiflu. In Guangxi province alone, some 350,000 hectares of farmland are devoted to the star anise tree with an annual output of 80,000 MT. It takes almost 30 kg of star anise to yield 1 kg of shikimic acid, enough to treat one person. It has been reported that star anise has antimicrobial, antifungal and antioxidant activities (Chouksey *et al.*, 2010; Benmalek *et al.*, 2013). Padmashree *et al.* (2007) indicated that powders of star anise and particularly their ethanol/water extracts have great potential as natural antioxidants. Yang *et al.* (2010) introduced *I. verum* as natural anti-microbials for the treatment of antibiotic pathogens. Abdallah *et al.* (2013) investigated the antiviral activity of anise oil against bovine herpes virus type 1- (BHV-1) in cell culture and they found that anise oil is non-toxic to MDBK cells up to 100 ug/ml, and also inhibited the growth and development of BHV-1. Sung *et al.* (2012) recommended star anise in the treatment of inflammatory diseases. Alhajj *et al.* (2015) indicated that Chinese star anise could be used as a natural additive to improve the immune responsiveness and performance of broiler chickens. One of the most important character of *I. verum* is digestive aid which may make the nursing mothers promote breast milk production, has the anti-bacterial and anti-fungal affection of asthma, bronchitis, and dry cough, refreshed the breath, and ensure a good sleep (Cheng and Changli, 2007; Ashraf *et al.*, 2012). Fagundes *et al.* (2014) concluded that anethole in the essential oil of *Illicium verum* Hook can be identified and determined by GC-MS, NMR and UV-VIS, and a superior HPLC method has been developed for the determination of the compound in rat plasma. Zhang *et al.* (2015) have examined the characteristics aromatic constituents of star anise, and they have confirmed forty seven compounds, with trans-anethole, estragole, and anisaldehyde the main aroma components. The content of trans-anethole was the highest (75.76%), followed by linalool (1.44%), Limonene (1.01%), and 4'-methoxypropiophenone (0.72%) were the lowest. Bhatti *et al.* (2017) concluded that the protocatechuic acid residing in *I. verum* most probably underlies its antioxidant action. Star anise volatile oil could be applied in different industries, like the cosmetic, the pharmaceutical or the food industry; in the latter it might replace the synthetic antioxidant used nowadays in order to overcome the adverse influence of the synthetic additives on the public health (Aly *et al.*, 2016). Economic and medicinal importance of Chinese star anise is shown in Table 3.

Table 3. Economic and medicinal importance of Chinese star anise.

1-	The anti-bacterial and anti-fungal properties of Chinese star anise are useful in the treatment of diseases like asthma, bronchitis and dry cough.
2-	Chinese star anise can also be used as for its sedating properties to secure a good sleep.
3-	Its osil is appropriate in providing relief from rheumatism and lower back pain.
4-	It can also be used as a natural breath freshener.
5-	There is a compound present in Chinese star anise which is called Shikimic acid, and it is used for preparing drug for curing influenza or the flu virus.
6-	Another important compound present in Chinese star anise which contains anti-oxidants properties is Linalool, and it is good for overall health.
7-	The chemical compounds which derived from this important herb also have anti-oxidant, disease preventing and health promoting properties.
8-	Anethole is the most important compounds in this herb, but other important compounds found in the seeds include extragol, p-anisaldehyde, anise alcohol, acetophenone, pinene and limonene.
9-	In traditional Chinese and Asian medicine, it mainly uses as stomachic, anti-septic, anti-spasmodic, carminative,

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- digestive, expectorant, stimulant and tonic.
- 10- The seeds are excellent source of many essential B-complex vitamins such as pyridoxine, niacin, riboflavin, and thiamin.
 - 11- Seeds are also great source of minerals like calcium, iron, copper, potassium, manganese, zinc, and magnesium.
 - 12- This important spice is also contain good amounts of anti-oxidant vitamins such as vitamin-C and vitamin-A.
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Shikimic acid which extracted from *I. verum* is one of the main ingredients in the antiviral drug Tamiflu used to fight avian influenza (Ohira *et al.*, 2009; Borah, 2013). *I. verum* has been reported to possess antioxidant properties (Chempakam and Balaji, 2008) as well as significant anticancer potential (Shu *et al.*, 2010). Antioxidant properties may be recommended in enhancing shelf life of products such as spices (Prakash *et al.*, 2011). Natural antioxidants are known to protect cells from damage induced by oxidative stress, which is generally considered to be a cause of ageing, degenerative disease, and cancer (Ringman *et al.*, 2005). Dinesha *et al.* (2014) concluded that the extracts of star anise exhibited effective prevention ability against H₂O₂ induced cell death and DNA protection, and these activities of extracts may due to the presence of polyphenols, proteins and flavonoids in star anise extracts. Chouksey *et al.* (2013) observed that the extracts of *I. verum* possess potent central nervous system (CNS) depressant action and anxiolytic effect without interfering with motor coordination. Park *et al.* (2015) suggested that treatment with *Illicium v.* maybe the basis of a novel therapeutic strategy for hyperlipidemia-atherosclerosis. Diza *et al.* (2014) suggested that the combination of chamomile and star anise can be used as an alternative antidiarrheal treatment. Shu *et al.* (2010) discovered that star anise polysaccharides could inhibit the growth of Sarcoma 180 tumor in vivo. The tumor inhibition ratio of high dose polysaccharides (720 mg/kg) was 30.92%. Kanatt *et al.* (2014) reported that star anise extract exhibit high reducing power indicating good antioxidant potential, and antioxidant potential of star anise extract was better than lemon grass extract, and the extracts were able to protect against radiation induced DNA damage in pBR322 plasmid. *Illicium verum* extract may contribute for development of phytotherapeutic products that could be more cost effective, safer, and more accessible and provide a lower risk of resistance than conventional therapeutic drugs (Sri *et al.*, 2015). Ritter *et al.* (2014) also found that anethole which has been found in both star anise and anise exerts a peripheral antinociceptive effect without causing sedation. They did propose anethole as an interesting therapeutic alternative in inflammatory and painful diseases. Li *et al.* (2017) showed that *I. verum* fruit extracts exhibit considerable potential for *M. persicae* control programs. Huang *et al.* (2016) indicated that the cellulase-ultrasonic assisted extraction technology has the potential be used for the industrial production of flavonoids from *I. verum*. Chinese star anise is commonly used in Iranian traditional medicine as antimicrobial (Amin, 2005), while *I. verum* has long been used in traditional Chinese medicine with the actions of dispelling cold and relieving pain (Wang *et al.*, 2011). Lenora *et al.* (2016) concluded that commercial use of star anise could be an alternative for the management of water hyacinth, contributing to solve environmental and economic problems caused by it. Zhou *et al.* (2016) have found that star anise extracts showed significant inhibitory effects on aerobic bacteria counts; besides, star anise extracts showed antimicrobial activity against amine producers. Peng *et al.* (2016) have suggested that the SJYB extractives of *I. verum* had a function in activating the acquired immune response and a huge potential in biomedicine. Diaz *et al.* (2014) have found that the mixture of star anise and chamomile decreased the completion percentage of the activated carbon, delayed the appearance of diarrhea and decreased the number of evacuations in comparison with the control treatments. They have finally proposed that the combination of chamomile and star anise can be used as an alternative anti-diarrheal treatment. Yadav and Bhatnagar (2007) indicate that the treatment with star anise rescues the tumor burden, lowers oxidative stress and increases the level of phase II enzymes, which may contribute to its anti-carcinogenic. Both the essential oil from Chinese star anise fruit and trans-anethole are major constituents and exhibit potent inhibitory effect against all test fungi indicating that most of the observed anti-fungal properties was due to the presence of trans-anethole in the oil, which could be developed as natural fungicides for plant disease control in fruit and vegetable preservation (Huang *et al.*, 2010; Vecchio *et al.*, 2016).

3. Anise

3.1. Occurrence and cultivation

China has important potential to produce aromatic and medical plants and herbs due to its various biological diversity and different climatic conditions (Chen *et al.*, 2013; Ogbaji *et al.*, 2013; Shahrajabian *et al.*, 2017; Yong *et al.*, 2017). Aromatic plants such as anise seed have a long traditional use in both folk and conventional medicine and of course in the pharmaceutical industry (Abouzid and Mohamed, 2011; Ibrahim *et al.*, 2017). Anise (*Pimpinella anisum*) is a herbaceous annual plant, native to Mediterranean region and primarily grown for both fruits and seeds (Zand *et al.*, 2013). It has been reported, it is also indigenous to Iran, India and Turkey

(Kucukkurt *et al.*, 2009). Its fruits, known also as aniseed, were used as traditional medicine in China as early as in the 5th century. Fruits of this plant contain fatty oil, proteins, carbohydrates and cellulose fibers. In European countries consumption of anise fruits is more than its production so the amount of imported anise fruits reached about 2000 t in 2004 (Ullah *et al.*, 2014). Among other countries Germany remains the largest spice importer of anise (Rapisarda 2004). Sirisha and Sujathamma (2018) noticed that anise usually grows on dry rocky places, rocky crevices, fields, meadows, mountains pastures and grasslands, and its seed germination in nature is very poor. The *Pimpinella anisum* has common names in different countries such as: Anis vert (France); Anise seed (Japan); Anise and Star anise (the USA); Annesella (Italy); Anisa, Badian, Kuppi, Muhuri, Saunf and Sop (Iran and India); Boucage anis, Petit anise (North Africa), and anise (England) (Ross, 2001; Khare, 2007). Anise is shown in Figure 2.

Classification of *Pimpinella L.*

Kingdom: Plantae

Subkingdom: Tracheobionta

Super division: Spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Sub class: Rosidae

Order: Apiales

Family: Apiaceae

Genus: *Pimpinella*



Figure 2. Anise.

3.2. Anise nutritional composition and chemical constituents

Anethole which is used in pharmaceutical, food, perfumery and flavouring industry, is the most important constituent of anise (Ozkan and Chalchat, 2006; Tuncturk and Yildirim, 2006). The yield and anethole content of aniseed are affected by the genotype, the ecological conditions and especially by agricultural practices such as the irrigation, plant population, fertilizer and planting date (Asadi-kavan *et al.*, 2009; Ozel, 2009; Acimovic *et al.*, 2014). Apart from anethole, anise is well-known for essential oil which gives it the characteristic odor and aroma. Although, the major component of anise oil is trans-anethole (75-90%), other constituents include coumarins (umbelliferone, umbelliprenine, bergapten, and scopoletin), lipids (fatty acids, beta-armylin, stigmaterol and its salts), flavonoids (flavonol, flavone, glycosides, rutin, isoorientin and isovitexin), protein and carbohydrate (Yamini *et al.*, 2008; Picon *et al.*, 2010). It has been reported that apiaceae seed are used in food industry such as bread, biscuits and cookies as ingredients, and in meat industry, Apiaceae are favorable spices. (Acimovic *et al.*, 2015). Mean values or components of anise essential oil analyzed by GC-MS is presented in Table 4. Anise methanolic extract and molecular formula is shown in Table 5. Oil content and fatty acid composition of anise is presented in Table 6.

Table 4. Mean values or components of anise essential oil analyzed by GC-MS (Ullah *et al.*, 2013).

No.	Components	Kovats retention index	%
1	Estragol	1197	0.33
2	Cis-Anethole	1252	0.14
3	Trans-Anethole	1287	82.1
4	δ -Elemene	1333	0.45
5	β -Elemene	1388	0.08
6	α -Himachalene	1449	0.71
7	γ -Himachalene	1478	7.0
8	α -Amorphane	1482	0.15
9	(E)-Methylisoeugenol	1489	0.14
10	α -Zingiberene	1493	0.77
11	β -Himachalene	1499	0.44
12	α -Muurolene	1502	0.15
13	β -Bisabolene	1506	0.38
14	β -Sesquiphellandrene	1522	0.05
15	Spathulenol	1580	0.04
16	Unknown	1629	0.05
17	α -Cadinol	1651	0.08
18	Unkown	1831	5.95
19	Unknown	1886	0.92

No. of identified compounds.

Table 5. Anise methanolic extract and molecular formula.

No.	Compound Name	Molecular Formula
1	Anethole	$C_{10}H_{12}O$
2	Varidiflorene	$C_{15}H_{24}$
3	Eicosane	$C_{20}H_{42}$
4	Docosane	$C_{22}H_{46}$
5	Nonadecane	$C_{19}H_{40}$
6	Pentadecane	$C_{15}H_{32}$
7	Butanoic acid	$C_{15}H_{20}O_3$
8	Heneicosane	$C_{21}H_{44}$
9	Octacosane	$C_{28}H_{58}$
10	Hexadecane	$C_{20}H_{42}$
11	Cyclohexane	$C_{26}H_{50}$

Table 6. Oil content and fatty acid composition of anise (Alfekaiki, 2018).

Element	Mineral contents (%)
Carbon	34.5
Oxygen	21.1
Nitrogen	ND
Aluminum	20.5
Bromine	14
Iron	ND
Copper	3.63
Lanthanum	5.85
Palladium	0.35
Sulfur	0.15
Potassium	ND
Magnesium	ND

3.3. Potential health benefits, medicinal uses of anise in modern medicine industry

Seeds of anise are used as analgesic in migraine and also as carminative, aromatic, disinfectant and diuretic in traditional medicine (Amin, 2005). In some traditional texts, anise is mentioned for melancholy, nightmare, and also in treatment of epilepsy and seizure (Mirheydar, 2001). Shobha (2013) noticed that aniseed is a potent anti-oxidative and anti-diabetic agent and thereby, possess a vast spectrum of applications and exploitations in the food and drug industry. Ciftci *et al.* (2005) showed that anise oil has anethole as active ingredients and also eugenol, methylchavicol, anisaldehyde and estragole. Rebey *et al.* (2017) revealed that aniseeds might constitute a novel source of natural antioxidants and could be used as food additive. Acimovic *et al.* (2014) found that drought cause a significant decrease in thousand seed weight, germination energy and total germination as well as essential oil content in anise. Contrary to this finding, the content of trans-anethole was significantly higher in the dry year. Ibrahim (2008) reported that according to the traditional thinking, drinking anise by boys maybe harmful to their reproductive system. Kreydiyyeh *et al.* (2003) found that extracts of the aniseeds are used as medicine for their diuretic and laxative effect, expectorant and anti-spasmodic action, and their ability to ease gastric pain and flatulence. Ibrahim *et al.* (2017) reported that waste residues of anise and star anise are promising new sources of phenolic antimicrobial compounds which offer new commercial opportunities to pharmaceutical industry. They have suggested that combination of anise waste extracts with some antibiotics leads to new choice for treatment of infectious diseases and waste extracts may act as activity modifying agent for antibiotics. Islam *et al.* (2016) reported that aniseed extracts showed positive antibacterial effects on only three bacteria, named, *Bacillus cereus*, *Bacillus subtilis* and *Streptococcus pneumoniae*. They have also found that the phytochemical analysis of the aqueous extract revealed the presence of alkaloids, flavonoids, saponins, tannins, terpenoids, phenolic compounds and cardiac glycosides. Fouda *et al.* (2014) indicated that the anise extract shows good performance as corrosion inhibitor 1 M HCl, and also the anise extract inhibits the corrosion by getting adsorbed on the metal surface following Langmuir adsorption isotherm. Uysal *et al.* (2007) reported that fruits of anise use for treatment of infections, angina, bronchitis, gastritis, laryngitis and migraine. Mohamed *et al.* (2015) showed that the petroleum ether, chloroform, ethyl acetate and methanol extracts of *P. anisum* (1:10 and 2:10) were highly active (30-40 mm) against *B. subtilis*. The ethyle acetate extract exhibited moderate activity (15 mm) against *E. coli* and low activity (13 mm) against *Ps. aeruginosa*. The methanol extract of *P. anisum* showed high activity (16 mm) against *E. coli*, low activity (13 mm) against *Ps. aeruginosa*, and the methanol extract have variable activity against all test organisms. Yazdani *et al.* (2009) concluded that anise can be a candidate for further studies due to their antifungal potencies. Rebey *et al.* (2019) indicated that the determination of optimal periods and provenances for antioxidant accumulation can be used to evaluate the quality of aniseeds and could be important for industries. Khudor *et al.* (2013) mentioned that *Pimpinella anisum* and some antibiotics by disc diffusion methods and minimum inhibitory concentration, the results showed these bacterial isolates were sensitive to the aqueous extract compared with methanol, acetone and petroleum ether and were more sensitive to vancomycin compared with other antibiotics. Karimzadeh *et al.* (2012) indicated the anticonvulsant and neuroprotective effects of anise oil, likely via inhibition of synaptic plasticity. Bagdassarian *et al.* (2013) stated that the seeds of anise are rich in phytochemical contents, which possessed high antioxidant and antimicrobial activities and they can be used for health supplement and pharmaceutical benefits. Aydemir *et al.* (2015) observed that trans-anethole has the potential to inhibit QS (Quorum sensing)-regulated virulence factors in *P. aeruginosa* by binding to LasR protein, similar to its natural ligand *N*-(3-oxododecanoyl)- γ -homoserine lactone. Mahood (2012) concluded that anise oil extract can decrease signs of polycystic ovary syndrome (PCOS) in the ovarian tissue and altered concentrations of luteinizing hormone. Singh *et al.* (2008) stated that the antioxidant potency of anise oil and its methanol and ethanol oleoresins, can be utilized for protecting fat-containing foods. Diaz *et al.* (2014) stated that mixture of chamomile and star anise decrease the completion percentage of the activated carbon, delayed the appearance of diarrhea and decrease the number of evacuations in comparison with the control treatments. They have suggested the combination of chamomile and star anise as an alternative antidiarrheal treatment. Ibrahim (2008) concluded that anise oil administration inhibited GST expression, besides decreasing testosterone, T3 and T4 hormones and inhibiting sperm counts and sperm motility. Al-Omari *et al.* (2018) concluded that anise possesses immunomodulatory activity when apply orally in mice and selectively activates cell-mediated immune mechanisms. Ciftci *et al.* (2005) indicated that anise is an annual herb indigenous to Iran, India, Turkey and many other warm regions and it could be considered as a potential natural growth promoter for poultry. Amina *et al.* (2016) showed that the aqueous extract of *P. anisum* L. can have a corrective effect against nephrotoxicity induced by lead, so *P. anisum* L. has a beneficial impact on the kidneys intoxicated with lead acetate. Mosaffa-Jahromi *et al.* (2017) suggested that anise oil could be a promising choice of treatment for depressed patients with irritable bowel syndrome. Shahamat *et al.* (2015) concluded that *P. anisum* possesses an

antidepressant-like activity similar to that of fluoxetine, which has a potential clinical value for application in the management of depression. Felsociova *et al.* (2015) reported that the most hopeful antifungal activity and killing effect against all tested penicillia was found to be *Pimpinella anisum* and *Origanum vulgare L.* Rattan *et al.* (2014) showed that a formulation of biscuits with anise extract was prepared for enhancing the healthy beneficial usage of biscuits and nutraceutical, in conditions like cough or sore throat with a simultaneous attainment of the other health benefits. Kargozar *et al.* (2017) stated that *Pimpinella anisum* is effective in the treatments of acute menopausal syndrome with different mechanisms. Barbalho *et al.* (2015) suggested that *P. anisum* has potential to be used to control lipid levels. Radaelli *et al.* (2016) the use of essential oil from anise might serve as an alternative to the use of chemical preservatives in the control and inactivation of pathogens in commercially produced food systems. Kucukkurt *et al.* (2009) demonstrated that aniseed could be used at 30 g/Kg level in quail diets an increased antioxidant activity with glutathion (GSH) and a decreased blood malondialdehyde (MDA) levels. Shahamat *et al.* (2016) suggested that *P. anisum* possesses an antidepressant-like activity similar to that of fluoxetine, which has a potential clinical value for application in the management of depression. Abdel-Reheem and Oraby (2015) found that *Pimpinella anisum* essential oil residuals have high inhibitory effect for *Salmonella typhi*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Escherichia coli* and *Micrococcus luteus*. Pavela (2014) stated has the essential oil from *Pimpinella anisum* fruits and trans-Anethole were toxic for *Daphnia magna* (62-92% mortality) and significantly reduced its fertility at high concentrations (35-50 $\mu\text{L mL}^{-1}$) and long exposure (48 h). However, no negative effect on *Daphnia* mortality or fertility was found at shorter exposure times (6 h) and lower concentrations (20 $\mu\text{L mL}^{-1}$). Womeni *et al.* (2013) found that the powder of *Pimpinella anisum* has a special potent antioxidants for stabilization of crude soybean oil. Changizi *et al.* (2017) observed that the simultaneous use of ethanolic extract of *P. anisum* during gentamicin (GM) administration is recommended to reduce its nephrotoxicity effects. Barbalho *et al.* (2015) reported that *P. anisum* has potential to be used to control lipid levels. Kadan *et al.* (2013) noted that anise could be one of the foods that attribute to cancer prevention and treatment. It could be a natural source of novel anticancer compounds with anti proliferative and apoptotic properties. Bekara *et al.* (2015) observed that aniseed aqueous extract was effective in reducing the level of some of biochemical parameters and ameliorate behavior of intoxicated rats by lead. Nahidi *et al.* (2012) concluded that *P. anisum* is effective on the frequency and severity of hot flashes in postmenopausal women. Hosseinzadeh *et al.* (2014) stated that *P. anisum* aqueous and ethanolic extracts can increase milk production in rats. Sharifi *et al.* (2008) reported that anise is commercially cultivated in Iran and has been used in medicinal applications; moreover, their oil can be effective for protection of fresh fruits facing fungi and its essential oil can be considered as a potential, broad spectrum and safe substitute of chemical agents. Ashraffodin Ghoshegir *et al.* (2015) showed the effectiveness of anise in relieving the symptoms of postpartum depression. Shirzadi *et al.* (2017) noted that *P. anisum* ethanolic extract is effective in suppression of morphine physical dependence and further studies are needed to find out the responsible constituents and also the exact mechanisms of actions. Nikoskhan *et al.* (2015) observed that 250 and 300 mg/kg of hydroalcoholic extract of *P. anisum* seed significantly increased the duration of open arm ledges and decreased the duration of closed arm ledges in maze; in addition, this treatment resolved anxiety and relieved anxiety in rats. Nikfarjam *et al.* (2016) described that *Pimpinella anisum* is one the most important native medicinal plants of Iran with anti-anxiety properties. Amini *et al.* (2018) identified components of the essential oils and obtained results showed that *Pimpinella anisum L.* showed the most fumigant toxicity on the storage pests. The pharmacological effects of *Pimpinella anisum* is shown in Table 7.

Table 7. The pharmacological effects of *Pimpinella anisum* (Shojaii and Abdollahi Fard, 2012).

System	Effect
Organism	Antibacterial Antifungal Insecticidal Antiviral
Muscle	Muscle relaxant of tracheal chain Antispasmodic and relaxant of anococcygeus smooth muscle
Nervous system	Anticonvulsant Analgesic Conditioned place aversion in morphine dependence
Gastrointestinal	Laxative Increase glucose absorption from the jejunum
Renal	Reduce volume of urine by increase activity of the renal $\text{Na}^+\text{-K}^+\text{-ATPase}$

Endocrine	Antidiabetic Hypolipidemic
Immune system	Antioxidant
Others	Reduction of menopausal hot flashes Growth promoter of day-old broilers Reduction of pain in dysmenorrhea

4. Conclusions

Aromatic and medicinal plants are gifts of nature which have been used against different diseases since the beginning of the history. Star anise (*Illicium verum* Hook. f.) is one of the most famous evergreen tree which has originally distributed in tropic and subtropic areas of Asia, especially China, and it is famous as in traditional Chinese medicine as well as traditional Asian medicine. Its fruit also commonly used spice. Chinese star anise together with the morphological similar Japanese star anise together with the morphologically similar Japanese star anise (*Illicium anisatum*), is also used for decoration purposes. The Japanese star anise is extremely toxic and is not edible in any form. It has been reported that (E)-Anethole, limonene, linalool, and α -pinene are major components of the essential oil of *I. verum*. The most important compounds of Chinese star anise are α -Pinene, β -Pinene, Myrcene, α -Phellandrene, 3-Carene, α -Terpinene, p-Cymene, Limonene, Trans-Ocimene, Cis- β -Ocimene, γ -Terpinene, Terpinolene, Linalool, γ -Terpineol, 4-Terpineol, α -Terpineol, Estragole, Cis-Anethole, Trans-Anethole, α -Cubebene, β -Clemene, Caryophyllene, Bergamotene, Δ -Cardinene, and α -Cadinol. Star anise is one of the many species that contain bioactive compounds as well as a number of phenolic and flavonoid compounds, having antioxidant, preservative and antimicrobial properties. Star anise considered as the main source of shikimic acid, which is the most important ingredient of Tamiflu drug. Chinese star anise has anti-bacterial and anti-fungal characters, and it is useful in treatment of diseases like asthma, bronchitis and dry cough, it is also good to having a good sleep; it is a natural breath fresher, one of its most compounds is Shikimic which is used as a drug in curing influenza and flu virus; it consists of Linalool which is good for overall health because of its anti-oxidants characters. Its seeds are good source of minerals like calcium, iron, copper, potassium, manganese, zinc, and magnesium. Important compounds found in anise seed include estragol, p-anisaldehyde, anise alcohol, acetophenone, pinene, and limonene, but the most important volatile oil that gives the characteristic sweet, aromatic flavor to seeds is anethole. The recent studies have shown that anise seeds and essential oil have antioxidant, antibacterial, antifungal, anticonvulsant, anti-inflammatory, analgesic, gastro-protective, antidiabetic and antiviral activities. Other important benefits of anise seeds are stimulant, carminative, expectorant, insecticide, vermifuge, digestive, antispasmodic, anti-rheumatic, antiseptic, anti-epileptic, anti-hysterical, culinary significance, keeps the heart strong by its importance role to control the blood pressure, one of the best gas-releasing agent, easing many hormonal problems in females, hair benefits, skin benefits and it may reduce symptoms of depression. Anise seed and its extract also use in savory dishes, baked goods, and different drinks in both ancient and modern time. Anise seeds are good source of many essential B-complex vitamins such as pyridoxine, niacin, riboflavin and thiamin. The seeds are also important source of minerals like calcium, copper, potassium, iron, manganese, magnesium and zinc. Anti-oxidant vitamins such as vitamin C and A are also foundable in the spice. Combined with a nutritious diet, other traditional Chinese and Asian medicine, Chinese star anise and anise seed may improve various aspects of health.

Conflict of interest

None to declare.

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