Acupuncture and Herbal Medicine

Star anise (*Illicium verum* Hook. f.): dual therapeutic and nutritional potential in food and medicine

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Abstract

Star anise (*Illicium verum* Hook. f., SA) is a well-known culinary seasoning in China and Vietnam. Actually, SA also has been widely used as a traditional Chinese medicine in China with a long history. Phytochemical analysis has revealed that SA contains a high concentration of essential oils, phenols, flavonoids, and other bioactive compounds that contribute to its diverse pharmacological properties. These properties include antibacterial, anti-inflammatory and analgesic, anti-oxidation, antiviral, anti-cancer, anti-diabetes, antidiarrheal, and promoting hair growth. Various preclinical studies have shown that SA extracts and their active constituents may have potential therapeutic applications in preventing and treating various diseases. However, a comprehensive report on the relationship between the active ingredient, biological activity, and food characteristics of SA is rare. The medicinal value of SA has not been well valued and developed. This review provides an overview of the botanical chemistry and pharmacological properties of SA, as well as its potential innovative applications in food and personal care products, aiming to provide theoretical support for its further development and utilization.

Keywords: Homology of medicine and food, Pharmacology, Phytochemistry, Star anise

Graphical abstract: http://links.lww.com/AHM/A149

Introduction

Star anise (*Illicium verum* Hook. f., SA) is the dried ripe fruit of the Magnoliaceae plant *Illicium verum* Hook. f. It has anise-scented star-shaped fruit, which is a famous spice[1] and is widely distributed in China and Vietnam[2]. SA also can be found in the United States of America, Germany, Japan, and other countries, according to the database of the Global Biodiversity Information Facility (https://www.gbif.org/). The mature anise herb of Guangxi Province has better biological activity, so SA from Guangxi Province is called "Daodi herbs" in traditional Chinese medicine. There are 10 famous "Daodi herbs" in Guangxi Province, collectively called "Gui Shi Wei." Unlike the Japanese SA *Illicium anisatum*, Chinese SA *Illicium anisatum* has no neurotoxins in fruits and seeds[3], and no toxic side effects, such as nausea and vomiting, tonic-clonic seizures[4], and epileptic seizures[5]. It is a natural plant used for both medicine and food[6,7].

Numerous contemporary investigations on the phytochemistry of extracts or active ingredients from *Illicium* plants have been carried out in recent years. Research has focused on identifying chemical substances and pharmacological effects of SA. Up to now, phenols, terpenoids, alkaloids, and secondary metabolites, for example, phenylpropanoids, flavonoids, neolignans, monoterpenes, and sesquiterpenes, have been isolated from SA[8].

Additionally, numerous *in vivo* and/or *in vitro* investigations have demonstrated that extracts and compounds from *Illicium* plants and their volatile oils possess a wide range of pharmacological activities, including antiviral[9], antibacterial[10], anti-inflammatory[11], antioxidative[12], antidiabetic[13], hair promotive, and immune-boosting activities, etc. Apart from its application in the Traditional Chinese Medicine system, anise fruit is also mentioned in the Indian Traditional Medicine system, mainly for the treatment of indigestion, intestinal gas, spasmodic colic, dysentery, cough, asthma, rheumatoid arthritis, facial paralysis, etc[14].

However, the brilliance of SA as a cooking seasoning conceals its medicinal value, resulting in the need for more attention and in-depth development of the therapeutic value of SA. Thus, an overview of the phytochemistry and pharmacology properties of SA is presented in this review, including its chemical composition,

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mechanism of action, and potential clinical applications, to offer a scientific basis and theoretical guidance for the future development of more therapeutic drugs, novel natural edible products, and functional foods from SA.

Methods

The PRISMA guidelines were followed in the preparation of this review. A literature search was conducted using databases, including Web of Science, PubMed, the China National Knowledge Infrastructure (CNKI), and Wan-fang database. Keywords used were SA, *Illicium verum* Hook.f., star anise essential oil (SAEO), Homology of medicine and food, pharmacology, phytochemistry, and antibacterial, anti-inflammatory, analgesic, anti-oxidation, antiviral, anti-cancer, anti-diabetes, antidiarrheal, and promoting hair growth, etc, and combinations of these keywords. All selected articles were from 2002 to 2024, and we excluded conference abstracts and hypothesis articles. We summarized the method in Figure 1.

Phytochemistry of SA

As a commonly used cooking spice at home and abroad, SA can be described as a treasure of the whole body. Regardless of roots, leaves, and fruits, they are rich in chemical components (Tables 1–3). The most widely used is its fruit, which is the traditional medicinal and food homologous material in China and other Southeast Asian countries, and its chemicals are also the most extensive. However, due to the inclusion of *Illicium anisatum* (Japanese SA), numerous adverse neurological reactions have been in infants treated with SA tea[36]. Therefore, it is necessary to distinguish between the two types of SA. In the study of Howes et al.[26], thermal desorption-gas chromatography-mass spectrometry (TD-GC-MS) analysis was used to identify three common volatile components in both types of SA (limonene, 1,8-cineole, β-caryophyllene). In addition, three unique components (estragole, trans-anethole, foeniculin) were detected in *Illicium verum* (Bajiao Huixiang) and six unique chemical components (Safrole, eugenol, asaricin, methoxyeugenol, eugenol derivative, and methoxyeugenol derivative) were detected in *Illicium anisatum* (Riben Mangcao). Ultimately, four components, including methoxyeugenol, asaricin, eugenol derivatives, and methoxyeugenol derivatives, were identified to distinguish the chemical compositions of the fruits of *Illicium verum* and *Illicium anisatum* (Riben Mangcao).

In recent years, most of the research on SA has focused on the extraction, isolation, identification, and biological activities of essential oil components in its fruit. The main extraction methods of SA essential oil were steam distillation[37], supercritical CO_2 extraction[38], simultaneous hydrodistillation and static headspace liquid-phase microextraction[30], liquid carbon dioxide, microwave-assisted soxhlet extraction[32], and others. SAEO has been shown to have good anti-inflammatory[39], antibacterial[40], and antioxidant[41] biological activities. In addition, SA fruit is abundant in phenols, flavonoids[42], terpene, essential oils, coumarins, alkaloids, and other chemical composition (Table 3). Thus far, no systematic studies have been conducted to clarify the correlation between these active ingredients and the biological activity of *Illicium verum* Hook. f. (Bajiao Huixiang).

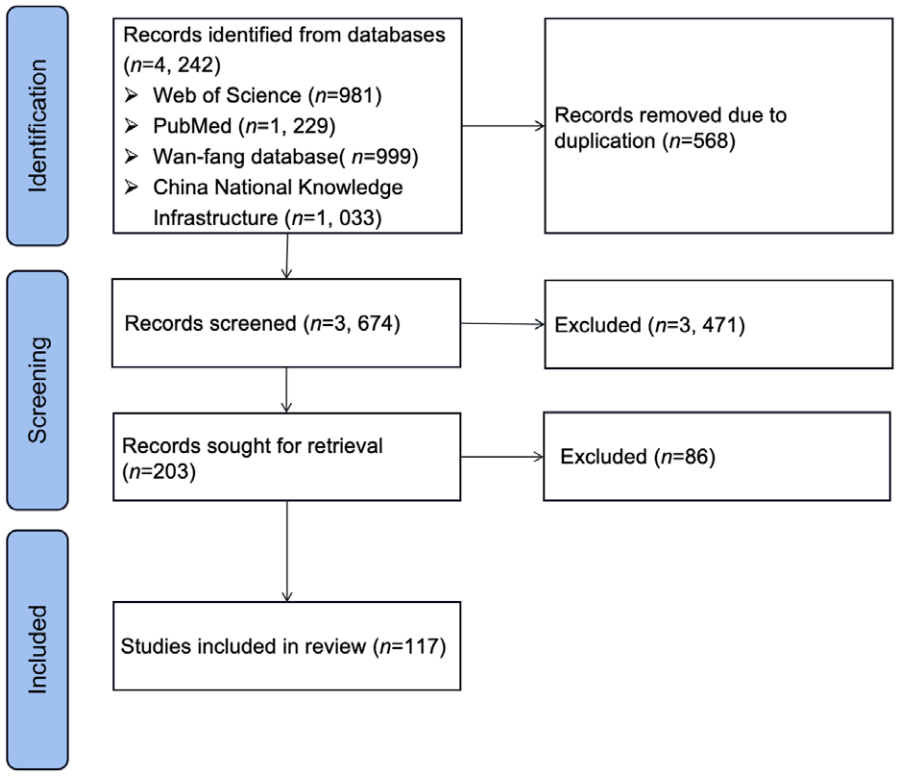
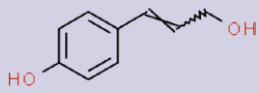
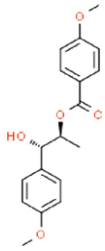
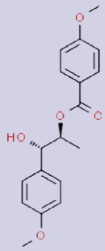
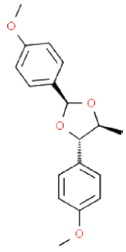
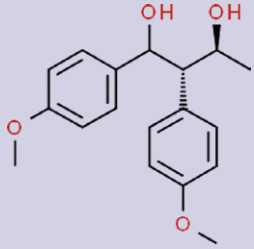
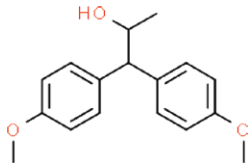
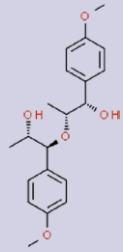


Figure 1. Flow diagram of literature search according to PRISMA guidelines. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1

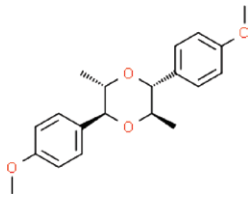
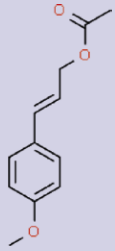
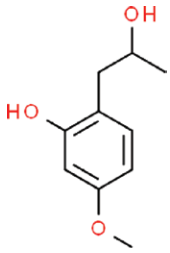
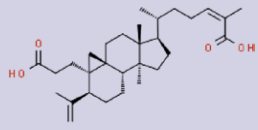
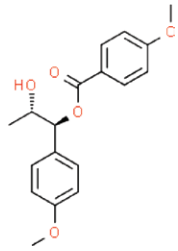
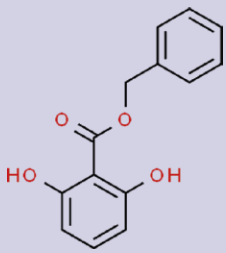
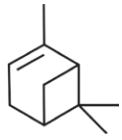
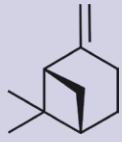
The chemical composition of SA leaves

Category	Name	CAS	Structure	Extraction method	Reference
Phenylpropanoid	p-Coumaryl alcohol	3690-05-9		The fresh sample (1.2 kg) was ground to a fine powder under liquid N_2 and extracted with CH_2Cl_2 over several days. The organic extract was then dried and evaporated under reduced pressure to yield a dark green oil (26.5 g; 2.2% w/w).	[15]
	verimol A	212516-34-2		The extraction method is the same as above.	[15]
	Verimol B	212516-35-3		The extraction method is the same as above.	[15]
	Verimol C	/		The extraction method is the same as above.	[15]
	Verimol D	212516-37-5		The extraction method is the same as above.	[15]
	Verimol F	212516-39-7		The extraction method is the same as above.	[15]
	Verimol G	/		The extraction method is the same as above.	[15]

(*Continued*)

Table 1

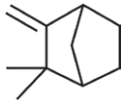
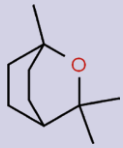
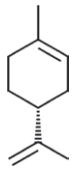
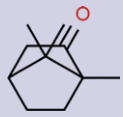
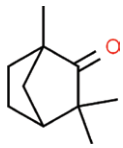
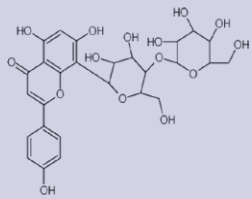
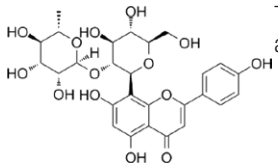
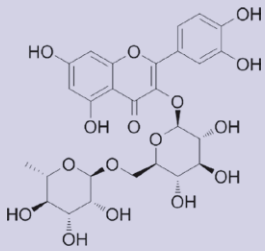
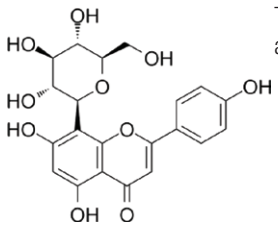
(Continued)

Category	Name	CAS	Structure	Extraction method	Reference
	Verimol H	/		The extraction method is the same as above.	[15]
	Verimol I	53484-54-1		The extraction method is the same as above.	[15]
	Verimol J	212516-43-3		The extraction method is the same as above.	[15]
	Nigranoic acid	39111-07-4		The extraction method is the same as above.	[15]
	Schizandronic acid	55511-14-3		The dichloromethane extract of the leaves of *Illicium verum*	[16]
Phenols	Verimol K	85985-75-7		The fresh sample (1.2 kg) was ground to a fine powder under liquid N_2 and extracted with CH_2Cl_2 over several days. The organic extract was then dried and evaporated under reduced pressure to yield a dark green oil (26.5 g; 2.2% w/w).	[15]
Monoterpenoids	α-Pinene	2437-95-8		Hydrodistillation-headspace solvent microextraction followed by GC-MS	[17]
Flavonoids	β-Pinene	18172-67-3		5 g of ground leaf powder and 130 mL of 67% ethanol (V:V) were mixed using microwave-assisted extraction	[17]

(*Continued*)

Table 1

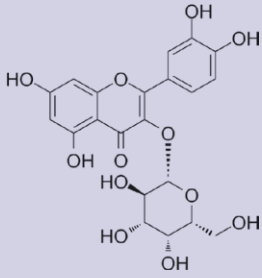
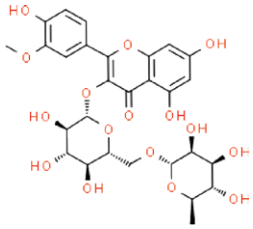
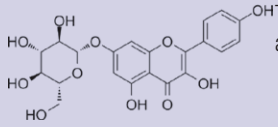
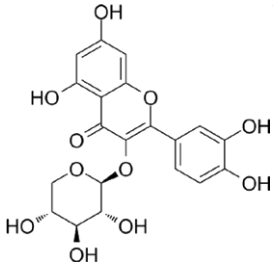
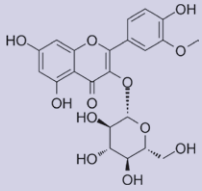
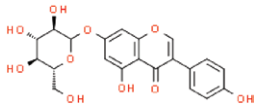
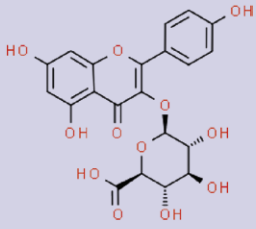
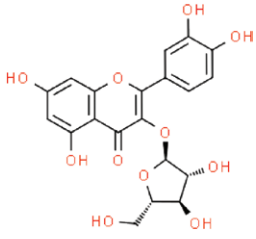
(Continued)

Category	Name	CAS	Structure	Extraction method	Reference
	Camphene	79-92-5		The extraction method is the same as above.	[17]
	1,8-Cineole	470-82-6		The extraction method is the same as above.	[17]
	D-Limonene	5989-27-5		The extraction method is the same as above.	[17]
	Camphor	76-22-2		The extraction method is the same as above.	[17]
	L-Fenchone	1195-79-5		The extraction method is the same as above.	[17]
	Vitexin-4“-O-glucoside	178468-00-3		The extraction method is the same as above.	[17]
	Vitexin-2”-O-rhamnoside	64820-99-1		The extraction method is the same as above.	[18]
	Rutin	153-18-4		The extraction method is the same as above.	[18]
	Vitexin	3681-93-4		The extraction method is the same as above.	[18]

(*Continued*)

Table 1

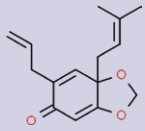
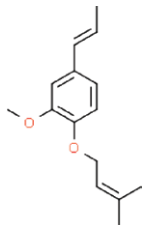
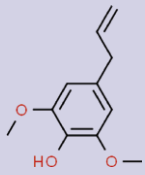
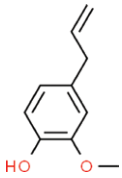
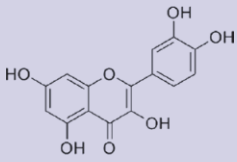
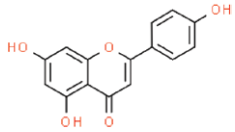
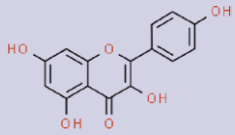
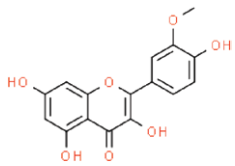
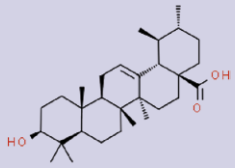
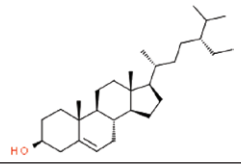
(Continued)

Category	Name	CAS	Structure	Extraction method	Reference
	Hyperoside	482-36-0		The extraction method is the same as above.	[18]
	Isorhamnetin-3-O-rutinoside	604-80-8		The extraction method is the same as above.	[18]
	Kaempferol-7-glucoside	16290-07-6		The extraction method is the same as above.	[18]
	Quercetin-3-O-xylopyranoside	549-32-6		The extraction method is the same as above.	[18]
	Isorhamnetin-3-O-glucoside	5041-82-7		The extraction method is the same as above.	[18]
	Genistin	529-59-9		The extraction method is the same as above.	[18]
	Kaempferol-3-O-arabinoside	22688-78-4		The extraction method is the same as above.	[18]
	Avicularin	5041-68-9		The extraction method is the same as above.	[18]

CAS: Chemical abstracts service; GC-MS: Gas chromatography-mass spectrometry; SA: Star anise.

Table 2

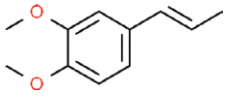
The chemical composition of SA roots

Category	Name	CAS	Structure	Extraction method	Reference
Phenylpropanoid	Illicinone A	219538-93-9		The dried roots of I. verum (8.0 kg) were powdered and extracted with 90 % EtOH (50 L × 3) under reflux.	[19]
	Illiverin A	915287-61-5		The extraction method is the same as above.	[19]
	Methoxyeugenol	6627-88-9		The extraction method is the same as above.	[20]
	Eugenol	202-589-1		The extraction method is the same as above.	[20]
Flavonoids	Quercetin	117-39-5		The extraction method is the same as above.	[20]
	Apigenin	520-36-5		The extraction method is the same as above.	[20]
	Kaempferol	208-287-6		The extraction method is the same as above.	[20]
	3′-Methoxyquercetin	207-545-5		The extraction method is the same as above.	[20]
Triterpenes	Ursolic acid	77-52-1		The extraction method is the same as above.	[20]
Others	β-Sitosterol	5779-62-4		The extraction method is the same as above.	[20]

(*Continued*)

Table 2

(Continued)

Category	Name	CAS	Structure	Extraction method	Reference
	1-Hexacosanol	506-52-5		The extraction method is the same as above.	[20]
	Methylisoeugenol	93-16-3		The extraction method is the same as above.	[20]

CAS: Chemical abstracts service; SA: Star anise.

Pharmacology of SA

Illicium verum Hook. f. (Bajiao Huixiang) is a traditional Chinese herbal medicine that has been widely studied for its pharmacological properties. Research has shown that SA has an array of biological effects, including antiviral, antibacterial, anti-inflammatory, antioxidant, antidiabetic, antidiarrheal, hair growth promoting, and immunity boosting, etc (Figure 2).

Antiviral activity

Essential oils are complex mixtures of volatile compounds, such as monoterpenes, sesquiterpenes, and phenylpropanoids[43], with the presence of phenylpropanes and sesquiterpenes contributing to the antiviral activity against Herpes simplex virus (HSV)[9]. SA is often praised for its antiviral properties, as it is the source of the precursor molecule shikimic acid, which is used to produce the anti-influenza drug oseltamivir (Tamiflu®) for both type A and B influenza[44]. Furthermore, SAEO and its isolated compounds exhibit potent antiviral effects. SAEO can exert its antiviral activity against HSV-1 by directly inactivating viral particles. This activity is dose-dependent and modulated through viral particle interactions[45]. In addition to directly inactivating viral particles, β-caryophyllene and isoeugenol present in SAEO may also interfere with the viral envelope structure or mask the viral structures necessary for adsorption or entry into host cells[46].

Research by Astani et al.[9] has shown that β-caryophyllene in SAEO is one of the most active antiviral compounds and can be used as a topical treatment for recurrent herpes infections. Its antiviral effect involves disrupting herpes virus adsorption and inactivating it before HSV enters cells, thus exerting antiviral activity but its antiviral mechanism is still unclear. Acyclovir was reported to inhibit viral DNA synthesis by acting as a substrate analog, terminating viral DNA chain elongation and ultimately inhibiting viral replication (Figure 3). Moreover, the components of SAEO, such as limonene, β-caryophyllene, and anethole, exhibit high antiviral activity against HSV-1, with a direct relationship between their lipophilicity and virus envelope disruption.

Currently, antiviral drugs generally face the problem of drug resistance, and the antiviral mechanisms of SAEO differ from those of existing clinical antiviral drugs. Therefore, in the context of a lack of effective treatments for viral infections, SAEO may be a potential alternative option.

Antibacterial activity

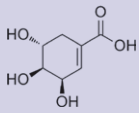
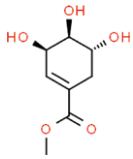
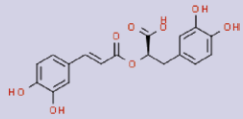
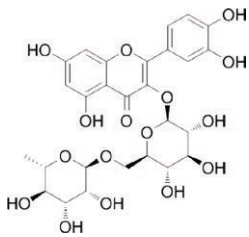
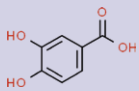
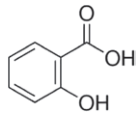
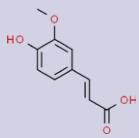
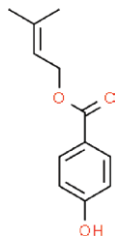
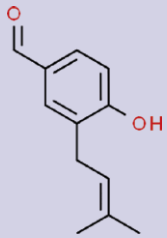
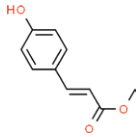
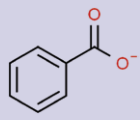
SA has essential oil components with strong antibacterial properties[47], which makes it can be used as a natural food-related antibacterial products (Figure 4), oral and skin antibacterial products, etc. Foodborne bacteria, such as *Staphylococcus aureus* (*S. aureus*), *Escherichia coli* (*E. coli*), and *Pseudomonas aeruginosa*, communicate with one another through quorum sensing (QS) systems to regulate microbial behavior, including the secretion of virulence factors and biofilm formation. SAEO inhibits the production of exopolysaccharide (EPS), weakens the *flhDC* master regulatory function of *E. coli*, *Salmonella*, and *Yersinia*, reduces cell differentiation, and decreases collective motility, ultimately impeding or even halting the growth of bacterial biofilm structures, thereby exhibiting antibacterial activity against foodborne pathogens. In addition, SAEO induces changes in membrane fluidity and integrity by causing damage to the cell membrane and reducing protein content. SAEO also inhibits key enzymes (CS, IDH, SDH, and G6PDH) in the tricarboxylic acid (TCA) cycle and hexose monophosphate (HMP) pathway in *E. coli* and *S. aureus*, reducing ATP synthesis and NADPH generation and eventually disrupting the mitochondria in bacteria, limiting the growth of *E. coli* and *S. aureus*[48].

The development of oral diseases is closely related to oral microbiology[49]. Preventing dental diseases is usually associated with a reduction in certain Gram-positive bacteria (such as *Streptococcus mutans* and *Lactobacillus*), Gram-negative bacteria (such as *Porphyromonas gingivalis* and *Actinobacillus*), and anaerobic bacteria. SAEO inhibits the maturation of *S. aureus* biofilm on enamel surfaces and reduces its prevalence within the oral cavity by lowering the expression levels of three GTF genes that are associated with biofilm formation. Tardugno et al.[50] formulated an alcohol-free mouthwash made from SAEO and tested its inhibitory activity against *Lactobacillus* using agar diffusion method. The results showed that SAEO kills oral microbiota by inhibiting enzyme activity, destroying cell walls, and inhibiting coaggregation between bacteria and biofilm formation[50].

Furthermore, protein profiling studies have revealed that for fungi, SAEO inhibits growth and ultimately leads to the death of *Aspergillus niger* by disrupting its energy metabolism by reducing ATP levels and cellular vitality and blocking the synthesis pathway of NAD. Therefore, SAEO can directly affect the cell membrane and metabolic pathways of fungi and bacteria, inhibiting their growth and reproduction and exhibiting antibacterial and antifungal activities. In addition to the essential oil of SA, there are flavonoids, terpenoids, and phenolic compounds in SA with antibacterial activity. Flavonoids and their hydroxylated derivatives exert antibacterial effects by interfering with bacterial receptor function[51]. Terpenoids and terpenes penetrate bacterial cells,

Table 3

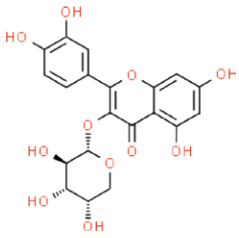
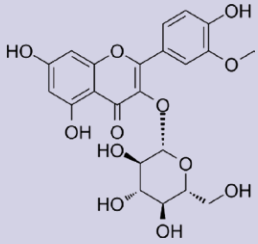
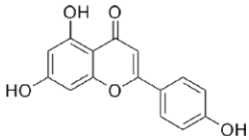
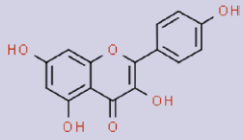
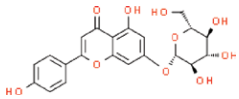
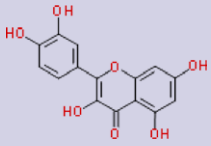
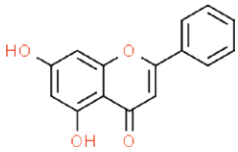
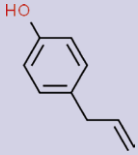
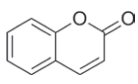
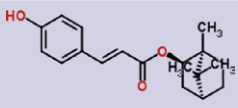
The chemical composition of SA fruits

Category	Name	CAS	Structure	Extraction method	Reference
Phenols	Shikimic acid	138-59-0		95% EtOH (3 × 40 L, each for 7 days) at room temperature, 90% methanol sonication	[21–22]
	Methyl shikimate	40983-58-2		95% EtOH (3 × 40 L, each for 7 days) at room temperature	[21]
	Rosmarinic acid	20283-92-5		Extracted by pressed warm water (37°C/18 h). The collected extract was sterilized using a sterile membrane (0.23 μm), and lyophilized by a Dura-Dry MP freeze-dryer	[23]
	Rutin	153-18-4		Extracted by pressed warm water (37°C/18 h)	[23]
	Protocatechuic	202-760-0		Extracted by pressed warm water (37°C/18 h)	[23]
	Salycilic	6934-3-8		Extracted by pressed warm water (37°C/18 h)	[23]
	(E)-Ferulic acid	97274-61-8		Extracted by pressed warm water (37°C/18 h)	[23]
	3-Methylbut-2-enyl-4-hydroxybenzoate	69844-87-7		95% EtOH (30L × 4) reflux extraction at room temperature	[8]
	4-Hydroxy-3-(3-methyl-2-buten-1-yl) benzaldehyde	54730-30-2		95% EtOH (30L × 4) reflux extraction at room temperature	[8]
	(E)-Methyl p-coumarate	3943-97-3		95% EtOH (30L × 4) reflux extraction at room temperature	[8]
	Benzoate	766-76-7		Methanol (three times) room temperature immersion extraction	[24]

(*Continued*)

Table 3

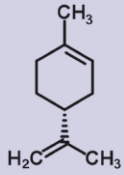
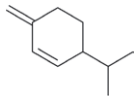
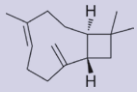
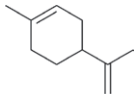
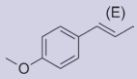
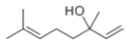
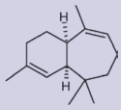
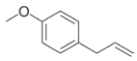
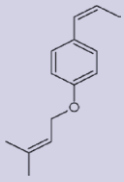
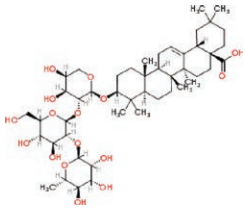
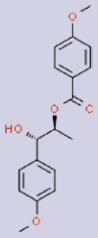
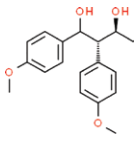
(Continued)

Category	Name	CAS	Structure	Extraction method	Reference
Flavonoids	Quercetin-3-O-a-L-arabinopyranoside	22255-13-6		95% EtOH (3 × 40 L, each for 7 days) at room temperature	[19]
	Isorhamnetin-3-O-B-D-galactopyranoside	5041-82-7		95% EtOH (3 × 40 L, each for 7 days) at room temperature	[19]
	Apigenin	520-36-5		Extracted by pressed warm water (37°C/18 h). The collected extract was sterilized using a sterile membrane (0.22 μm), and lyophilized by a Dura-Dry MP freeze-dryer	[23]
	Kaempferol	520-18-3		/	[25]
	Apigenin-7-glucoside	209-430-5		Extracted by pressed warm water (37°C/18 h)	[23]
	Quercetin	117-39-5		Extracted by pressed warm water (37°C/18 h)	[23]
	Chrysin	480-40-0		Extracted by pressed warm water (37°C/18 h)	[23]
	Chavicol	501-92-8		Hydrodistillation—static headspace liquid-phase microextraction—gas chromatography-mass spectrometry	[26]
Coumarins	Coumarin	91-64-5		Pressed warm water (37°C/18 h). The collected extract was sterilized using a sterile membrane (0.23 μm), and lyophilized by a Dura-Dry MP freeze-dryer	[23]
Terpene	(-)-Bornyl p-coumarate	55511-08-5		95% EtOH (30L × 4) reflux extraction at room temperature	[8]
	δ-3-Carene	13466-78-9		Microwave extraction technique; hydrodistillation method	[27–28]

(*Continued*)

Table 3

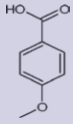
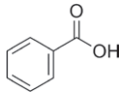
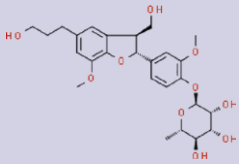
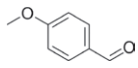
(Continued)

Category	Name	CAS	Structure	Extraction method	Reference
	β-Limonene	5989-27-5		The extraction method is the same as above.	[27–29]
	β-Phellandrene	555-10-2		The extraction method is the same as above.	[27–28]
	β-Caryophyllene	87-44-5		The extraction method is the same as above.	[27–28]
	Limonene	138-86-3		Soxhlet extraction with ethyl acetate as solvent	[30–31]
Esential oil	Trans-anethole	4180-23-8		Ethyl acetate Soxhlet extraction; Microwave-assisted Soxhlet extraction	[23,30,32]
	Linalool	78-70-6		Simultaneous distillation-extraction method	[27–28]
	γ-Himachalene	53111-25-4		Hydrodistilled anise oil	[29]
	Estragole	140-67-0		Hydrodistillation	[23, 27–29,33]
	Foeniculin	78259-41-3		Hydrodistillation (3 h), using a Clevenger type apparatus	[19,23, 27–28]
Others	Anemonenorin A	89412-79-3		95% EtOH (30L × 4) reflux extraction at room temperature	[8]
	Verimol A	212516-34-2		95% EtOH (30L × 4) reflux extraction at room temperature	[8]
	Verimol D	212516-37-5		95% EtOH (30L × 4) reflux extraction at room temperature	[8]

(*Continued*)

Table 3

(Continued)

Category	Name	CAS	Structure	Extraction method	Reference
	Anisic acid	1335-08-6		95% EtOH (30L × 4) reflux extraction at room temperature	[8]
	Benzoic acid	65-85-0		Methanol (three times) room temperature immersion extraction	[24]
	Icariside E4	126253-42-7		95% EtOH (3 × 40 L, each for 7 days) at room temperature	[21]
	4-Methoxybenzaldehyde	123-11-5		Ethyl acetate Soxhlet extraction; Microwave-assisted Soxhlet extraction	[30,34–35]

CAS: Chemical abstracts service; SA: Star anise.

causing bacterial deformation and functional impairment, and inhibit biofilm formation, thereby exhibiting antibacterial activity[52]. Phenolic compounds exert antibacterial effects by influencing cell permeability, inducing enzyme-hydrogen binding within cells, and affecting normal bacterial function[53]. Moreover, the bacterial biofilm is disrupted by phenolic compounds in SA, reducing bacterial pathogenicity and simultaneously preventing bacterial resistance[54]. The other potential related antimicrobial mechanisms of SA are summarized in Figure 5 and Table 4.

Anti-inflammatory and analgesic activity

In addition to volatile components with good antibacterial activity, SA also contains shikimic acid and other phenolic substances. Shikimic acid is not only the key starting material for the semi-total synthesis of oseltamivir for treating and preventing influenza[58] but also has many other biological activities, such as anti-inflammatory activity. Several studies have demonstrated the anti-inflammatory activity of shikimic acid *in vitro* and *in vivo*. For example, a study by You et al.[59] conducted *in vitro* anti-inflammatory activity experiments on shikimic acid using the lipopolysaccharide (LPS)-induced RAW 264.7 cell inflammatory model. The results showed that in RAW 264.7 cells, shikimic acid played an anti-inflammatory role by inhibiting LPS-induced cell viability, reducing nitrite accumulation and the production of pro-inflammatory cytokines, such as inhibiting the activation of the mitogen-activated protein kinase (MAPK) and nuclear factor-κB (NF-κB) pathways induced by IL-1β and inhibiting the increase of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX2) protein expression induced by IL-1β[59].

In another study, Sun et al.[60] showed that shikimic acid exhibited significant anti-inflammatory activity in mice with acetic acid-induced colitis and inflammation induced by xylene. Those may be due to the inhibition of ERK1/2 and P38 phosphorylation by shikimic acid, thereby reducing the production of pro-inflammatory factors(such as TNF-α, IL-1β, and NF-κB), thereby inhibiting the inflammation cascade reaction to play an anti-inflammatory role, while reducing TNF-α and prostaglandin (PGE)-induced inflammation and mechanical pain sensitivity[61]. In addition, the hot plate test and acetic acid-induced abdominal twisting experiment further confirmed the central and peripheral analgesic activity of shikimic acid.

Excessive fat accumulation leads to inflammatory reactions, and non-alcoholic fatty liver disease (NAFLD) characterized by lipid accumulation and liver inflammation is becoming a global epidemic[62]. Kim et al.[63] found that shikimic acid reduced the mRNA expression of lipid production-related genes (such as FAS, SREBP-2c, and LXR-α) in HepG1 cells and the protein expression of SREBP-1c and LXR-α in 2T3-L3 cells, that is, it inhibited lipid production-related genes at the mRNA and protein levels simultaneously. In addition, shikimic acid can also play a good role in reducing lipid synthesis by activating the cell energy charge sensor and "metabolic master switch" AMPK and its downstream ACC phosphorylation in HepG2, Huh7, and 3T3-L1 cells[63]. The current potential anti-inflammatory activity mechanisms of SA and related information are summarized in Figure 6 and Table 5.

However, there is currently a lack of mechanistic studies on using SA to prevent and treat metabolic diseases such as fat inflammation. Further studies are needed to fully elucidate the mechanisms underlying the anti-inflammatory activity of SA and explore its potential as a therapeutic agent for treating inflammatory disorders.

Antioxidant activity

An abundance of flavonoids is present in the SA. Kanatt et al.[67] reported that the phenolic content in the aqueous extract of SA was 237.69 mg/g extract, and the flavonoid content was 115.8 mg/g extract. Iftikhar et al.[68] employed the Folin-Ciocalteu method and aluminum chloride colorimetric method to evaluate the total phenolic (TP, using gallic acid as a standard) and total

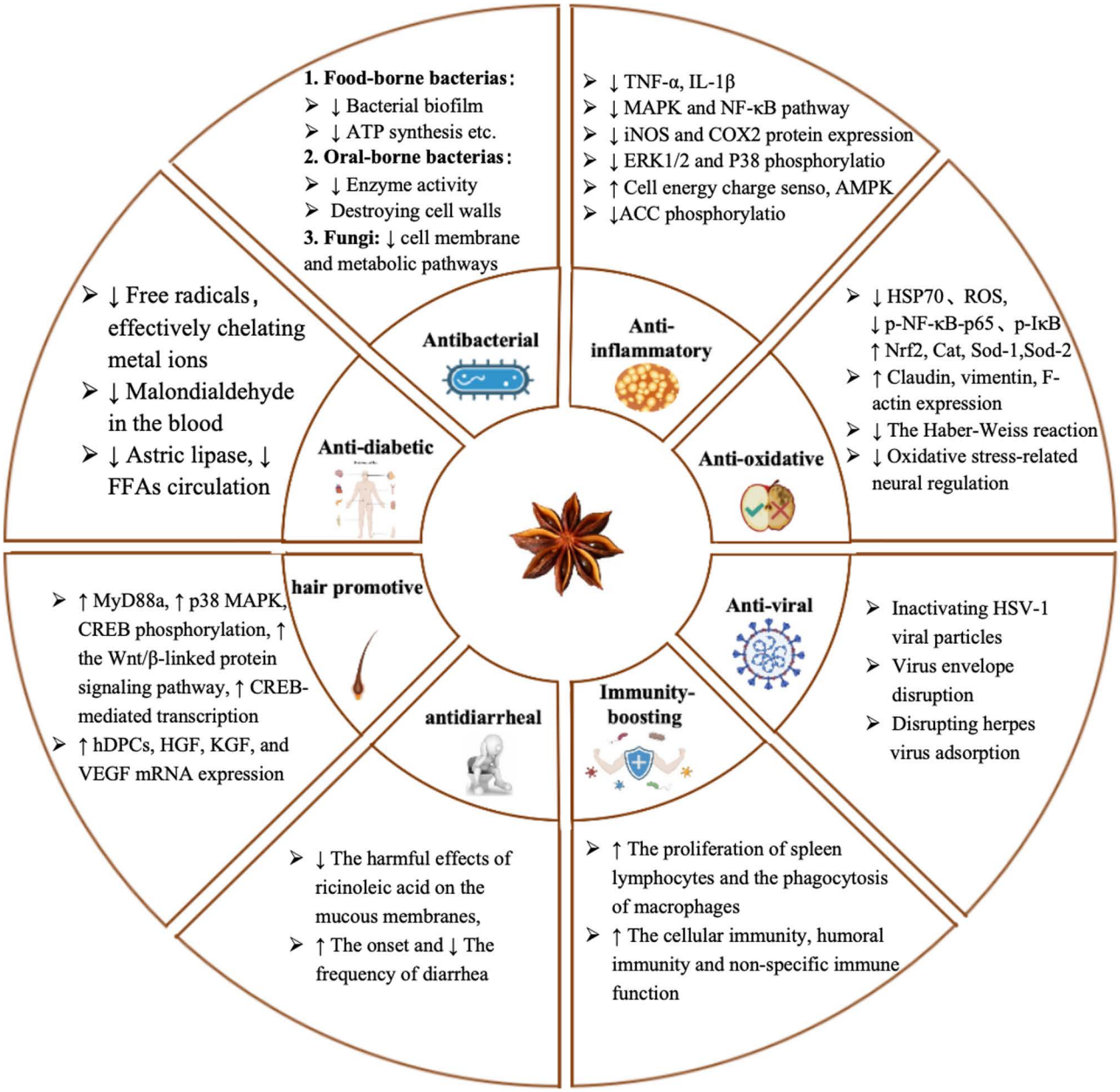


Figure 2. Summary of the biological effects of SA. SA possesses a wide range of pharmacological activities, including antiviral, antibacterial, anti-inflammatory, antioxidative, antidiabetic, antidiarrheal, hair promotive, and immune-boosting activities, etc. ACC: Acetyl-CoA carboxylase; AMPK: AMP-activated protein kinase; ATP: Adenosine triphosphate; Cat: Catalase; CREB: Cyclic-AMP response binding protein; FFA: Free fatty acids; hDPC: Human dermal papilla cell; HGF: Hepatocyte growth factor; HSP: Heat shock protein; HSV: Herpes simplex virus; IL: Interleukin; iNOS: Inducible nitric oxide synthase; KGF: Keratinocyte growth factor; MAPK: Mitogen-activated protein kinase; NF: Nuclear factor-κB; ROS: Reactive oxygen species; SA: Star anise; TNF: Tumor necrosis factor.

flavonoid (TF, using catechin as a standard) content in the aqueous extract of SA, respectively. The results showed that the total phenolic content in the aqueous extract accounted for 0.83 mg/g of dry plant material, and the total flavonoid content accounted for 1.24 mg/g of dry plant material[68]. These data collectively indicate that, in addition to high phenolic content, the aqueous extract of SA also contains a substantial number of flavonoids. In daily life, SA is often used similarly to water extraction when cooking meat, suggesting that the nutrients we consume from SA are predominantly phenolics and flavonoids.

Numerous studies have shown that flavonoids and flavonoid-like compounds exhibit potent antioxidative biological activities[69] and are recommended for defense against oxidative stress related to aging, allergies, and diabetes, among other physiological and pathological conditions[70]. These activities may be attributed to the chelation of flavonoid compounds with transition metal ions and/or the scavenging of reactive oxygen species (ROS) and enzyme inhibition. SA fruit contains flavonoids such as apigenin, quercetin, and luteolin (Table 3). Previous reports suggest that oxidized flavonoid monomers, such as apigenin and luteolin, can reduce blood sugar through their antioxidative activities. Studies have shown that the antilipid peroxidation activity of apigenin is related to its ability to scavenge 2,2-diphenyl-1-picrylhydrazyl radicals and its half-peak oxidation potential (E-p/2)[70]. Moreover, the 5 and 7 hydroxyl groups in the apigenin structure can chelate

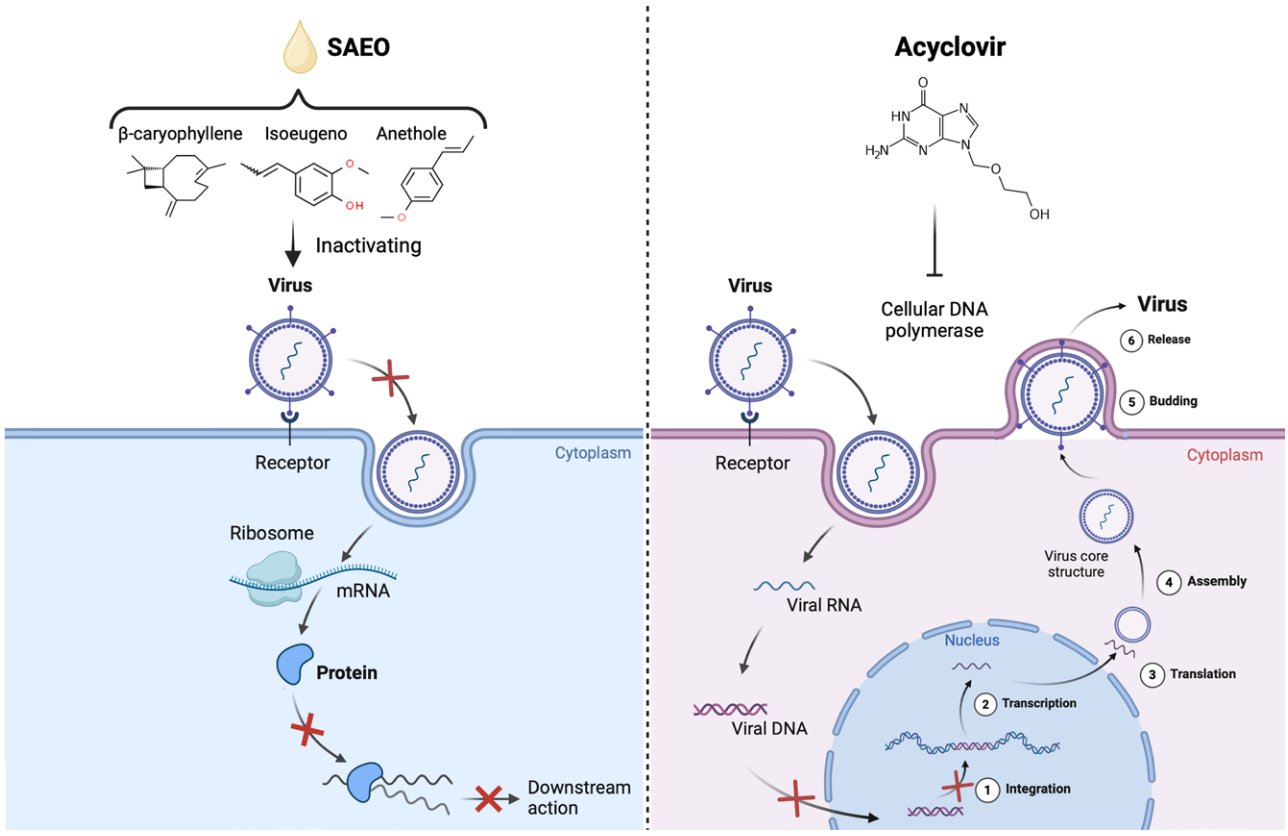


Figure 3. Antiviral effect of SA and the antiviral mechanism of acyclovir. The SAEO and its components β-caryophyllene, isoeugeno, and anethole exhibit antiviral activity by interfering with the viral envelope structure or masking the viral structures required for attachment to host cells, owing to their lipophilic properties and viral envelope-disrupting effects. Additionally, they disrupt the attachment of HSV and inactivate it before entry into the cells, thereby exerting antiviral effects. This mechanism is distinct from the mode of action of acyclovir, which acts by interfering with cellular DNA polymerase to inhibit viral replication. Created by BioRender.com. HSV: Herpes simplex virus; SA: Star anise; SAEO: Star anise essential oil.

transition metal ions (eg, intracellular Fe^{2+} or Cu^{+}), thereby reducing the capacity of H_2O_2 to transform into hydroxyl radicals *via* the Haber-Weiss reaction and exerting antioxidative effects. Consequently, apigenin has a protective effect on liver cells treated with tert-butyl hydroperoxide.

Furthermore, Liu et al.[71] found that quercetin and orcinol effectively intervened in spermatogenesis disorders through three pathways targeting oxidative stress, ROS metabolic processes, and the NF-κB pathway. The primary mechanisms involve reducing HSP70 and ROS expression levels in Sertoli cells, decreasing p-NF-κB-p65 and p-IκB levels, upregulating claudin, vimentin, and F-actin expression in Sertoli cells, and protecting Sertoli cell structure. These effects ultimately mitigate the decline in cell viability induced by heat stress[71]. In addition, quercetin can significantly improve hyperglycemia, dyslipidemia, and antioxidative status in type 2 diabetes by reducing endoplasmic reticulum oxidative stress, β-cell death, and inhibiting porcine pancreatic α-amylase and mammalian α-glucosidase[69]. Quercetin also exerts antioxidative effects by downregulating ROS levels and upregulating antioxidant gene expression (Nrf2, Cat, Sod-1, and Sod-2)[72]. Other flavonoids, such as hesperidin, have been shown to exert effective antioxidative and neuroprotective effects in STZ-induced diabetes by reducing oxidative stress-related neural regulation. The antioxidant activity of SA is likely primarily attributed to the presence of flavonoids and polyphenols. This potential mechanism can be succinctly summarized as follows: 1. scavenging free radicals; 2. chelating metal ions; 3. inhibiting oxidase activity; 4. enhancing antioxidant enzyme activity (Figure 7).

In addition to the above applications of SA antioxidant biological activities, it has also shown good application against gastric ulcers, which are mainly caused by oxidative damage. Ibrahim et al.[73] found that in two ulcer models, alcoholic gastric mucosal injury and aspirin gastric mucosal injury, SA extract increased glutathione reductase, superoxide dismutase, and peroxidase activities in the gastric mucosa of rats by promoting the production of reduced glutathione to alleviate gastric ulcer. It also significantly reduced the production of lipid peroxides and exerted good anti-gastric ulcer effects with the synergistic effect of various phenolic compounds[73].

Anti-diabetes activity

Khan et al.[74] used human serum albumin-fructose glycosylation assay to determine the anti-glycosylation activity of SA *in vitro*. The results showed that the anti-glycation activity of the ethanol extract of SA was five times that of the standard inhibitor rutin, showing good anti-glycosylation activity and inhibiting the formation of cross-linked advanced glycation end products (AGEs) in the model protein system. In addition, SA contains several phenolic and flavonoid compounds, which can inhibit the glycosylation of biomolecules by

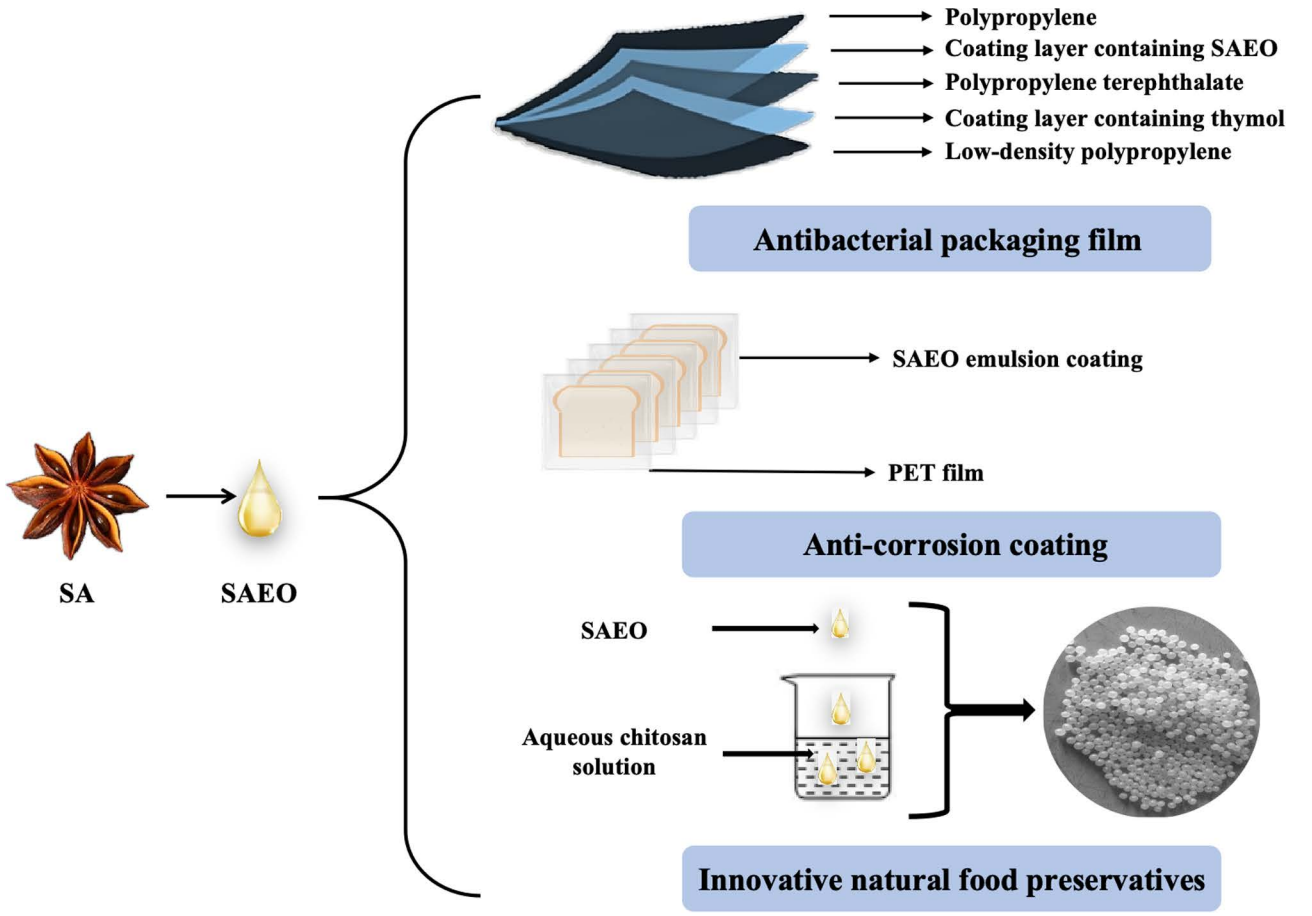


Figure 4. Innovative food materials of SA. SEAO is widely used in various food-related fields, such as food packaging, anti-corrosion coating, and innovative preservatives, due to its excellent antibacterial properties and bioactivity. PET: Polyethylene terephthalate; SA: Star anise.

scavenging free radicals and/or effectively chelating metal ions[75], and also effectively reduce the amount of malondialdehyde in the blood of STZ-induced diabetic rats[76]. In addition, the ethanolic extract of SA contains many phenolic substances. A study by Kamoun et al.[77] found the flavonoid myricitrin-5-methyl ether to be capable of inhibiting the catalytic activity of gastric lipase, lowering the levels of circulating FFAs associated with insulin resistance in obese patients, and thus treating obesity and diabetes.

In summary, SA's phenolic and flavonoid compounds inhibit biomolecular glycation, scavenge free radicals, and/or effectively chelate metal ions, thus demonstrating good anti-glycation activity and inhibiting the formation of AGEs. Additionally, SA can reduce the levels of malondialdehyde in the blood of diabetic rats, inhibit the catalytic activity of gastric lipase, and lower the levels of free fatty acids associated with insulin resistance, thereby treating obesity and diabetes (Figure 8).

Antidiarrheal activity

Acute diarrhea is mainly caused by the toxins produced by microorganisms in the intestinal lumen, which allows excessive mucosal secretion, and by underlying inflammation that alters the permeability of the gastrointestinal mucosal, leading to a decrease in the absorption of exudates[78]. Anise has a long history of use in treating toothache and indigestion[79]. Díaz et al.[80] studied the antidiarrheal effects of a combination of chamomile and anise tea in a castor oil-induced diarrhea model. The presence of flavonoids, glycosides, and phenylpropanoids in the composition of chamomile and anise reduced the harmful effects of ricinoleic acid on the mucous membranes, prolonging the onset and reducing the frequency of diarrhea, thus providing a good treatment for diarrhea[80].

Promoting hair growth activity

With the increase in life pressure, the prevalence of hair loss has increased sharply, with the patients' age decreasing, making treating hair loss a vital challenge facing clinical dermatology today. Currently, the available therapies for hair loss are oral nonsteroidols and topical minoxidil. Interestingly, the shikimic acid component of SA has also been effective in preventing and curing hair loss in some studies. In their study, Choi et al.[81] evaluated the effect of shikimic acid on the progression of hair in C57BL/6 mice. The topical shikimic acid interacted with mannose receptor (MR) on the cell surface that is effective in promoting hair growth by the following potential molecular mechanism: First activates myeloid differentiation primary response 88 (MyD88), which then promotes downstream p38 MAPK and CREB phosphorylation, ultimately regulating the Wnt/β-linked protein signaling pathway and stimulates CREB-mediated transcription, respectively[81]. Additionally,

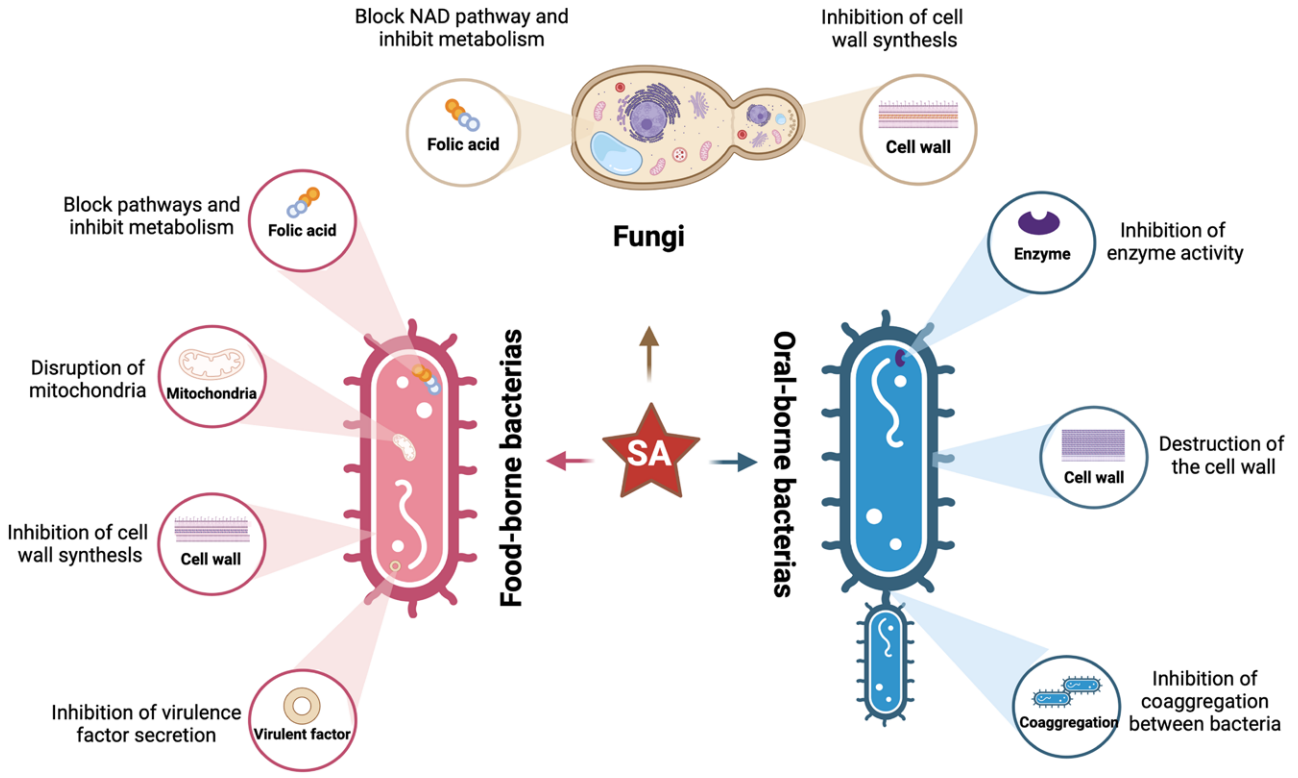


Figure 5. Potential antibacterial mechanism of SA. SA inhibits the secretion of virulence factors and the formation of biofilms, reducing ATP synthesis and NADPH generation, as well as key enzymes (CS, IDH, SDH, and G6PDH) in the TCA cycle and HMP pathway. It disrupts bacterial mitochondria and damages the structure of bacterial biofilms, exerting antimicrobial effects against foodborne pathogens. Additionally, SA inhibits enzyme activity, disrupts cell walls, and inhibits coaggregation and biofilm formation among bacteria, thereby suppressing the proliferation of oral bacteria. Moreover, SA directly affects the cell membrane and metabolic pathways (ATP, NAD) of fungi and bacteria, inhibiting their growth and reproduction. Created by BioRender.com. ATP: Adenosine triphosphate; HMP; Hexose monophosphate; NAD: Nicotinamide adenine dinucleotide; NADPH: Triphosphopyridine nucleotide; SA: Star anise; TCA: Tricarboxylic acid.

well-known substances that encourage hair growth include hepatocyte growth factor (HGF), keratinocyte growth factor (KGF), and vascular endothelial growth factor (VEGF)[82]. Human dermal papilla cells (hDPCs) c-myc, HGF, KGF, and VEGF mRNA expression were all considerably upregulated by SA topical treatment, promoting hair development. It demonstrated that SA could promote hair growth both in mouse models and in human hair follicles (HFs), making SA a potential agent for the therapies of hair loss.

Boost immunity activity

The demand for functional foods has increased in recent years due to growing knowledge of healthy eating, which has driven the food sector to search for new functional goods with positive health effects. The State Administration for the Market Regulation of China's databases indicate that SA is utilized as a food supplement in domestic health food items, with benefits for weariness and increased immunity [Table S1, http://links.lww.com/AHM/A138]. SA's anethole and other components can improve human immunity[14]. The pharmacological experiments revealed that the main mechanism is to promote the proliferation of spleen lymphocytes and the phagocytosis of macrophages in mice, and finally strengthen the cellular immunity, humoral immunity, and non-specific immune function of the body[83].

In conclusion, SA possesses a diverse range of pharmacological activities, making it a promising candidate for developing new drugs and therapies. Further research is needed to elucidate the underlying mechanisms of these activities and explore their potential clinical applications.

Applications of SA

Food industry

Daily food products

SA, renowned as a "drug homologous food"[84], possesses medicinal and dietary functions, and is widely utilized as a spice and flavor enhancer in culinary applications[1]. SA is commonly used as a seasoning for marinating and stewing meat dishes in China. Incorporating SA into meat stews imparts a spicy flavor primarily by altering the composition and ratio of volatile compounds. Spices, including SA, can mitigate or rectify off-flavors in meat ingredients, harmonizing the flavors of meat products and imparting distinctiveness[85], as observed in traditional Chinese cuisine's "Four Famous Chickens." Moreover, SA is frequently employed as the principal spice or condiment in various popular cuisines, such as those of Thailand, India[86], Vietnam, and Malaysia, to enhance overall flavor profiles[87].

Besides being a staple in meat seasoning (eg, Chinese five-spice powder in China), SA finds application in various everyday consumables, including pastries, teas, coffee, jams[88], chocolates, fruit preserves, and desserts, owing to its distinct flavor profile and sweetness. SA herbal teas

Table 4

Summary of SA antimicrobial mechanisms

Form of medication	Bacteria	Mechanism	Reference
Aqueous extracts + essential oil	*Escherichia coli* and *Staphylococcus aureus*	Secondary metabolites such as flavonoids and terpene groups are present in water extracts and essential oils, and their hydroxyl groups exert antibacterial effects by interfering with the function of bacterial receptors	[51]
Essential oil	*Acinetobacter baumannii*	The SAEO can inhibit the formation of plankton and biofilm cells of *Acinetobacter baumannii*, disperse pre-formed biofilms, and reduce the ability of bacterial cells to adhere to polystyrene	[55]
Vacuum-freeze-dried powder	*Aeromonas hydrophila*	SA contains many hydrophobic compounds, such as terpenes, terpenes, phenylpropylene, and isothiocyanates, which can penetrate bacterial cells, causing cell malformations and dysfunction, thereby exerting antibacterial effects	[52]
Essential oil	*S. aureus* and *Staphylococcus lutea*	The supercritical fluid extract and essential oil of SA are more sensitive to gram-positive bacteria than gram-negative bacteria, because lipid teichoic acid exists in the cell membrane, which can promote the penetration of hydrophobic substances such as SAEO, to destroy the bacterial structure and achieve the purpose of bacteriostasis	[56]
Essential oil + acetone extracts	*Penicillium citrinum, Aspergillus flavus*, and *Penicillium viridicatum* (75%); *Aspergillus niger* (50%); *Penicillium citrinum* and *Penicillium viridicatum* (50%)	The trans-anethol in SA essential oil contains aromatic nuclei of polar functional groups that have the use of inhibiting bacterial growth	[57]
Essential oil	Methicillin-resistant *S. aureus*	The presence of phenolic compounds affects the permeability of cell membranes, induces intracellular enzyme-hydrogen binding, and thus affects its normal function; Causes permanent damage to coagulation of the plasma membrane and cell contents, and/or loss of the integrity of the membrane stiffness	[53]
Dried powder	*S. aureus* (87%); *Penicillium aeruginosa* (80%); *Salmonella typhimurium* (60%)	Compared to the effect on *S. typhimurium* and *Pseudomonas aeruginosa* biofilms, SA extract has a great destructive effect on the structure of *Staphylococcus aureus* biofilms. *Escherichia coli* K-12 and *P. aeruginosa virtual PAO1* biofilms are inhibited in the same way by polyphenol extracts and can significantly reduce bacterial virulence and prevent bacterial resistance	[54]

SA: Star anise; SAEO: Star anise essential oil.

(*I. verum*) are prevalent in Mexico and the southwestern United States and are known for their efficacy in alleviating symptoms like infantile colic and stomach pain.

Health food

The growing awareness of healthy eating has led to an increased demand for functional foods, prompting the food sector to seek new products with beneficial health effects. In China, there have been some health-functional foods approved by the State Food and Drug Administration that contain SA, mainly in two types: health-function medicinal liquor and health care tablet. The anethole and other components in SA have the function of improving human immunity[14]. The pharmacological experiments revealed that the main mechanism is to promote the proliferation of spleen lymphocytes and the phagocytosis of macrophages in mice, and finally strengthen the cellular immunity, humoral immunity, and non-specific immune function of the body[83].

Innovative food materials (food packaging)

SA is utilized as both raw material and powder in culinary practices, daily food preparation, and health food supplements. Additionally, it serves as a natural antimicrobial agent in packaging films, anti-corrosion coatings, and as an innovative preservative, offering a viable alternative to chemically synthesized food packaging materials. This is attributed to its antibacterial, anthelmintic, and antiseptic properties, as well as its safe and non-toxic composition. Consequently, this review paper examines recent advancements in SA-based food packaging materials (Figure 4), laying the groundwork for future investigations into natural food materials.

Antibacterial food packaging film

Currently, the popularity of COVID-19 has created a great interest in cooking at home, which is increasing the overall demand for packaged products. Most of the food packaging films commonly used on the market are

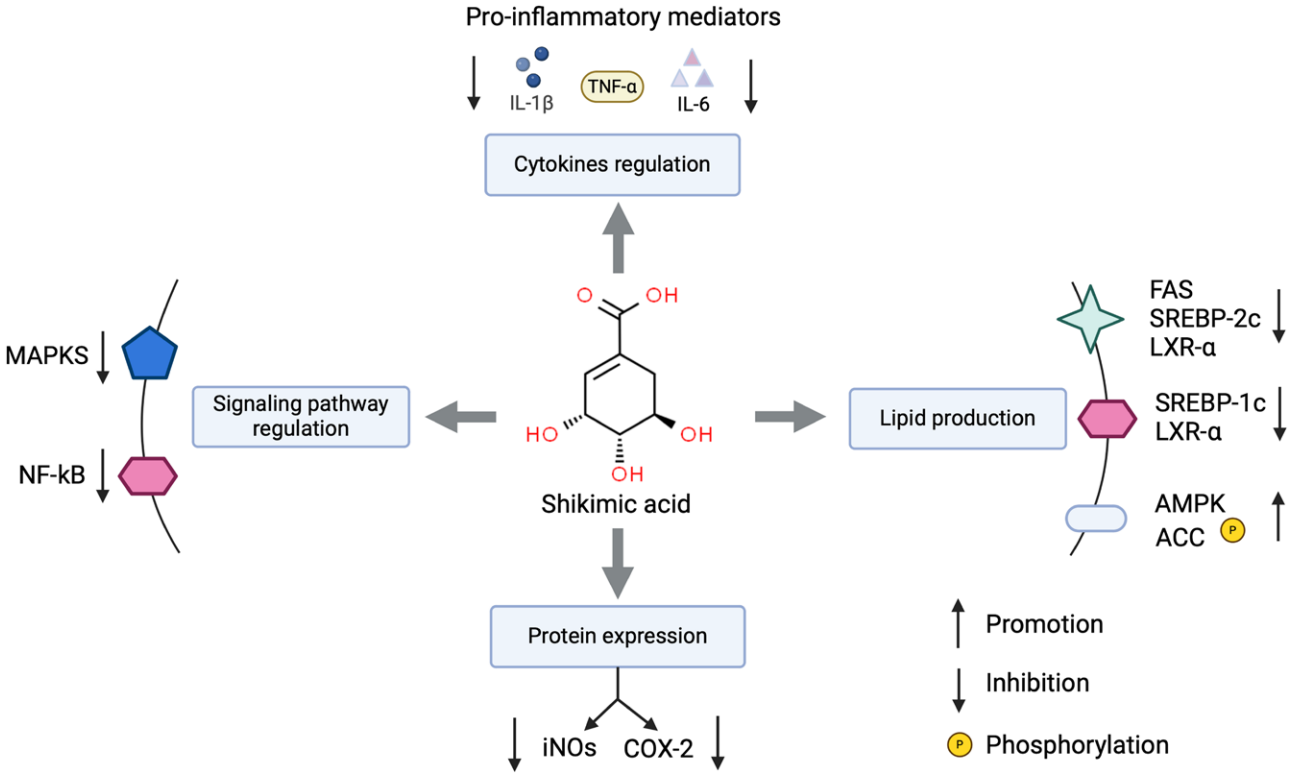


Figure 6. Potential anti-inflammatory mechanism of SA. The shikimic acid of SA exerts anti-inflammatory effects by inhibiting the regulation of cytokines (TNF-α, IL-1β, IL-6), suppressing the increase in iNOS and COX2 protein expression induced by IL-1β, inhibiting the modulation of MAPK and NF-kB signaling pathways, and reducing mRNA expression of genes associated with lipid production (such as FAS, SREBP-2c, and LXR-α) as well as protein expression of SREBP-1c and LXR-α kinase in 2T3-L3 cells. Created by BioRender.com. ACC: Acetyl CoA carboxylase; AMPK: AMP-activated protein kinase; COX2: Cyclooxygenase-2; IL: Interleukin; iNOS: Inducible nitric oxide synthase; MAPK: Mitogen-activated protein kinase; NF: Nuclear factor-κB; SA: Star anise; TNF-α: Tumor necrosis factor-α.

made of plastic and/or chemical synthesis[89]. In addition to polluting the environment, they also harm human health[90]. When subjected to high-temperature cooking or other cooking methods, the chemical components may be transferred to the food. With the pursuit of healthy living, people are increasingly favoring the use of safe and reliable edible products obtained from natural plant extracts. The SAEO is emulsified and encapsulated by β-cyclodextrin and other ways to make multilayer multifunctional food packaging films together with base films such as polyethylene terephthalate film (PET), which have good antibacterial activity.

Rahman et al.[54] prepared food packaging films from anise essential oil and found that the highest biofilm inhibition was 87% for this multilayer film at a concentration of 3 mg/mL, and around 80% and 60% for *Pseudomonas aeruginosa* and *Salmonella typhimurium*, respectively. It simultaneously reduces colony motility, reducing the aggregated motility zone of *S. aureus* by 95.5% and reducing the decline in *Salmonella typhimurium* colony motility by 80%. Due to the anti-QS and anti-biological activity of SA extracts against the above foodborne pathogens, it is a promising natural food packaging film for the preservation of cheese, formulated yogurt, flavored milk, and other food products[54].

Lee et al.[91] used SAEO as an insect repellent, the antimicrobial agent and *trans*-anethole (99%) (TH) as an antimicrobial agent, PET film as a base film, low-density polyethylene film (LDPE) and polypropylene film (PP) (29.3 ± 1.2 μm) as laminate film. As an active food packaging material, a multifunctional multilayer film with five layers and a total thickness of 101.00 ± 1.33 μm was created and applied to sliced wheat bread. The larvae of *P. interpunctella* larvae have sharp and strong mandibles that can perforate food packaging materials[92] and inhibit the growth of surface microorganisms. The above experimental results suggest that this multifunctional film can be utilized as an active food packaging material to improve food products' safety and shelf life.

Neto et al.[93] created a double-bottom antimicrobial package with a β-cyclodextrin (β-CD) complex (ICs) containing essential oils of palm (ICp) or anise (ICsa) and a lift-off lid, which addresses the short shelf life of apples in developing countries such as Brazil due to insufficient freezer capacity, primarily by slowing the growth of Penicillium. It was found that this innovative double-bottom antimicrobial package had 1/3 less fungal growth, less than 50% weight loss, less ethylene and CO_2 production, less than 25% loss of hardness, increased TA and SSC and reduced pH than the control, indicating that DBAP with ICp or ICsa maximized its shelf life[93]. This is mainly related to the presence of essential oils and antibacterial ingredients such as *trans*-anisole in SA.

Wyrwisz et al.[94] mixed different gas types of food packaging gases for the gas packaging and then combined them with active packaging (anise essential oil, cinnamon essential oil, and clove essential oil) to extend the shelf life of gluten-free cakes. The shelf life of the gluten-free cake with high β-glucan content was significantly delayed by the combination of the three herbal oils

Table 5

Summary of SA anti-inflammatory and analgestic mechanisms

Model classification	Molding	Mechanism	Reference
Inflammatory models	Xylene-induced ear edema in mice. Causes the release of pro-inflammatory mediators such as histamine and serotonin, promotes vasodilation, leukocyte infiltration, and plasma leakage	SA exhibits anti-inflammatory activity by inhibiting vasodilation, leukocyte infiltration	[60]
	Carrageenan-induced paw edema in rats. In the early stages, histamine and serotonin are released, peaking at 3 h to release kinin-like substances, while in the late stages, PGEs, proteases, and lysozymes are released	SA significantly inhibited the formation of paw edema in rats both in the early and late stages, probably due to the inhibition of cyclooxygenase involved in PGE formation, and the level of PGE was significantly reduced by CSA treatment2; in addition, MDA levels were significantly reduced after SA treatment, possibly due to SA's activity in scavenging superoxide anions and hydroxyl radicals	[60]
	Inflammation of human keratinocytes and HaCaT cells induced by TNF-α/IFN-γ	Inhibits the expression of TNF-α/IFN-γ-induced chemokines, pro-inflammatory cytokines, and adhesion molecules by blocking NF-κB, STAT1, MAPK and Akt activation, thereby exerting anti-inflammatory effects	[64]
	Human keratinocytes line HaCaT cell inflammation model induced by IFN-γ	It inhibits IFN-γ-induced ICAM-1 expression by blocking the JAK/STAT pathway in HaCaT human keratinocytes and plays an anti-inflammatory role	[65]
	Croton oil-induced ear edema	Exerts an anti-inflammatory effect by inhibiting the production and/or release of PGE (2) and NO, inhibiting the formation of exudates and the activity of myeloperoxidase	[66]
	Carrageenan-induced pleurisy	Reduces the volume of pleural exudate and the number of migrating leukocytes by reducing NO and PGE (2) levels in inflammatory exudates.	[66]
	Carrageenan-induced rat paw edema	IV-Ext-3 exhibits the most potent anti-inflammatory effects in SA extract, mainly due to its antihistamine and antioxidant potential	[24]
	Carrageenan-induced paw edema test (Carrageenan, histamine, serotonin, and PGEs)	Related to the phytochemical components (shikimic acid, benzoate, benzoic acid, and anethole) of IV-Ext-3 in SA that exert antioxidant activity, its antioxidant activity contributes to its anti-inflammatory effect	[24]
Analgesic models	The hot plate test is suitable for the evaluation of central-acting analgesics	The analgesic activity of SA may be due to the central nervous system sedative effect	[60]
	Acetate-induced abdominal twisting is a visceral pain model used to assess the peripheral analgesic activity of drugs	SA produces peripheral analgesia by inhibiting the release of chemical mediators and/or cytokines	[60]

IFN-γ: Interferon-γ; NO: Nitric oxide; PGE: Prostaglandin; SA: Star anise; TNF-α: Tumor necrosis factor-α.

at 60% CO_2/40% N_2, which also maintained the texture and color of the bread. It suggests that combining the aerosol packaging with the active packaging containing SAEO did extend the shelf life of the gluten-free cake and is a promising food packaging material for practical applications.

Another study by Zhang et al.[95] showed that a composite film was prepared by an ethanol extract of SA and hydroxypropyl-β-CD inclusion complex together with sodium alginate. That film was found to maintain a high vitamin C content and reduce the weight loss of fresh-cut Chinese yam. The association energy between the inclusion complex and the sodium alginate molecule was calculated. It is shown that this composite film containing SA alcohol extract has good potential for food packaging applications.

In summary, SAEO has been widely used in the field of food packaging films. In the future, it may be possible to combine various SA edible essential oils with biological activity to produce natural food films with a wider range of functions, which are safe, effective, natural, and reliable, and worthy of further exploration and research transformation.

Food anti-corrosion coating

Except for use as food packaging, SAEO is also widely used as a food coating due to its antibacterial, antimicrobial activity, and edibility[96]. Huang et al.[97] applied SAEO to grass carp fillets during refrigeration. It was found that anise essential oil was effective in delaying the increase in TVB-N, TBA, putrescine, and *K* values

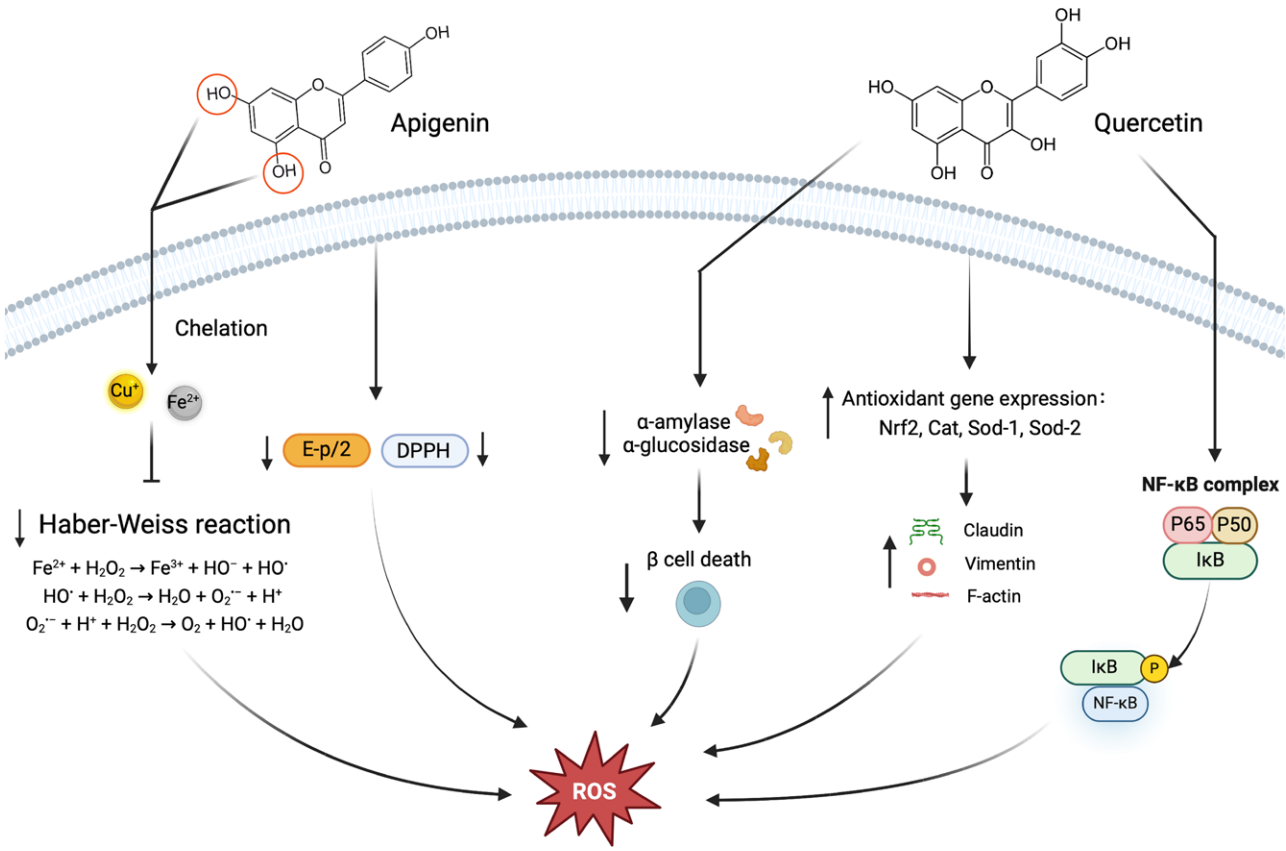


Figure 7. Potential antioxidant mechanism of SA. The flavonoid compound apigenin in SA exhibits antioxidant properties by chelating with transition metal ions and/or scavenging ROS. It reduces the ability of H_2O_2 to generate hydroxyl radicals through the Haber-Weiss reaction and exerts antioxidant effects by scavenging DPPH and lowering the half-wave oxidation potential (E-p/2). Furthermore, quercetin in SA protects supporting cells by decreasing the expression levels of HSP70 and ROS, reducing the levels of p-NF-κB-p65 and p-IκB, and upregulating the expression of laminin, fibronectin, and F-actin in supporting cells. This protection helps maintain the structural integrity of supporting cells. Quercetin also reduces endoplasmic reticulum oxidative stress, β-cell death, and inhibits porcine pancreatic α-amylase and mammalian α-glucosidase. It decreases ROS levels and upregulates the expression of antioxidant genes (*Nrf2*, *Cat*, *Sod-1*, and *Sod-2*), thereby exerting antioxidant effects. Created by BioRender.com. DPPH: 2,2-diphenyl-1-picrylhydrazyl radicals; HSP70: Heat shock protein 70; ROS: Reactive oxygen species; SA: Star anise.

to inhibit microbial. It also extended the shelf life of the fillets by 2 days, demonstrating its potential as a natural preservative[97].

Zhang et al.[96] prepared an edible coating to prevent spoilage and browning of fresh-cut fruits and vegetables by encapsulating SAEO in hydroxypropyl-β-cyclodextrin (HPCD) to make its dispersion in xanthan gum more uniform and stable. Experimental studies have shown that the encapsulated SAEO increased the water solubility by 47.5 times and decreased the weight loss of fresh-cut yam samples by more than 30% while increasing the inhibition of browning and polyphenol oxidase activity of the samples by nearly 8 and 7 times, respectively[96]. The above study proved that the coating has a good effect on weight loss and inhibition of browning of fresh-cut yam, and SAEO in HPCD is promising for practical application as a preservative for fresh fruits and vegetables.

It is worth mentioning that Lin et al.[98] combined polylysine and lactic acid streptococcal peptides as complex antimicrobial agents with SAEO to design edible nanoemulsion coatings containing natural antimicrobial agents to inhibit bacterial growth during storage of ready-to-eat meat products and thereby increasing their shelf life. A comprehensive characterization of meat in terms of bacterial testing, physicochemical properties (water content, pH, total volatile basic nitrogen), bacterial load, and sensory properties revealed that the use of this coating resulted in good color, odor, and overall acceptability of the meat samples. The extension of shelf life from 8 to 16 days confirmed that the nanoemulsion edible coating containing SAEO, polylysine and lactic acid streptococcal peptides is an ideal coating to improve the quality and shelf life of perishable ready-to-eat meat products, with far-reaching implications for the development of food preservative coatings.

Lee et al.[99] applied SAEO emulsion coatings with insect-repellent properties to the surface of PET films and then laminated the PET substrates with three laminates (LDPE20, PP20, and PP30). The experimental study found that the infestation rate of insect larvae on the surface and inside of bread packaging made with PP30/IEC25/PET was only around 29.2% of that of the control film packaging, indicating that the PP30/IEC25/PET film has significant insect-repellent activity as food packaging and has great potential for active packaging in real food systems[99].

It is obvious that SAEO has been quite widely implemented in food packaging due to its bioactivity and safe edibility, not only as an antibacterial packaging film to isolate various foodborne organisms but also as an anti-corrosion coating in direct contact with food to prevent spoilage, thus extending the shelf life of food.

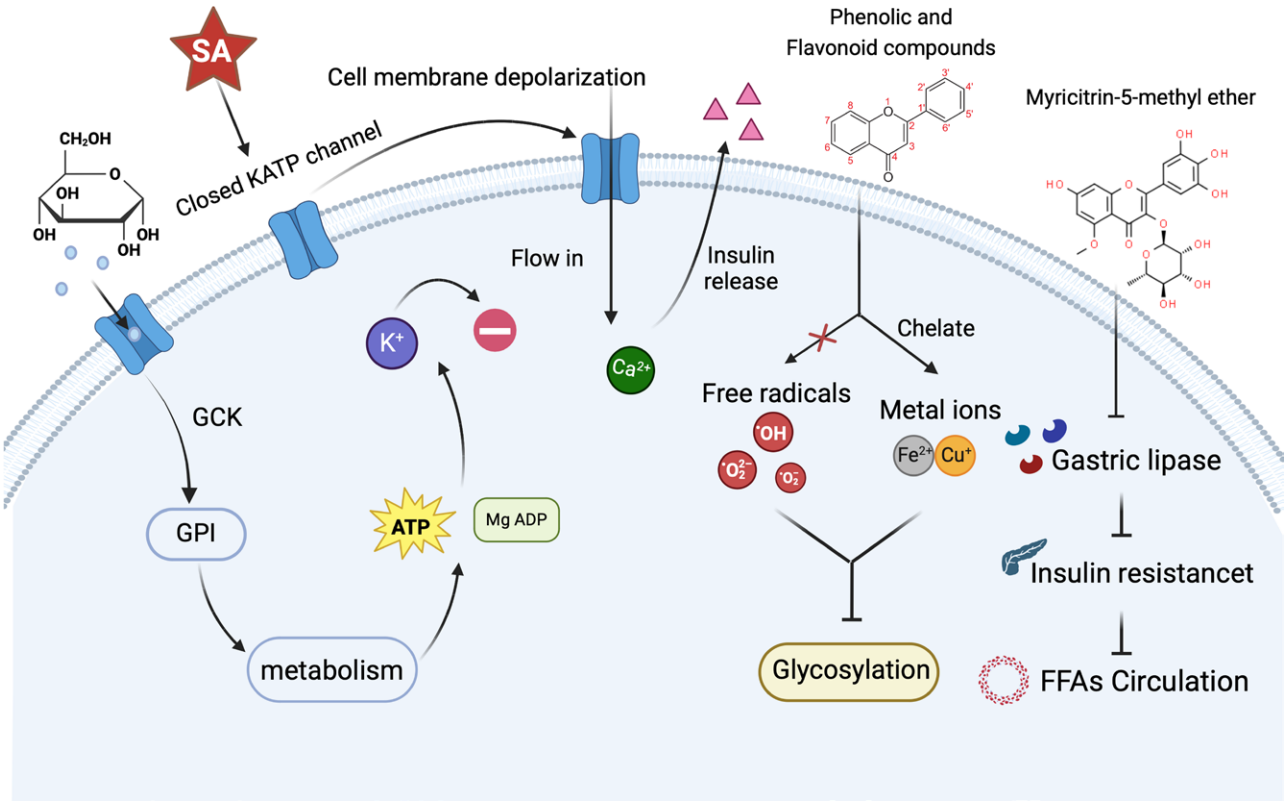


Figure 8. The potential mechanism of SA anti-diabetes. SA's phenolic compounds and flavonoids can effectively inhibit biomolecular glycation by scavenging free radicals and/or chelating metal ions. Additionally, the flavonoid myricitrin-5-methyl ether found in SA exhibits antidiabetic activity by inhibiting the catalytic activity of gastric lipase, thereby reducing circulating levels of free fatty acids associated with obesity and insulin resistance in patients with diabetes. Created by BioRender.com. GCK: Glucokinase; GPI: Glycosylphosphatidylinositol; FFA: Free fatty acids; SA: Star anise.

Innovative natural food preservative

Trans-anethole and anisaldehyde, two primary active components of SAEO, exhibit antipyretic, antioxidant, antibacterial, antifungal, and antiparasitic characteristics. As a result, they are considered excellent candidates for use as natural preservatives in various foods. SAEO showed a wide range of inhibitory effects against common foodborne molds, mainly because anethole was the main compound in the essential oil composition accounting for 89.12%, followed by estragole accounting for 4.859%[100]. Kedia et al.[101] encapsulated SAEO in gel form and lyophilized form in nanocapsules, resulting in enhanced effectiveness of SAEO as a fungal inhibitor and aflatoxin inhibitor, inhibiting aflatoxin B1 secretion. It was found that the amount of encapsulated aflatoxin B1 was 0.2 μL/mL, which was more than 2 times lower than that of unencapsulated SAEO. It also had a considerable inhibitory effect on staphylococci. Furthermore, the acute toxicity study of SAEO experiments revealed that the acute LD_{50} of SAEO was higher than that of other EOs (eg, *Foeniculum vulgare* Mill seed essential oil)[101], *Mentha spicata* essential oil[78], *Mentha cardiaca* L. essential oil[102]. This indicates that SAEO has a good safety profile. This study demonstrates the practical value of nano-encapsulated SAEO as a plant-based preservative and food preservation enhancer.

Moreover, by exploiting the unique molecular structure of CDs, that is, hydrophilic exterior surface and hollow hydrophobic core, Guan et al.[103] enabled the preparation of HP-β-CD selected host molecules with the active ingredients in SA alcohol extractives (SAAE) to obtain a stable SAAE/HP-β-CD inclusion to overcome the instability and insolubility of free SAAE. It was found that HP-β-CD can improve water solubility, thermal stability, and photostability by complexing, which makes it possible for the SAAE/HP-β-CD complex system to become a preservative in food systems[103].

Daily products

Perfumes and oral care products often utilize the masking and deodorizing properties of SA, as well as its ability to enhance fragrance and freshness. The presence of trans-anethole and shikimic acid compounds in SA contributes to these effects. Furthermore, essential oil extracts from the fruit, seeds, and leaves of SA demonstrate the potential in regulating skin conditions and providing deodorizing effects[39]. Shikimic acid can inhibit unpleasant odors by suppressing lipase activity and fatty acid production[104]. The prevention of oral diseases is associated with reducing specific bacteria, and star anise extract (SAE) has been shown to inhibit biofilm formation and bacterial proliferation[105]. Additionally, SAEO has been used to produce alcohol-free mouthwashes, exhibiting the potential to inhibit oral microorganisms and biofilm formation[50].

The concept of "green cosmetics" has prompted consumers to prefer environmentally friendly, safe, and effective three-in-one skincare products. Trans-anethole, by inhibiting the activity of ORAI1 and preventing UV-induced melanogenesis, offers skin-whitening effects[106]. Shikimic acid derived from plant healing tissue enhances skin remodeling by reprogramming human

dermal fibroblasts into multipotent skin-derived progenitor cells, activating dryness markers, and reinforcing the extracellular matrix composition to achieve regenerative human skin[107]. This contributes to wound healing and enhanced skin repair in human artificial skin models, providing a solid scientific basis for cosmetic medicine and medical aesthetics.

Furthermore, the Cosmetic Ingredient Database (CosIng) of the European Commission and the database of the China Food and Drug Administration (CFDA) indicate that *Illicium verum* can be used in the production of skincare and cosmetic products [Table S2, http://links.lww.com/AHM/A138]. The Flavor and Extract Manufacturers Association (FEMA)[108] and the Food and Drug Administration (FDA) have granted *Illicium verum* and trans-anethole the status of safe ingredients, marked with the Generally Recognized as Safe (GRAS) symbol. Therefore, SA and its derivatives can meet the multifaceted demands of consumers, presenting broad market prospects in the cosmetics and skincare industry.

Moreover, in skin and beauty care, dermatitis and allergic reactions are also significant concerns for consumers, for example, the common atopic dermatitis (AD), a chronic inflammatory skin disease that often occurs in infants and children[109]. Sung et al.[110] induced AD-like skin lesions in NC/Nga mice using topically house dust mite extract and demonstrated experimental research that fennel extract suppresses AD-like skin lesions by inhibiting the expression of chemokines, cytokines, and adhesion molecules. Due to their deodorizing, antimicrobial, and protective properties, SAE and SAEO offer promising applications in topical products, such as perfumes, oral care, and skincare.

Other application

SA is not only used in human food, clinical and household products but also poultry farming and crop pest control as a cheap, environmentally friendly alternative to pesticides in poultry farms[111]. The trans-anethole in SAEO can be used as a potential insecticide to poison *Myzus persicae* (Hemiptera: Aphididae), a major pest of many vegetables and crops[112], and *Ornithonyssus sylviarum* (Acari: Macronyssidae), a common ectoparasite that feeds on the blood of poultry[111], and the house fly[113], also a pest of avian spoilage. The Coleoptera *Alphitobius diaperinus* (Panzer)[114], a common meat and poultry pest, can be rendered immobile by the trans-anethole in SAEO at 1% or more concentrations. SA is also a natural acaricide against nymphs of *I. Ricinus*[115]. Soonwera et al.[116] found that the combination of soybean oil and SAEO acted as natural ovicidal and repellent agents against *Periplaneta americana* L. In addition, SAEO at concentrations above 6.0 μL/g can completely inhibit aflatoxin production, prevent fungal contamination, and be used as a potential natural fumigant for preserving lotus seeds[117].

Therefore, SA can be developed not only as a biopesticide for veterinary use but also as a feed additive to inhibit various types of pests in poultry farming, and likewise as a natural fumigant for the preservation and storage of Chinese herbs, with a wide range of applications.

Conclusions

As a medicinal and edible botanical with a long history, SA is rich in resources and has excellent development value. Although relevant papers have reviewed the research progress of SA, they are not comprehensive and in-depth enough, and their timeliness also needs to be improved. Compared with other reviews on SA, our paper fills the gap in the application of SA in health food applications, daily necessities, etc, and comprehensively sorts out the pharmacodynamic effects and mechanisms of SA active monomers and related compounds.

There is still a lack of in-depth research on the following aspects of SA: 1) There is very little clinical experimental data on SA, the safe usage, dosage, and adverse reactions of SA in special populations such as the elderly, children, and pregnant women require further investigation in terms of food safety. 2) There are currently few studies on the absorption, metabolism, excretion, and bioavailability of SA in the human body. 3) The structure-biological relationships of some active monomers in SA are not yet clear, and their quality markers (Q-Marker) remain undefined.

Therefore, it is recommended that researchers use network pharmacology, metabolomics, chinmedomics methods, and other advanced multi-disciplinary technological methods to carry out more in-depth research to solve the above problems. Our team is currently exploring the Q-Marker of SA and its medicinal value, hoping to provide a scientific reference value for its future development and application.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

Lin Zhu: Data curation, formal analysis, writing-original draft. Yu Luo: review & editing. Hua Luo: Supervision, writing-review & editing. Yitao Wang: Funding acquisition, project administration. Chun Yao: Funding acquisition, project administration. Jian Xiao: Project administration. Erwei Hao: Project administration, Jinmin Zhao: Supervision. All authors read and approved the final version of the paper.

Ethical approval of studies and informed consent

Not applicable.

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None.

Data availability

All data generated or analyzed during this study are included in this published article and its supplementary information files.

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