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# Sedum aizoon L.: a review of its history, traditional uses, nutritional value, botany, phytochemistry, pharmacology, toxicology, and quality control

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In China, Russia, Mongolia, Japan, North Korea, and Mexico, *Sedum aizoon* L. (*S. aizoon*) is used as an edible plant. Up to now, over 234 metabolites, including phenolic acids, flavonoids, triterpenes, phytosterols, and alkaloids, among others, have been identified. In addition to its antioxidant, anti-inflammatory, anti-fatigue, antimicrobial, anti-cancer, and hemostatic activities, *S. aizoon* is used for the treatment of cardiovascular disease. This paper provides an overview of the history, botany, nutritional value, traditional use, phytochemistry, pharmacology, toxicology, and quality control of *S. aizoon*.

KEYWORDS

Sedum aizoon L., pharmacological activities, quality control, hemostatic activity, active metabolites

## Highlights

- *S. aizoon* L. is frequently prescribed in both China and other countries as a traditional folk herbal remedy for various diseases
- *This review contributes to updating the herbalogical textual research, traditional use, botany, phytochemistry, pharmacology, toxicity, and nutritional value and quality control of* S. aizoon *L.*
- *In earlier literature, there was no systematic review of* S. aizoon *L*

## 1 Introduction

Sedum aizoon L. (Chinese name:景天三七) is a perennial herbaceous plant that is widely distributed in China, Russia, Mongolia, Japan, North Korea, and Mexico. It is a member of the *Sedum* genus in the *Sedum* family (*Crassulaceae*) (Guo and Lin, 2007). Its name is also consistent with the plant name recorded in "The Plant List" (http://www.theplantlist.org), which is now incorporated into the requirement for traditional medicine in the provinces of Jiangsu and Fujian (Jia et al., 2014). It is one of the renowned "Taibai seven medicine (太白七药)" in the Qinling Mountains, which has the effects of dispersing blood stasis, stopping bleeding, tranquilizing the mind, detoxifying, and analgesia, and is used in the treatment of various kinds of bleeding, palpitations, and insomnia. Growing in

**Traditional uses**
- resist fatigue
- enhance immunity
- Regulates blood lipids
- lowers blood pressure
- prevents heart disease

**Pharmacology**

*Sedum aizoon* L

**nutritional Value**

**Ethnomedicinal application**
- antioxidant,
- anti-inflammatory
- anti-fatigue
- antibacterial
- anti-cancer
- Hemostasis
- improving cardiovascular disease
- Others

- AA grade green food the China Green Food Development Centre.
- High calcium content, high absorption rate of calcium ions
- has been made into cookies, jellies, tea and other health products

**Phytochemistry**
- phenolic acids
- flavonoids
- Triterpenes and phytosterol
- Alkaloids
- Volatile oils
- other compounds

Graphical Abstract

GRAPHICAL ABSTRACT

the natural environment, *S. aizoon* is a unique pest-free plant that does not require pesticides during its whole phenological cycle and has been designated as AA grade green food by the China Green Food Development Center. Its fresh stems and leaves are consumed as vegetables (Xue, 2015).

Despite the fact that the phytochemistry and ethnopharmacology of *S. aizoon* have been previously reviewed, a comprehensive study linking its bioactive metabolites with its pharmacological properties is lacking. Therefore, this paper provides an overview of the history, botany, nutritional value, traditional use, phytochemistry, pharmacology, toxicology, and quality control of *S. aizoon*.
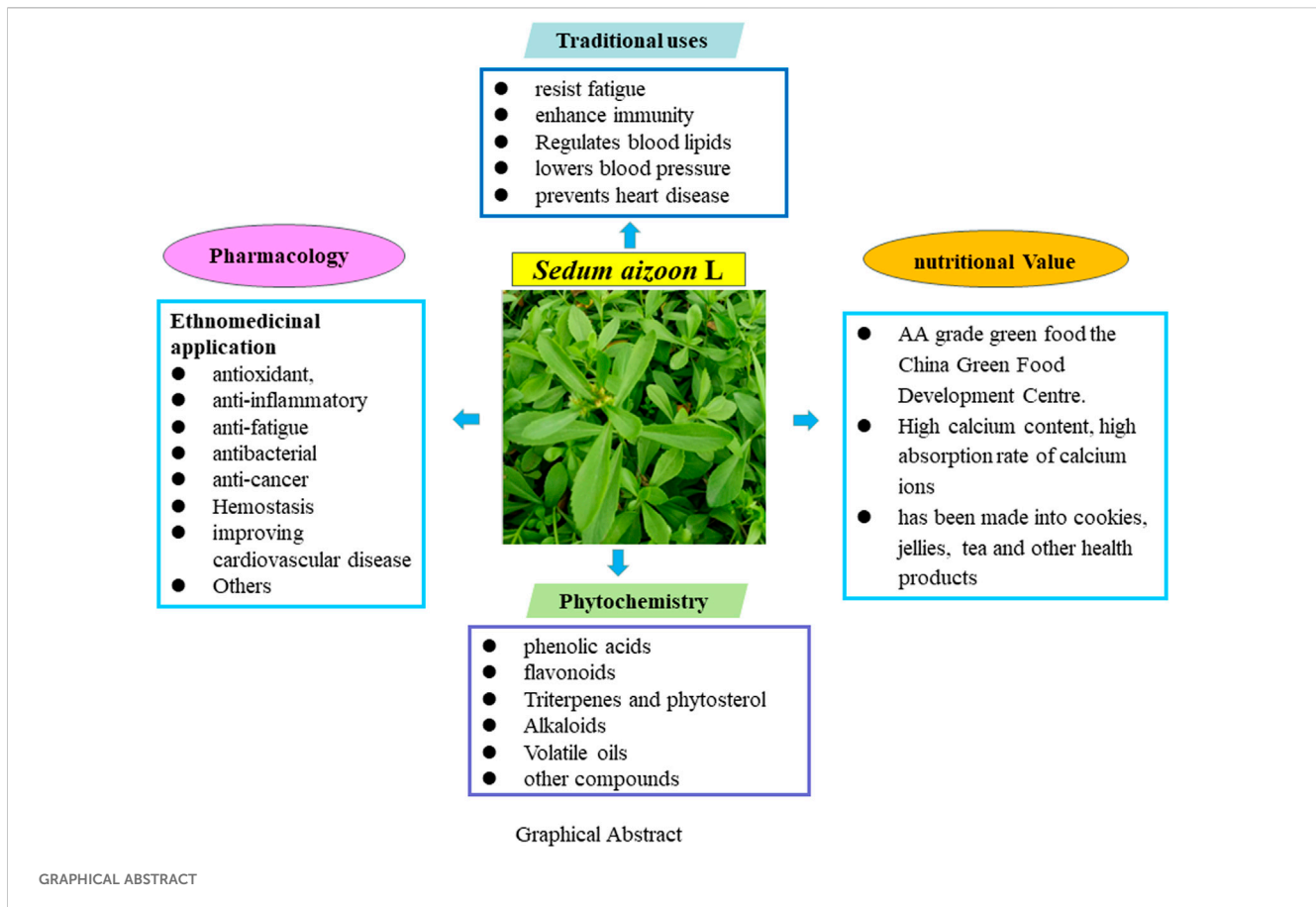
# 2 Materials and methods

Information about *S. aizoon* was gathered from scientific literature sources, including PubMed, Baidu Scholar, Google Scholar, Web of Science, SciFinder, CNKI, Wanfang, the Plant List (www.theplantlist.org), and books. The history, nutritional value, traditional uses, botany, phytochemistry, pharmacology, toxicology, and quality control or a combination between them was used as keywords to search for data up to July 2023. Approximately, 767 research studies of *S. aizoon* were gathered from various databases. With the removal of duplicate literatures, 300 literatures were selected according to research purpose, relevance, and article type. The articles which contained information apart from that mentioned above or written in

languages rather than English were also excluded. ChemBioDraw Ultra version 14.0 was used to draw chemical structures.

# 3 History and traditional uses

## 3.1 History

*S. aizoon* was first recorded in "*Jiu Huang Ben cao*" (救荒本草) (Ming Dynasty), which is the earliest book with agronomy and botany as its monograph on the history of China. Later, it was also included in many other famous works on Chinese herbal medicine, including "*Wild Vegetables Bo lu*" (野菜博录) (Ming Dynasty), "*Plants Ming Shi Tu Kao*" (植物名实图考), and "*Discussion on varieties of Chinese medicinal materials*" (中药材品种论述).

The medicinal parts of *S. aizoon* were roots and grass in *S. aizoon*, and *S. kamshaticum*. *S. aizoon* has more than 60 synonyms and is distributed in more than 20 provinces or autonomous regions. In addition, the herb and the syrup were included in the Pharmacopoeia of the People's Republic of China (Part I) (1977 edition) (Chinese Pharmacopoeia Committee, 2005).

## 3.2 Traditional uses

In folk medicine, the flat and sweet whole herb and the roots of *S. aizoon* are widely used for dispersing blood stasis and stopping
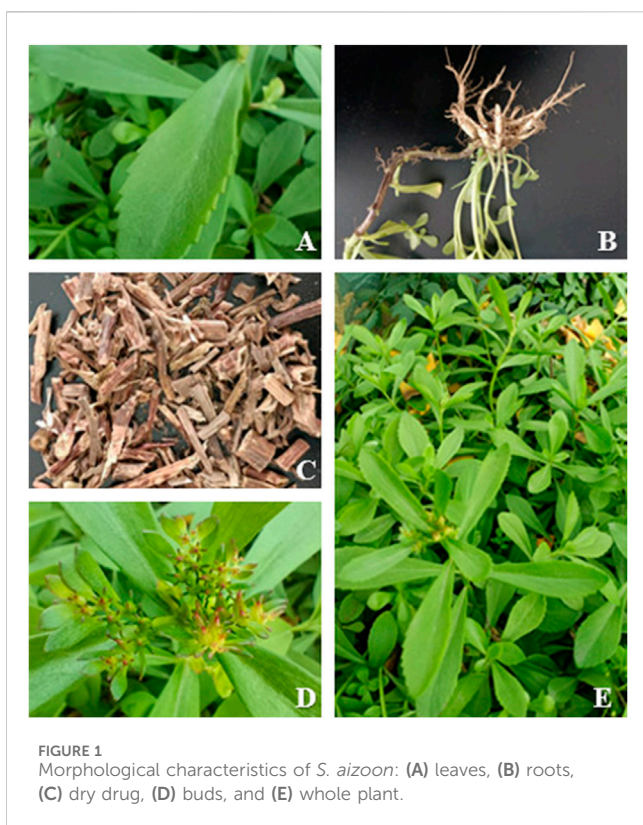
FIGURE 1
Morphological characteristics of *S. aizoon*: **(A)** leaves, **(B)** roots, **(C)** dry drug, **(D)** buds, and **(E)** whole plant.

blood bleeding. For instance, daily administration of 60–90 g of *S. aizoon* decoction can treat bleeding symptoms, including hemoptysis, bleeding gums, epistaxis, gingival bleeding, and internal bleeding. The fresh juice was effectively used for the treatment of leukemia, aplastic anemia, thrombocytopenic purpura, hemoptysis, and different forms of bleeding (i.e., gingival, digestive tract, and hematuria) (Chinese herbal medicine research group, 1971). In addition, ancient medical classics, such as Li Shizhen's "Compendium of Materia Medica" (本草纲目), Chen Shiduo's "New Compilation of Materia Medica" (本草新编), and Zhang Xichun's "Intergrating Chinese And Western Medicine" (医学衷中参西录), explicitly stated that *S. aizoon* had good hemostasis and analgesic function, which was known as "the god medicine for hemostasis" (止血神药). It is also used as a heart and mind tranquillizing agent with an excellent effect on hysteria palpitation, restlessness, hypertension, and rheumatic heart disease (Chen, 2003). Likewise, the detoxifying and clearing heat effects have also been reported.

Of note, *S. aizoon* has a long history as both an edible and medicinal herb. For example, vegetables with *S. aizoon*'s stems and leaves as metabolites have good nutritional value. "Jiu Huang Ben Cao" (救荒本草) in the Ming Dynasty stated that the regular consumption of the fresh, tender stems and leaves of *S. aizoon* can promote blood circulation and calm the heart.

# 4 Nutritional value

The tender stems and leaves contain moisture (87 g), protein (2.1 g), fat (0.7 g), carbohydrate (8.0 g), crude fiber

(1.5 g), ash (1.2 g), energy (196.65 KJ), Ca (315 mg), P (39 mg), Fe (3.2 mg), carotene (2.54 mg), vitamin B1 (0.05 mg), vitamin B2 (0.07 mg), vitamin PP (90 mg), and vitamin C (90 mg) (Yi, 2000; Liu et al., 2012). Owing to its unique aroma and taste, *S. aizoon* is used for the preparation of cookies, jellies, and tea (Wang, 2013).

# 5 Botany

## 5.1 Geographical repartition

*S. aizoon* belongs to the genus *Sedum* of the *Crassulaceae* family. There are approximately 600 species widely distributed in the temperate and subtropical regions of the northern hemisphere with Mexico being the largest center of origin and diversity of *Sedum* species.

## 5.2 Morphology

*S. aizoon* is an annual or perennial, succulent herb, growing in clusters and has a strong ability to bifurcate. *S. aizoon* has coarse, woody rhizomes that resemble ginseng in form. The stems are erect, cylindrical, and glabrous, which can reach heights of 15–50 cm. At each node, the stems carry just one leaf, which is nearly opposite on both sides. The leaves are 2.5–5 cm long, 5–12 mm wide, obovate or long oval in shape, and broad and thick with more juice. Additionally, they feature a cuneate base, a serrated border toward the apex, a moderately rounded top, and few sessile leaves. The loose, terminal verticillaster contains ten stamens that are around the same length as the petals, five distinct pistils that are slightly longer than the stamens, five orange–yellow petals with lancolate, sharp tips, and five sepals with blunt ends. Follicles are either reddish or brown in color and are grouped in a star pattern. Seeds are obovate, smooth, have wings along the edge, and have a wider apical. Flowers usually bloom in summer. The photos of *S. aizoon* are pictured and shown in Figure 1.

# 6 Phytochemistry

Up to now, more than 234 metabolites, including flavonoids (**1–48**), phenolic acids (**49–78**), triterpenes and phytosterols (**79–90**), alkaloids (**91–98**), volatile constituents (**99–216**), and others (**217–234**), have been preliminarily isolated or identified from *S. aizoon*. Among these, flavonoids are the main metabolites of *S. aizoon*. The main metabolites and their structure are given in Table 1 and Figures 2–5.

## 6.1 Flavonoids

So far, 48 flavonoid metabolites (**1–48**) with definite structure have been isolated and identified from *S. aizoon*, which are grouped into flavonols (**1–36**), isoflavones (**37–39**), flavones (**40–43**), flavanonols (**44–47**), and flavan-3-ol (**48**). Among flavonols, rhamnazin-3-O-β-D-

TABLE 1 Main active metabolites identified in *S. aizoon*.

| Metabolite | Plant part | Molecular formula | Reference |
|---|---|---|---|
| Flavonoid | | | |
| Trifolin | Leaves and stems | $C_{21}H_{20}O_{11}$ | Xu et al. (2019) |
| Rutin | | $C_{27}H_{30}O_{16}$ | |
| Isoquercitrin | | $C_{21}H_{20}O_{12}$ | |
| Isorhamnetin | | $C_{16}H_{12}O_7$ | |
| Astragalin | | $C_{21}H_{20}O_{11}$ | |
| Genistein | | $C_{15}H_{10}O_5$ | |
| Lonicerin | | $C_{27}H_{30}O_{15}$ | |
| Scutellarein | | $C_{15}H_{10}O_6$ | |
| Catechin | | $C_{15}H_{14}O_6$ | |
| Rhamnetin-3-O-β-D-glucopyranoside | Rhizome | $C_{22}H_{22}O_{12}$ | Li et al. (2020a) |
| Isorhamnetin-3-O-β-D-xylopyranoside | | $C_{21}H_{20}O_{11}$ | |
| Isorhamnetin-3-O-α-L-arabinopyranoside | | $C_{21}H_{20}O_{11}$ | |
| Rhamnazin-3-O-β-D-glucopyranoside | Aerial parts | $C_{23}H_{26}O_{12}$ | Xiong et al. (2019) |
| Quercetin | Aerial parts, rhizome, and leaves and stems | $C_{15}H_{10}O_7$ | |
| Myricetin | Aerial parts and leaves and stems | $C_{15}H_{10}O_8$ | |
| Luteoloside | N/A | $C_{21}H_{20}O_{11}$ | |
| Quercitrin | Aerial parts and leaves and stems | $C_{21}H_{20}O_{11}$ | Wolbi and Olszewska (1996), Li et al. (2007) |
| Myricitrin | Aerial parts | $C_{21}H_{20}O_{12}$ | |
| Quercetin-3-o-(2′-galloyl) rhamnoside | N/A | $C_{28}H_{30}O_9$ | Wolbi and Olszewska (1996) |
| Quercetin-3-O-α-L-arabinopyranoside | Leaves and stems and rhizome | $C_{20}H_{18}O_{11}$ | Han et al. (2017) |
| Myricetin-3-O-α-L-arabinopyranoside | Aerial parts | $C_{20}H_{18}O_{12}$ | |
| Kaempferol-7-O-glucoside | Leaves and stems | $C_{21}H_{20}O_{11}$ | |
| Kaempferol-3-O-β-D-glucopyranoside | | $C_{21}H_{20}O_{11}$ | |
| Herbacetin-3-O-α-L-arabinopyranoside | | $C_{20}H_{18}O_{10}$ | |
| Myricetin-3-β-D-glucopyranoside | Aerial parts and leaves and stems | $C_{21}H_{20}O_{13}$ | Li et al. (2008) |
| Myricetin-3-β-D-(6″-o-galloyl)-glucopyranoside | Whole grass | $C_{28}H_{24}O_{17}$ | |
| Myricetin-3-o-β-D-(6″-o-galloyl)-galactopyranoside | | $C_{28}H_{24}O_{17}$ | |
| Myricetin-3′-o-β-D-glucopyranoside | Leaves and stems | $C_{21}H_{20}O_{13}$ | Jia et al. (2014) |
| Kaempferol | Leaves and stems and rhizome | $C_{15}H_{10}O_6$ | Lin et al. (2014), Xiong et al. (2019) |
| Kaempferol-3-O-α-L-rhamnoside | Leaves and stems | $C_{21}H_{20}O_{10}$ | Zhang et al. (2010) |
| Herbacetin-8-O-α-D-lyxoside | | $C_{20}H_{18}O_{11}$ | |
| Herbacetin-8-O-β-D-xylopyranoside | | $C_{20}H_{18}O_{11}$ | |
| Luteolin | | $C_{15}H_{10}O_6$ | |
| Herbacetin-8-O-β-D-glucopyranoside | Aerial parts | $C_{25}H_{23}O_7D_3$ | Xu et al. (2015) |

TABLE 1 (*Continued*) Main active metabolites identified in *S. aizoon*.

| Metabolite | Plant part | Molecular formula | Reference |
|---|---|---|---|
| Herbacetin-3-O-β-D-glucopyranosyl-8-O-α-L-arabinopyranoside | | $C_{74}H_{105}O_{32}$ | |
| Herbacetin-3-O-α-L-rhamnopyranosyl-8-O-α-D-lyxopyranoside | | $C_{26}H_{28}O_{14}$ | |
| Herbacetin-3-O-α-L-arabinopyranosyl-8-O-β-D-xylopyranoside | | $C_{25}H_{26}O_{14}$ | |
| Gossypetin-3-O-β-D-glucopyranosyl-8-O-β-D-xylopyranoside | | $C_{73}H_{106}O_{34}$ | |
| 3′-Methoxyl-gossypetin-3-O-β-D-glucopyranosyl-8-O-β-D-xylopyranosie | | $C_{27}H_{30}O_{17}$ | |
| 6″-O-(E)-feruloyl isorhamnetin | Whole plant | $C_{32}H_{30}O_{15}$ | (Li J. X. et al., 2011) |
| 6″-O-(E)-feruloyl quercetin | | $C_{31}H_{28}O_{15}$ | |
| 3,4′,5,7-Tetrahydroxyflavone-7-O-α-D-xylopyranoside | Whole grass | $C_{20}H_{18}O_{10}$ | Han et al. (2021) |
| Sedacin A | Whole plant | $C_{28}H_{32}O_{7}$ | Li J. X. et al. (2011) |
| Sedacin B | | $C_{29}H_{34}O_{7}$ | |
| 1,3,8,10,10b-Pentahydroxy-5a-(4-hydroxy-3-methoxyphenyl)-9-(4-hydroxybenzoyl)-5a,10b-dihydro-11H-benzofuro[2,3-b]chromen-11-one | Roots | $C_{29}H_{21}O_{12}$ | Li et al. (2017) |
| 1,3,8,10,10b-Pentahydroxy-9-(4-hydroxybenzoyl)-5a-(4-hydroxyphenyl)-5a,10b-dihydro-11H-benzofurochromen-11-one | | $C_{28}H_{19}O_{11}$ | |
| 5a-(3,4-Dihydroxyphenyl)-1,3,8,10,10b-pentahydroxy-9-(4-hydroxybenzoyl)-5a,10b-dihydro-11H-benzofurochromen-11-one | | C28H19O12 | |
| 1,8,10,10b-Tetrahydroxy-5a-(4-hydroxy-3-methoxyphenyl)-9-(4-hydroxybenzoyl)-3-methoxy-5a,10b-dihydro-11H-benzofuro[2,3-b]chromen-11-one | | $C_{30}H_{23}O_{12}$ | |
| **Phenolic acids** | | | |
| Sedumol | Whole grass | $C_{12}H_{16}O_{8}$ | Han et al. (2021) |
| Vanillic acid | Aerial parts | $C_{8}H_{8}O_{4}$ | Lin (2014) |
| Protocatechuic acid | Aerial parts and leaves and stems | $C_{7}H_{6}O_{4}$ | |
| Caffeic acid | N/A | $C_{9}H_{8}O_{4}$ | |
| P-hydroxybenzoic acid | Aerial parts and leaves and stems | $C_{7}H_{6}O_{3}$ | Lin et al. (2014) |
| Pyrogallol | Aerial parts | $C_{6}H_{6}O_{3}$ | |
| 5,7-Dihydroxychromone | N/A | $C_{9}H_{6}O_{4}$ | |
| Glucosyringic acid | Leaves and stems | $C_{15}H_{20}O_{10}$ | Jia et al. (2014) |
| P-hydroxybenzoyl arbutin | | $C_{19}H_{20}O_{9}$ | |
| Pyroside | | $C_{14}H_{18}O_{8}$ | |
| Arbutin | Roots and leaves and stems | $C_{12}H_{16}O_{7}$ | |
| 4-Methoxy-3,5-dihydroxybenzoic acid | Whole grass | $C_{8}H_{8}O_{5}$ | Han et al. (2021) |
| 4-Hydroxybenzeneethanol | | $C_{8}H_{10}O_{2}$ | |
| 4-Hydroxybenzaldehyde | | $C_{7}H_{6}O_{2}$ | |
| cis-4-Coumaric acid | Aerial parts | $C_{9}H_{8}O_{3}$ | Xiong et al. (2019) |
| 2-O-(trans-caffeoyl) malic acid | | $C_{13}H_{12}O_{8}$ | |
| 2-O-(trans-caffeoyl)-malic acid 1-methyl-ester | | $C_{14}H_{14}O_{8}$ | |
| 2-O-(trans-caffeoyl)-malic acid 1,4-dimethyl ester | | $C_{15}H_{16}O_{8}$ | |
| Isolariciresinol-9-O-β-D-glucopyranoside | | $C_{26}H_{34}O_{11}$ | |
| Iriflophenone-2-O-β-D-glucopyranoside | | $C_{19}H_{20}O_{10}$ | |

(Continued on following page)

**TABLE 1 (*Continued*) Main active metabolites identified in *S. aizoon*.**

| Metabolite | Plant part | Molecular formula | Reference |
|---|---|---|---|
| Ethyl gallate | Aerial parts and leaves and stems | $C_9H_{10}O_5$ | |
| Gallic acid | Aerial parts, whole plant, and leaves and stems | $C_7H_6O_5$ | Zhang et al. (2010) |
| Methyl gallate | Aerial parts and leaves and stems | $C_8H_8O_5$ | |
| Echinochlorin A | Rhizome | $C_{26}H_{40}O_8$ | Li et al. (2020a) |
| 1-O-sinapoyl glucopyranoside | Aerial parts | $C_{17}H_{22}O_{10}$ | Xu et al. (2015) |
| Chrysophanol-8-O-β-D-glucoside | Whole grass | $C_{21}H_{20}O_9$ | Li et al. (2008) |
| Hydroquinone | Roots and whole grass | $C_6H_6O_2$ | |
| Vanilloloside | Leaves and stems | $C_{14}H_{20}O_8$ | Han et al. (2017) |
| Woodorien | | $C_{13}H_9N_3O_2$ | |
| Iriflophene | Aerial parts and rhizome | $C_{13}H_{10}O_5$ | Xiong et al. (2019), Li et al. (2020a) |
| **Triterpenes** | | | |
| Ginsenoside Re | Roots | $C_{48}H_{82}O_{18}$ | Gong (2020) |
| α-Amyrin | N/A | $C_{30}H_{50}O$ | |
| Ursolic acid | Roots | $C_{30}H_{48}O_3$ | Li et al. (2008) |
| Glutin-5-en-3-one | Leaves and stems | $C_{30}H_{48}O$ | |
| Isomoliol-3β-acetate | | $C_{32}H_{52}O_2$ | |
| Taraxerone | Rhizome | $C_{30}H_{48}O$ | Li et al. (2020a) |
| Isomotiol | | $C_{30}H_{50}O$ | |
| Oleanolic acid | Roots | $C_{30}H_{48}O_3$ | Lin (2014) |
| **Phytosterols** | | | |
| β-Sitosteryl linoleate | Rhizome | $C_{47}H_{80}O_2$ | Li et al. (2020a) |
| Daucosterol | Rhizome and whole grass | $C_{35}H_{60}O_6$ | |
| β-Sitosterol | Rhizome, leaves and stems, and roots | $C_{29}H_{50}O$ | Zhang et al. (2010) |
| Stigmasterol | N/A | $C_{29}H_{48}O$ | Cao (2011) |
| **Alkaloids** | | | |
| Sedinine | N/A | $C_{17}H_{25}NO_2$ | Kim et al. (1996) |
| Despun methylisopelletierine | | $C_9H_{17}NO$ | |
| Sedamine | Roots | $C_{14}H_{21}NO$ | Li et al. (2008) |
| Aizoonoside A | Aerial parts | $C_{18}H_{19}NO_8$ | Xu et al. (2015) |
| Thymine | Aerial parts | $C_5H_6N_2O_2$ | Lin et al. (2014) |
| Senecionine | Roots | $C_{18}H_{25}NO_5$ | Wu et al. (2008) |
| Seneciphylline | | $C_{18}H_{23}NO_5$ | |
| Integerrimine | | $C_{18}H_{25}NO_5$ | |

TABLE 1 (*Continued*) Main active metabolites identified in *S. aizoon*.

| Metabolite | Plant part | Molecular formula | Reference |
|---|---|---|---|
| Volatile oils | | | |
| 2,6-Di(tbutyl)-4-hydroxy-4-methyl-2,5-cyclohexadien-1-one | Whole plant | $C_{15}H_{24}O_2$ | Qian et al. (2018) |
| β-Ionone | | $C_{13}H_{20}O$ | |
| Epiglobulol | | $C_{15}H_{26}O$ | |
| α-Guaiene | | $C_{15}H_{24}$ | |
| Isophytol | | $C_{20}H_{40}O$ | |
| Squalene | | $C_{30}H_{50}$ | |
| Tritriacontane | | $C_{33}H_{68}$ | |
| Hexadecane | | $C_{16}H_{34}$ | |
| Pristane | | $C_{19}H_{40}$ | |
| Octadecane | | $C_{18}H_{38}$ | |
| Tricosane | | $C_{23}H_{48}$ | |
| Tetracosane | | $C_{24}H_{50}$ | |
| Pentacosane | | $C_{25}H_{52}$ | |
| Hexacosane | | $C_{26}H_{54}$ | |
| Heptacosane | | $C_{27}H_{56}$ | |
| Octacosane | | $C_{28}H_{58}$ | |
| Nonacosane | | $C_{29}H_{60}$ | |
| Hentriacontane | | C31H64 | |
| Cetyl palmitate | | $C_{32}H_{64}O_2$ | |
| 4, 8, 12, 16-Tetramethyl heptadecan-4-olide | | $C_{21}H_{40}O_2$ | |
| Cyclohexyl benzoate | | $C_{13}H_{16}O_2$ | |
| Methyl palmitoleate | | $C_{17}H_{32}O_2$ | |
| Methyl palmitate | | C17H$_{34}$O$_2$ | |
| Ethyl palmitate | | $C_{18}H_{36}O_2$ | |
| Methyl linolelaidate | | C19H34O2 | |
| Methyl oleate | | $C_{19}H_{36}O_2$ | |
| Methyl stearate | | $C_{19}H_{38}O_2$ | |
| Ethyl linoleate | | $C_{20}H_{36}O_2$ | |
| Ethyl oleate | | $C_{20}H_{38}O_2$ | |
| 1-Hexacosanol | | $C_{26}H_{52}O$ | |
| Hexahydrofarnesyl acetone | Whole plant and fresh herbs | $C_{18}H_{36}O$ | Guo et al. (2006), Qian et al. (2018) |
| 2-Undecanone | Fresh herbs | $C_{11}H_{22}O$ | Guo et al. (2006) |
| 2-Tridecanone | | $C_{13}H_{26}O$ | |
| Nerolidol | | $C_{15}H_{26}O$ | |
| (−)-Spathulenol | | $C_{15}H_{24}O$ | |
| Cedrol | | $C_{15}H_{26}O$ | |
| Globulol | | $C_{15}H_{26}O$ | |

TABLE 1 (*Continued*) Main active metabolites identified in *S. aizoon*.

| Metabolite | Plant part | Molecular formula | Reference |
|---|---|---|---|
| 1-Nonene | | C9H18 | |
| (十)-Aromadendrene | | C15H24 | |
| Calamenene | | $C_{15}H_{22}$ | |
| Caryophyllene epoxide | | $C_{15}H_{24}$ | |
| Bornyl acetate | | $C_{12}H_{20}O_2$ | |
| Geraniol acetate | | $C_{12}H_{20}O_2$ | |
| 15-ene-heptadecanal | | $C_{17}H_{48}O$ | |
| Hexadecanoic acid | | $C_{16}H_{32}O_2$ | |
| Phytol | Leaves, stems, fruits, and fresh herbs | $C_{20}H_{40}O$ | |
| 4-hepten-2-one | Aerial parts | $C_7H_{12}O$ | Chen et al. (2014) |
| Elsholtzia ketone | | $C_{10}H_{14}O_2$ | |
| 3-Methyl-2-butanol | | $C_5H_{12}O$ | |
| 2,3-Butanediol | | $C_4H_{10}O_2$ | |
| 1-Octanol | | $C_8H_{18}O$ | |
| 4-Terpineol | | $C_{10}H_{18}O$ | |
| 3-Hexen-1-ol | | $C_6H_{12}O$ | |
| Pentylfuran | | $C_9H_{14}O$ | |
| β-Phellandrene | | $C_{10}H_{16}$ | |
| 4-Carene | | $C_{10}H_{16}$ | |
| β-Terpinene | | $C_{10}H_{16}$ | |
| Isoterpinolene | | $C_{10}H_{16}$ | |
| α-Thujene | | $C_{10}H_{16}$ | |
| β-Farnesene | | $C_{15}H_{24}$ | |
| π-Muurolene | | $C_{15}H_{24}$ | |
| Heptanal | | $C_7H_{14}O$ | |
| Benzaldehyde | | $C_7H_6O$ | |
| Hexanal | | $C_6H_{12}O$ | |
| Furfural | | $C_5H_4O_2$ | |
| Octanal | | $C_8H_{16}O$ | |
| Benzeneacetaldehyde | | $C_8H_8O$ | |
| Nonanal | | $C_9H_{18}O$ | |
| Decanal | | $C_{10}H_{20}O$ | |
| 1-Octadecanol | Roots and leaves | $C_{18}H_{38}O$ | Chen and Qiang (2017) |
| (Z) 9-Octadecenoic acid, methyl ester | Roots and stems | $C_{19}H_{36}O_2$ | |
| 2,2′-Methylenebis(6-tert-butyl-4-methylphenol | Leaves, stems, and fruits | $C_{23}H_{32}O2$ | |
| Dimethyl phthalate | | $C_{10}H_{10}O_4$ | |
| Methyl tetradecanoate | | $C_{15}H_{30}O_2$ | |
| Heptadecanoic acid methyl ester | | $C_{18}H_{36}O_2$ | |
| Pentatriacontane | Leaves, stems, and roots | $C_{35}H_{72}$ | |

(Continued on following page)

TABLE 1 (*Continued*) Main active metabolites identified in *S. aizoon*.

| Metabolite | Plant part | Molecular formula | Reference |
|---|---|---|---|
| Heptadecane | Leaves, and whole plant | $C_{17}H_{36}$ | |
| 3-Ethyl-2,4-dimethyl-pentane | Leaves | $C_9H_{20}$ | |
| 2,6-Dimethyl-octane | | $C_{10}H_{22}$ | |
| 6,10,14-Trimethyl2 pentadecanone | | $C_{18}H_{36}O$ | |
| 1-Pentadecanol | | $C_{15}H_{32}O$ | |
| Oxacycloheptadec-8-en-2-one | | $C_{16}H_{28}O_2$ | |
| Tridecanoic acid, methyl ester | | $C_{14}H_{28}O_2$ | |
| 2,6,11-Trimethylodlodecane | | $C_{15}H_{32}$ | |
| 3-Methyl-undecane | | $C_{12}H_{26}$ | |
| Octadecane | Fruits | $C_{18}H_{38}$ | |
| 2,6,10,14-Tetramethyl-hexadecane | | $C_{20}H_{42}$ | |
| Icosane | Stems | $C_{20}H_{42}$ | |
| Nonadecane | | $C_{19}H_{40}$ | |
| 3,8-Dimethyl-decane | | $C_{12}H_{26}$ | |
| 4-Methyl-pentadecane | | $C_{16}H_{34}$ | |
| 1-Octadecene | | $C_{18}H_{36}$ | |
| 2-Methyl-tridecane | | $C_{14}H_{30}$ | |
| Tetratetracontane | | $C_{44}H_{90}$ | |
| Tetradecane | | $C_{14}H_{30}$ | |
| Pentadecane | Leaves and stems | $C_{15}H_{32}$ | |
| 2,4,4-Trimethylhexane | | $C_9H_{20}$ | |
| 2,4-Dimethylhexane | | C8H18 | |
| 4,6-Dimethyl-dodecane | | $C_{14}H_{30}$ | |
| Heneicosanoic acid-methyl ester | | $C_{22}H_{44}O_2$ | |
| Tricosanoic acid, methyl ester | | $C_{24}H_{48}O_2$ | |
| 2,4-bis(1,1-Dimethylethyl)-phenol | | $C_{14}H_{22}O$ | |
| Hexadecyl-oxirane | | $C_{18}H_{36}O$ | |
| 3,3- Dimethylhexane | | $C_8H_{18}$ | |
| 3, 3-Dimethyl-heptane | Roots | $C_9H_{20}$ | |
| Tetratriacontane | | $C_{34}H_{70}$ | |
| 1-Heptadecanol | | $C_{17}H_{36}O$ | |
| Octacosanoic acid, methyl ester | | $C_{29}H_{58}O_2$ | |
| Octadecanal | | $C_{18}H_{36}O$ | |
| 2-Hexadecyl-1,1′-bi-cyclopentyl | | $C_{26}H_{50}$ | |
| P-Cymene | Aerial parts | $C_{10}H_{14}$ | |
| Pentadecanoic acid, methyl ester | Roots, leaves, stems, and fruits | $C_{16}H_{32}O_2$ | |
| Dibutyl phthalate | | $C_{16}H_{22}O_4$ | |
| (Z,Z,Z)-9, 12, 15-octadecatrienoic acid, methyl ester | | $C_{19}H_{32}O_2$ | |
| Eicosanoic acid, methyl ester | | $C_{21}H_{42}O_2$ | |

(Continued on following page)

**TABLE 1** (*Continued*) Main active metabolites identified in *S. aizoon*.

| Metabolite | Plant part | Molecular formula | Reference |
|---|---|---|---|
| Docosanoic acid, methyl ester | | $C_{23}H_{46}O_2$ | |
| Tetracosanoic acid, methyl ester | | $C_{25}H_{50}O_2$ | |
| Hexacosanoic acid, methyl ester | | $C_{27}H_{54}O_2$ | |
| Others | | | |
| Glucose | Whole grass | $C_6H_{12}O_6$ | Zheng (1975) |
| Fructose | | $C_6H_{12}O_6$ | |
| Sedoheptulose | | $C_7H_{14}O_7$ | |
| Sucrose | | $C_{12}H_{22}O_{11}$ | |
| (3S,5R,6R,7E,9S)-megastigman-7-ene-3,5,6,9-tetrol 9-O-β-D-glucopyranoside | Aerial parts | $C_{28}H_{35}O_4D$ | Xu et al. (2015) |
| (3S,5R,6R,7E,9S)-megastigman-7-ene-3,5,6,9-tetrol 3-O-β-D-glucopyranoside | | $C_{28}H_{35}O_4D$ | |
| Picein | Leaves and stems | $C_{14}H_{18}O_7$ | Jia et al. (2014) |
| Koaburaside | | C14H20O9 | |
| Hexacosoic acid | Whole grass | $C_{26}H_{52}O_2$ | Li et al. (2008) |
| Salidroside | | $C_{14}H_{20}O_7$ | |
| Malic acid | N/A | $C_4H_6O_5$ | Xuan (2014) |
| N-triacontanoic acid | Roots and stem | $C_{33}H_{66}O_2$ | Li et al. (2020a) |
| 1-Hexadecanol | | $C_{16}H_{34}O$ | |
| Dioctadecylsulfide | | $C_{36}H_{74}S$ | |
| 1-Naphthalen-2-yl-ethanone | Whole grass | $C_{12}H_{10}O$ | Lin et al. (2011) |
| Lotaustralin | Aerial parts | $C_{11}H_{19}NO_6$ | Xiong et al. (2019) |
| Butanedioic acid | | $C_4H_6O_4$ | |
| 9(Z)-octadecenamide | | $C_{18}H_{35}NO$ | |

N/A: not applicable or not explicitly stated.

glucopyranoside (**4**), myricitrin (**10**), myricetin-3-O-α-L-arabinopyranoside (**14**) (Xiong et al., 2019), herbacetin-8-O-β-D-glucopyranoside (**26**), herbacetin-3-O-β-D-glucopyranosyl-8-O-α-L-arabinopyranoside (**27**), herbacetin-3-O-α-L-rhamnopyranosyl-8-O-α-D-lyxopyranoside (**28**), herbacetin-3-O-α-L-arabinopyranosyl-8-O-β-D-xylopyran-oside (**29**), gossypetin-3-O-β-D-glucopyranosyl-8-O-β-D-xylopyranoside (**31**), and 3′-methoxyl-gossypetin-3-O-β-D-glucopyranosyl-8-O-β-D-xylopyranosie (**35**) (Xu et al., 2015) were obtained mainly from the aerial part of *S. aizoon*. Later, Xu et al. (2019) successfully identified four flavonols [i.e., trifolin (**1**), rutin (**2**), astragalin (**32**), and isoquercitrin (**5**)], two flavones [i.e., lonicerin (**43**) and scutellarein (**46**)], and one isoflavone [i.e., genistein (**39**)] in the leaves and stems of *S. aizoon*. Two new prenylated isoflavones, sedacin A (**37**) sedacin B (**38**), and two flavonols, sedacin C (6″-O-(E)-feruloyl quercetin) (**33**) and sedacin D (6″-O-(E)-feruloyl isorhamnetin) (**34**), were isolated from the whole plant of *S. aizoon* (Li W. L. et al., 2011). Among them, sedacin A and sedacin B had the function of scavenging DPPH and ABTS+ free radicals (Li J. X. et al., 2011). Rhamnetin-3-O-β-D-glucopyranoside (**3**), quercetin-3-O-α-L-arabinopyranoside (**8**), isorhamnetin-3-O-β-D-xylopyranoside (**22**), and isorhamnetin-3-O-α-L-arabinopyranoside (**23**) have also been detected in rhizomes (Li et al.,

2020a). Four flavanonols (**44–47**) with rare dimeric structures, with the character of an iriflophene unit and a flavonoid unit connecting via a furan ring, were isolated from the roots and identified using NMR, IR, UV, HRESIM, DEPT, HSQC, HMBC, and CD methods. In addition, studies were conducted to assess the activity of these four substances, and they revealed that 5a-(3,4-dihydroxyphenyl)-1,3,8,10,10b-pentahydroxy-9-(4-hydroxybenzoyl)-5a,10b-dihydro-11H-benzofurochromen-11-one (**46**) and 1,8,10,10b-tetrahydroxy-5a-(4-hydroxy-3-methoxyphenyl)-9-(4-hydroxybenzoyl)-3-methoxy-5a,10b-dihydro-11H-benzofuro[2,3-b]chromen-11-one (**47**) had good anti-proliferative activities *in vitro* against the tumor cell lines BXPC-3, A549, and MCF-7 (Li et al., 2017). The structures of flavonoids from *S. aizoon* are displayed in Figure 2.

## 6.2 Phenolic acids

Phenolic acids are the most important chemical derivatives of plant secondary metabolites. Currently, 31 phenolics (**49–78**) have been found from *S. aizoon*, including phenolic acids (**49–58, 60**), lignans (**61**), phenylpropanoids (**59, 62–63**), and other phenolics (**64–78**). Two phenolic acids, namely, sedumol (**49**) and 4-methoxy-
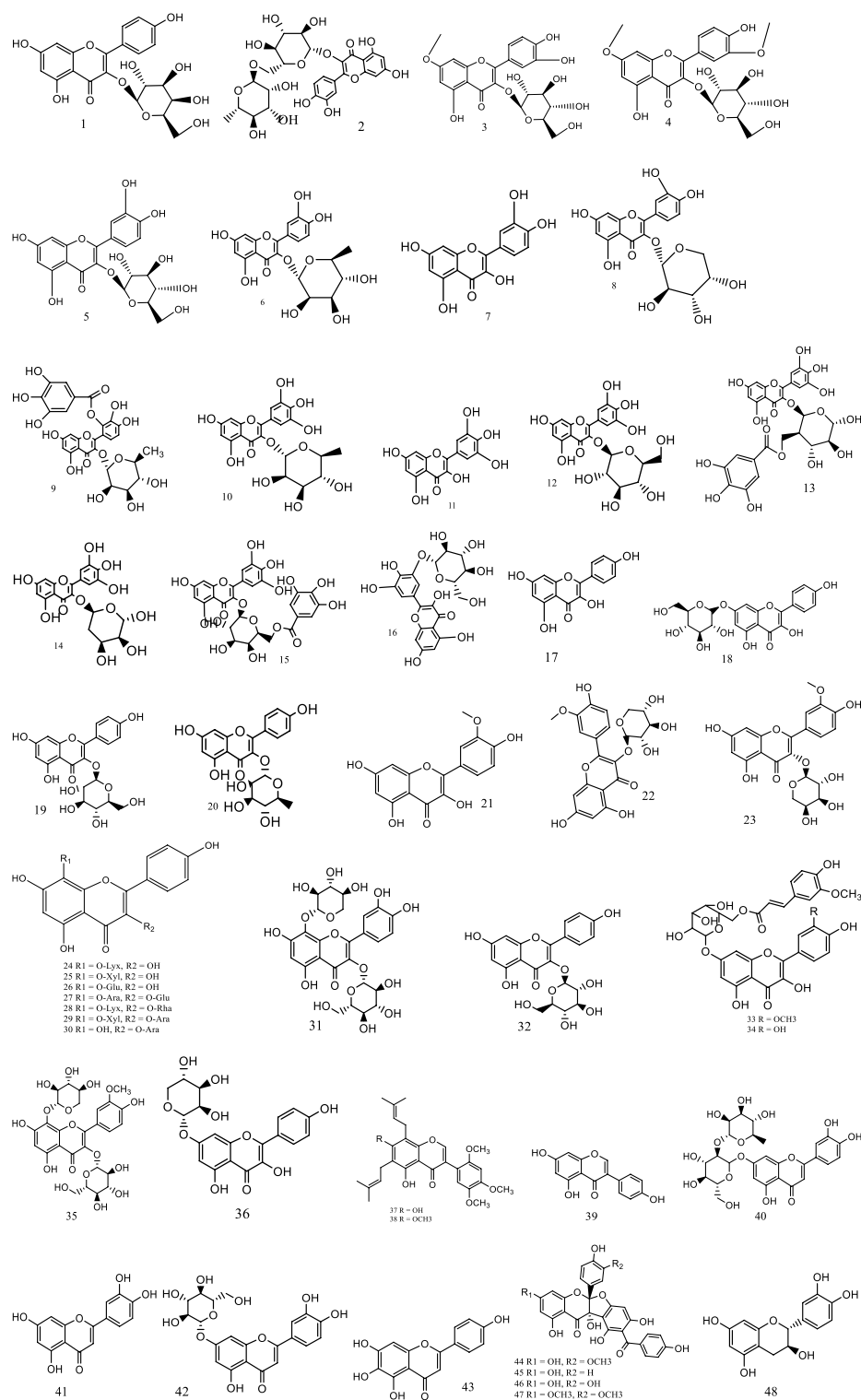
**FIGURE 2**
Structures of flavonoids from *S. aizoon* (**1–48**).

3,5-dihydroxybenzoic acid (**56**) (Han et al., 2021), were obtained from the 95% ethanol extract of *S. aizoon*'s whole grass. Other phenolic acids, including vanillic acid (**50**) (Lin, 2014), protocatechuic acid (**51**), cis-4-coumaric acid (**52**), p-hydroxybenzoic acid (**54**) (Xiong

et al., 2019), and caffeic acid (**53**) (Lin et al., 2014), were isolated from the aerial part of *S. aizoon*. Isolariciresinol-9-O-β-D-glucopyranoside (**61**) is classified as cyclolignans, which was obtained from the 70% ethanol extract via silica gel column chromatography (300–400 mesh).
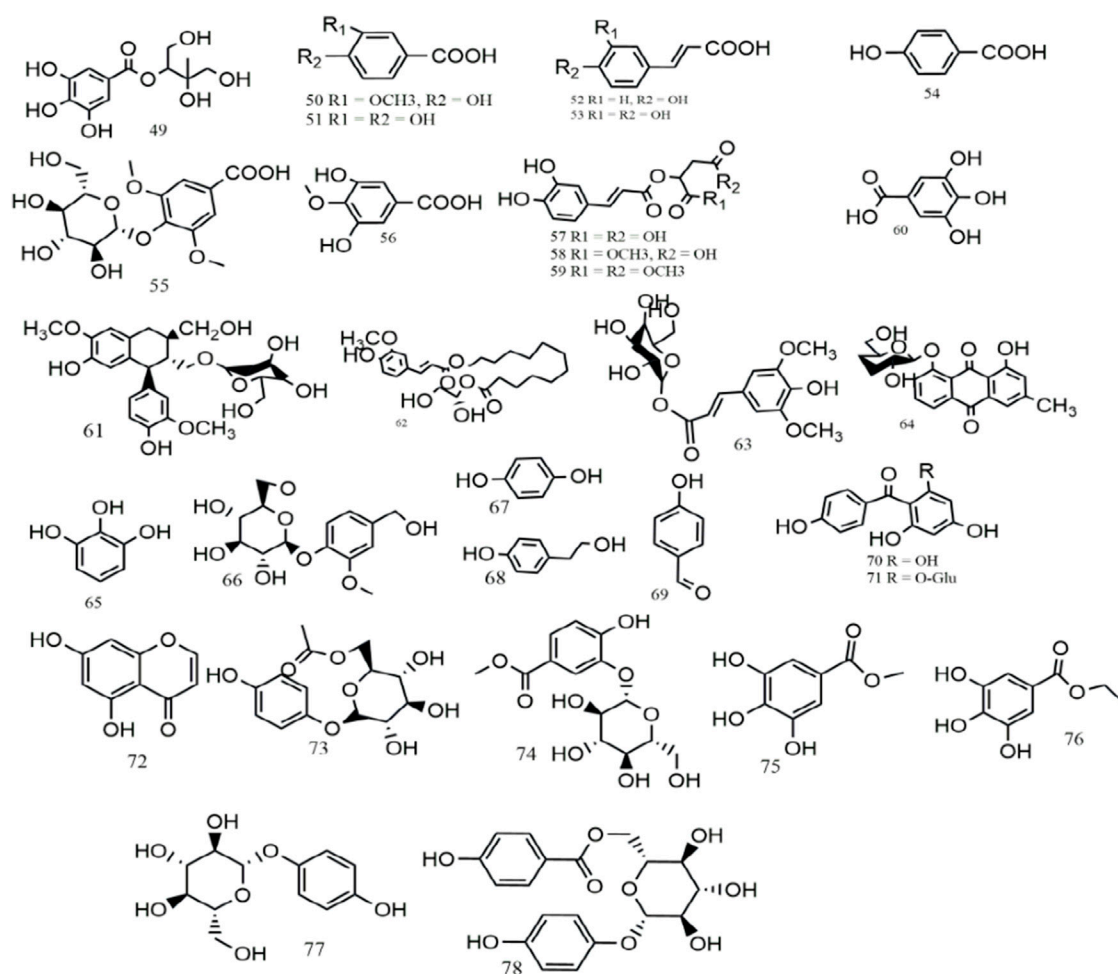
FIGURE 3
Structures of phenolic acids from *S. aizoon* (**49–78**).

2-O-(trans-caffeoyl)-malic acid 1,4-dimethyl ester (**59**) (Xiong et al., 2019), echinochlorin A (**62**) (Li et al., 2020a), 1-O-sinapoyl glucopyranoside (**63**) (Xu et al., 2015), and chrysophanol-8-O-β-D-glucoside (**64**) (Li et al., 2008) have been identified in *S. aizoon*. The structures of phenolic acids from *S. aizoon* are displayed in Figure 3.

## 6.3 Triterpenes and phytosterol

### 6.3.1 Triterpenes

A type of terpenoids known as triterpenoids has a parent nucleus that contains 30 carbon atoms. Triterpenoids exist in plants in free form or as glycosides or esters and have various biochemical activities. Up to now, eight triterpenes (**79–86**) were separated from *S. aizoon*, including one tetracyclic triterpenes (**79**) and seven pentacyclic triterpenes (**80–86**). The only tetracyclic triterpene, ginsenoside Re (**79**), is a dammarane-type triterpene. Seven pentacyclic triterpenes are divided into four groups: ursane type (**80**), oleanane type (**81–83**), friedelane type (**84**), and fernane type (**85–86**). In the studies of Li et al. (2008, 2020a), glutin-5-en-3-one (**84**), isomoliol-3β-acetate (**86**), taraxerone (**82**), and isomotiol

(**85**) were isolated from *S. aizoon* for the first time. The structures of triterpenoids from *S. aizoon* are displayed in Figure 4.

### 6.3.2 Phytosterols

Up to now, a total of four phytosterols (**87–90**) have been identified in *S. aizoon*. These include β-sitosteryl linoleate (**87**) (Li et al., 2020a), daucosterol (**89**) (Guo et al., 2010; Lin et al., 2011), β-sitosterol (**88**), and stigmasterol (**90**) (Cao, 2011). The structures of phytosterol from *S. aizoon* are displayed in Figure 4.

## 6.4 Alkaloids

Eight alkaloids (**91–98**) have been isolated and identified from *S. aizoon*. In 1996, Kim et al. (1996) examined the alkaloids in *Sedum* species and discovered the presence of three alkaloids, namely, sedinine (**91**), sedamine (**92**), and despun methylisopelletierine (**93**) in *S. aizoon*. Thymine (**95**) was obtained from the ethyl acetate fraction of aqueous extracts of *Sedum aizoon* L. In the study of Gao et al. (2006), three pyrrolizidine alkaloids (PAs), namely, senecionine (**96**), seneciphylline (**97**), and integerrimine
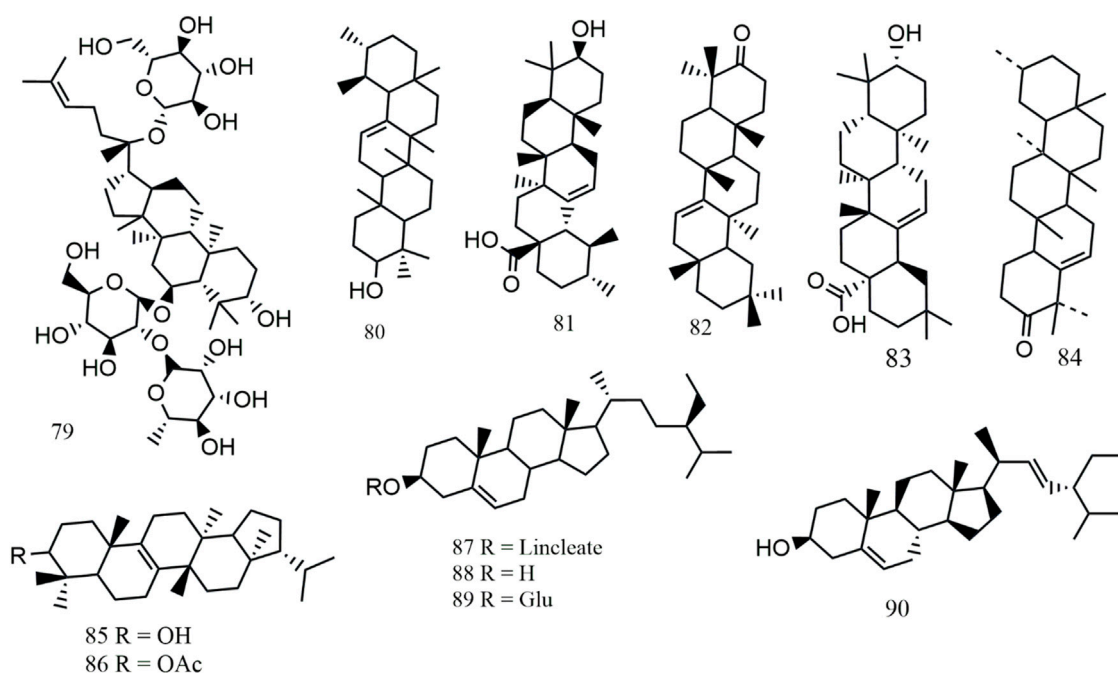
**FIGURE 4**
Structures of triterpenoids (**79−86**) and phytosterol (**87−90**) from *S. aizoon*.
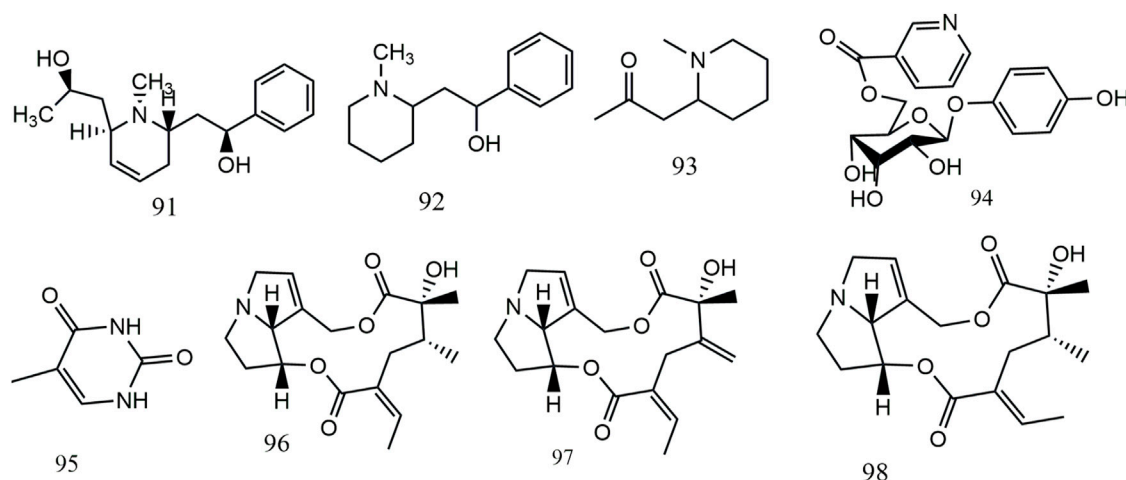


**FIGURE 5**
Structures of alkaloids (**91−98**) from *S. aizoon*.

(**98**) were identified in the extracts of *S. aizoon*'s root, which had strong hepatotoxicity. The structures of alkaloids from *S. aizoon* are displayed in Figure 5.

# 7 Pharmacological activities

According to pharmacological studies, *S. aizoon* has a wide range of pharmacological activities, including antioxidant, anti-fatigue, and anti-inflammatory activities, improving cardiovascular disease, and other activities. The related biological activities and main effects are listed in Table 2.

## 7.1 Antioxidant activity

*S. aizoon* has excellent antioxidant activity, as demonstrated by several pharmacological studies *in vitro* and *in vivo*. An in-depth *in vivo* study showed that the juice from the stems and leaves of *S. aizoon* increased the peroxidase (POD) and superoxide dismutase

TABLE 2 Biological activities of the *S. aizoon* extracts and bioactive metabolites.

| Tested substance | Model | Key result | Reference |
|---|---|---|---|
| Ethanol extract | *In vitro*, total antioxidant capacity, superoxide anion, OH radical scavenging assay, and blood antioxidant | Obvious antioxidant activity | Ma et al. (2019), Qi et al. (2022) |
| | Stomach bleeding model in mice, clean grade healthy ICR Mice | Reduced gastric mucosal injury and shortened the bleeding time and clotting time in mice | Zhong et al. (2014) |
| | *In vitro*, *aeromonas*, *Rhizopus nigricans*, *Botrytis cinerea*, *Penicillium italicum*, *Pseudomonas fragi*, and *Shewanella putrefaciens* isolated from sea food | Exhibited antibacterial activity, caused membrane damage, disruption of mycelial morphology, the bacterial surface, and internal ultrastructure, resulted in the leakage of sugars and proteins, retarded the microbial growth, and delayed meat spoilage | Xu et al. (2019), Luo et al. (2020), Wang et al. (2020), Wang et al. (2022a), Wang et al. (2022b), Wang et al. (2023c), Ge et al. (2023) |
| | Human liver cancer cell line | The inhibitory rate of liver cancer cells was as high as 52.04% with 200 μg/mL ethanol extract | Wang et al. (2013) |
| | ICR mice weigh 18~20 g | Reduced the weight gain of mice and TC and TG levels increased HDL-C levels | Wang et al. (2013) |
| | Type 1 diabetes mellitus mice | Significantly restored body weight gain, improved food utilization, decreased the coefficients for both the liver and kidney, the levels of TC and TG, and the MDA content, increased the levels of HO-1 and NQO1 in the livers of mice, activated the Nrf2 pathway, thereby regulating the expression of downstream proteins, and regulated glucose metabolism in T1DM mice | Qi et al. (2022) |
| | *In vitro*, MDRPA, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Micrococcaceae*, *Escherichia coli*, *Salmonella paratyphi* B, *bacillary dysentery*, *Proteus mirabilis*, *Clostridium perfringens*, *Bacillus subtilis*, *Bacillus anthracis*, *Candida parapsilosis*, *Candida tropicalis*, and *Candida albicans* | The MIC50 for *pseudomonas aeruginosa* was 0.125 g/mL, which exerted definite bacteriostatic effects on bacteria and weak effect on fungus | Zhang et al. (2011), Zhang et al. (2012) |
| Sap | *In vivo*, the liver in *Cyprinus carpio* Linnaeus | Increased SOD, POD activities, and MDA content | Zhang and Wang (2012) |
| | College students who have completed exhaustive exercise | Prolonged the time of extreme exercise in mice, decreased BUN and MDA levels and LDH, increased SOD, muscle glycogen content, and liver glycogen content, play an anti-fatigue role, increased the amount of blood return and the content of hemoglobin in the blood, reduced the blood flow at the end of the limb and the concentration of cortisol and serum creatine kinase in the blood, improved the ability of metabolic regulation and response speed, accelerated fatigue recovery, and prevented and relieved fatigue | Ding, 2019; Ren (2020) |
| | *In vivo*, rats with gastrointestinal tract hemorrhage induced by aspirin | Turned positive rat fecal occult blood into negative, increased PC, GPIIb/IIIa, P selectin, PLT, IL8, ET-1, and platelet number and aggregation, decreased PAF, significantly shortened TT and APTT, and significantly increased FIB | Liu et al. (2011), Liu et al. (2015), Bai et al. (2016) |
| | Senile stroke patients | Promoted blood circulation, removed blood stasis, and reduced blood pressure | Chen (2000) |
| Ethyl acetate extracts | LPS-stimulated RAW 264.7 cells | Inhibited LPS-induced NO, TNF-α, and IL-6 production | Lin et al. (2015a) |
| | α-Glucosidase activity assay | Inhibit α-glucosidase activity | Cao (2011) |

TABLE 2 (*Continued*) Biological activities of the *S. aizoon* extracts and bioactive metabolites.

| Tested substance | Model | Key result | Reference |
|---|---|---|---|
| N-Butanol extracts | α-Glucosidase activity assay | Inhibit α-glucosidase activity | Cao (2011) |
| Methanol extracts | α-Glucosidase activity assay | Inhibit α-glucosidase activity | Cao (2011) |
| | *In vivo,* male ICR mouse croton oil-induced ear edema, rat CGN-induced paw edema, TPA-induced ear edema assay of sub-chronic inflammation, mouse acetic acid-induced writhing, and LPS-stimulated RAW 264.7 cells | Inhibited PGE2 production by the downregulation of COX-2 expression and COX-2 induction and inhibited acute as well as sub-chronic inflammation dose-dependently | Kim et al. (2004) |
| | *In vivo,* H/R model in neonatal rat cardiomyocytes | Decreased the LDH, apoptosis, and caspase-3 activity, activated P13K/Akt, increased eNOS phosphorylation, NO, and the Bcl-2/Bax ratio, reduced H/R-induced cardiomyocyte damage, and protected cardiomyocytes | Qiang (2013) |
| *S. aizoon* tablet | 244 cases with peptic ulcer bleeding | Increased the PC and shortened bleeding time | Xu (2012) |
| Aqueous extracting—ethanol precipitating extract | Stomach bleeding model in mice | Exerted the strongest protective effects on gastric mucosa | Zhong et al. (2014) |
| Petroleum ether | Stomach bleeding model in mice | Reduced gastric mucosal injury and shortened the bleeding time and clotting time in mice | Chen et al. (2012) |
| Ethyl acetate of water extraction | Clean grade healthy ICR mice | Good hemostatic effect | Chen et al. (2012) |
| Aqueous extracts | Stomach bleeding model in mice | Reduced gastric mucosal injury and shortened the bleeding time and clotting time in mice | Chen et al. (2012) |
| | *In vitro*, MDRPA, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* | Have certain bacteriostasis, and the MIC50 for *pseudomonas aeruginosa* was 0.5 g/mL | Tan et al. (2001) |
| | *In vivo*, male Kunming mice | Increased the amount of sleeping mice and decreased the autonomic activities in mice | Guo et al. (2009) |
| | Esophageal carcinoma cells | Destroyed the structure of phospholipid and resulted in the damage of the ultrastructure of esophageal carcinoma cells | Fu et al. (2008) |
| | *In vivo*, patients with cardiovascular and cerebrovascular diseases | Protected blood vessels, removed blood stasis, and prevented blood clots | Xuan (2015) |
| Herbacetin-3-O-α-L-rhamnopyranosyl-8-O-α-D-lyxopyranoside | *Escherichia coli*; *Staphylococcus aureus* Rosenbach and *Bacillus subtilis* | Showed certain growth inhibition, and it showed more potency against Gram-positive than against Gram-negative bacteria | Xu et al. (2015) |
| Myricetin-3-O-β-D-glucopyranoside | *Escherichia coli*, *Staphylococcus aureus* Rosenbach, and *Bacillus subtilis* | Showed more potency against Gram-positive than against Gram-negative bacteria | Xu et al. (2015) |
| Gossypetin-3-O-β-D-glucopyranosyl-8-O-β-D-xylopyranoside | *Escherichia coli*, *Staphylococcus aureus* Rosenbach, and *Bacillus subtilis* | Showed more potency against Gram-positive than against Gram-negative bacteria | Xu et al. (2015) |
| Ethyl acetate from alcohol extract | *In vivo*, male Kunming mice | Obviously decreased the autonomic activities in mice, prolonged the sleeping time, and increased the amount of sleeping mice | Guo et al. (2010) |
| N-butanol extracted from alcohol extract | *In vivo*, the male Kunming mice | Obviously decreased the autonomic activities in mice, prolonged the sleeping time, and increased the amount of sleeping mice | Guo et al. (2010) |
| Yangxincao Anshen Granule | *In vivo*, Kunming mice | Significantly decreased spontaneous activity, prolonged sleep time, and | Zhang et al. (2015b) |

TABLE 2 (*Continued*) Biological activities of the *S. aizoon* extracts and bioactive metabolites.

| Tested substance | Model | Key result | Reference |
|---|---|---|---|
| | | increased rates of sleeping in mice on the high (12 g/kg/d) and medium dosages (6 g/kg/d) | |
| *S. aizoon* (30 g) and *Semen Ziziphus Spinosa* (15 g) | *In vivo*, Kunming mice | Extented the sleep time significantly and increased the sleep rate | Zhang et al. (2015a) |
| *S. aizoon* (22.5 g) and *Semen Ziziphus Spinosa* (22.5 g) | *In vivo*, Kunming mice | Extended the sleep time and increased the sleep rate | Zhang et al. (2015a) |
| Myricetin-3-O-β-D-glucopyranoside | *In vitro*, human hepatoma cell line (HepG2), human breast cancer (MCF-7), and human lung carcinoma (A549) tumor cell lines | Had anti-proliferative activities on cell proliferation with IC50 values of 46.30, 75.27, and 49.76 μmol/L, respectively | Xu et al. (2015) |
| 5a-(3,4-Dihydroxyphenyl)-1,3,8,10,10b-pentahydroxy-9-(4-hydroxybenzoyl)-5a,10b-dihydro-11H-benzofuro chromen-11-one, an iriflophene unit, and a quercetin unit connecting via a furan ring | *In vitro, in situ* pancreatic adenocarcinoma cell (BXPC-3), A549, and human breast cancer (MCF-7) tumor cell lines | Exhibited moderate cytotoxic activities against BXPC-3, A549, and MCF-7 tumor cell lines with IC50 ranging from 24.84 to 37.22 μmol/L | Li et al. (2017) |
| 1,8,10,10b-Tetrahydroxy-5a-(4-hydroxy-3-methoxyphenyl)-9-(4-hydroxybenzoyl)-3-methoxy-5a,10b-dihydro-11H-benzofuro [2,3-b]chromen-11-one, an iriflophene unit and a rhamnazin unit connecting via a furan ring | *In vitro*, anti-proliferative activities against BXPC-3, A549, and MCF-7 tumor cell lines | Exhibited moderate cytotoxic activities against BXPC-3, A549, and MCF-7 tumor cell lines with IC50 ranging from 24.84 to 37.22 μmol/L | Li et al. (2017) |
| EtOAc fraction of aqueous extract | *In vitro*, LPS-stimulated RAW 264.7 macrophages | Inhibited the release of NO from inflammatory cells | Lin (2014) |
| 3′,4′,5,7-Tetrahydroxy | *In vitro*, LPS-stimulated RAW 264.7 macrophages | Inhibited the release of TNF-α | Lin (2014) |
| Galuteolin | *In vitro*, LPS-stimulated RAW 264.7 macrophages | Inhibited the release of NO and TNF-α | Lin (2014) |
| Protocatechuic acid | *In vitro*, LPS-stimulated RAW 264.7 macrophages | Inhibited the release of TNF-α, IL-6, NO, and IL-1β | Huang, 2014; Lin (2014) |
| Caffeic acid | *In vitro*, LPS-stimulated RAW 264.7 macrophages | Inhibited the release of TNF-α, IL-6, NO, and IL-1β | Huang, 2014; Lin (2014) |
| 6% *S. aizoon* | Renal hypertensive male rat model | Lowered SBP and MAP, thereby lowering blood pressure | Han et al. (2022) |
| 10% *S. aizoon* | Renal hypertensive male rat model | Decreased SBP, MAP, blood pressure, serum creatine kinase CK activity, left ventricular stroke index LVWI (LW/BW) and HWI (HW/BW), and the expression of AT1 protein, increased the expression of AT2 and catalase protein, reversed myocardial remodeling, and protected the heart | Han et al. (2022) |
| *Yangxincao* capsules | Hyperlipidemia rat model | Significantly decreased the levels of serum TC, TG, and LDL-C, decreased the level of apoB, and increased the levels of HDL-C and its subcomponents HDL2-C, HDL3-C, and the ratio of HDL-C/TC; significantly increased the activities of LCAT and LPL and the level of apoA in the serum | Liu et al. (2005) |
| Leaching solution | Rabbit and frog | Stimulated the action of the heart and reduced the toxicity of amphetamine | Zheng (1975) |
| Polysaccharide | Mice | Significantly improved thymus index and spleen index, T- and B-lymphocyte transformation and proliferation, and NK cell activity; increased the percentage values of CD3^{+}, CD4^{+}, CD19^{+}, and CD4+/CD8+ in the peripheral blood | Huang (2019) |

N/A, not applicable or not explicitly stated.

**FIGURE 6**
Schematic diagram of anti-fatigue effects of *S. aizoon*.
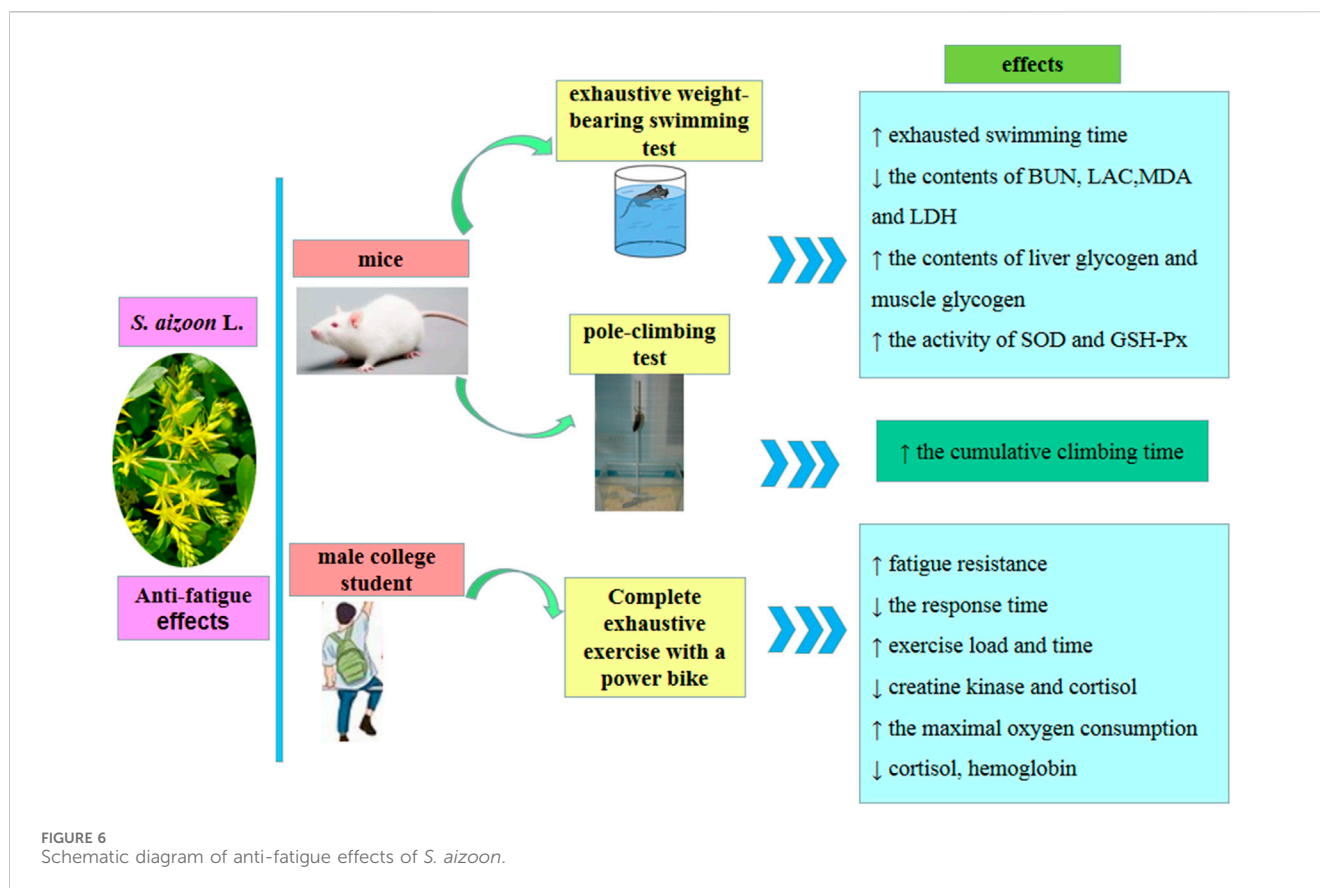
(SOD) of the liver in *Cyprinus carpio* Linnaeus as well as reduced the content of malondialdehyde (MDA), thus preventing the peroxidation damage of the liver cell membrane (Zhang and Wang, 2012). Experimental tests *in vivo* showed that ethanol extracts of *S. aizoon* were able to enhance antioxidant enzymes in T1DM mice and successfully alter the Nrf2/Keap1/ARE signaling pathway (Qi et al., 2022). Additionally, 95% ethanol extract of *S. aizoon* increased the activity of SOD, CAT, and GSH-Px and reduced the contents of MDA and ROS on the rat adrenal pheochromocytoma cell line (PC12) induced by $H_2O_2$, showing a protective effect on the cell (Zhao, 2015).

## 7.2 Anti-fatigue effects

As national fitness activities expand, more individuals participate in sports, and the negative consequences of exercise fatigue on the body become more obvious. The effective recuperation of the body and the rapid removal of exercise exhaustion are becoming increasingly vital to society. The animal experiments (mice) demonstrated that the extracts of *S. aizoon* (3.6 and 0.9 mL/kg, 30 days) prolonged the time of extreme exercise in mice, reduced the contents of blood urea nitrogen (BUN), lactic acid (LAC), MDA, and lactate dehydrogenase (LDH) in the serum of mice, improved the activity of SOD and GSH-Px, and increased the contents of liver and muscle glycogen of mice (Ding, 2019). In a human clinical trial, it has been found that the administration of the sap (0.225 mL/kg.d, 0.9 mL/kg.d, and 3.6 mL/kg.d, 28 days) of the aerial part from *S. aizoon* [5 mL/(60 kg.d), 14 days] reduced the response time

of male college students to the stimulus signal, improved fatigue resistance, and accelerated fatigue recovery by decreasing the content of blood perfusion index, cortisol, and creatine kinase in the serum and increasing hemoglobin and the load of final exercise (Ren, 2020). The above studies showed that *S. aizoon* improved exercise endurance, affected their metabolic activity, and produced anti-fatigue effect. *S. aizoon*'s probable anti-fatigue effects of action are shown in Figure 6.

## 7.3 Hemostatic activity

*S. aizoon* has an effect comparable to that of *Notoginseng* Radix in terms of reducing bleeding without causing stasis and nourishing blood. A series of experiments *in vivo* and *in vitro* revealed that extracts and preparations of *S. aizoon* exhibited good hemostatic activities. Previous studies showed that alcohol and aqueous extracts (6, 12 g/kg b.w) of *S. aizoon* could significantly shorten the bleeding time and clotting time of mice (Chen et al., 2012). The juice of the whole herb from *S. aizoon* could increase the levels of GP IIb/IIIa, P selectin, and ET-1 and the number of platelets and enhance the platelet aggregation and release function of the rats with aspirin-induced gastric hemorrhage, thus achieving hemostasis. Since *S. aizoon* could increase the level of IL-8, it was used in patients with bleeding accompanied by inflammation (Huang, 2014).

*S. aizoon* combined with other drugs can also be used for the treatment of bleeding diseases. Patients with bleeding peptic ulcers was treated upon treatments with herbs *S. aizoon* in conjunction with omeprazole (Xu, 2012). After intravenous injection in rabbits

**FIGURE 7**
*S. aizoon*'s probable hemostatic activity.



**FIGURE 8**
*S. aizoon*'s probable antimicrobial action.
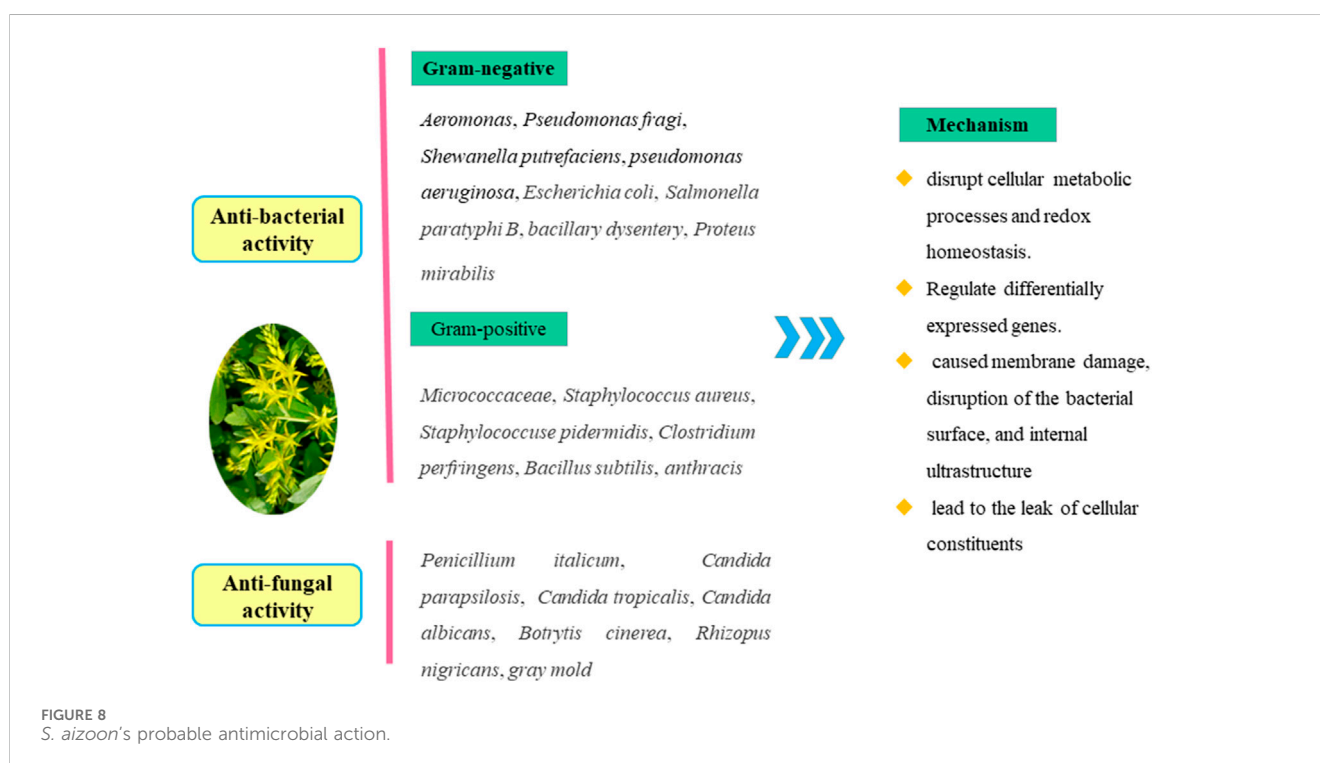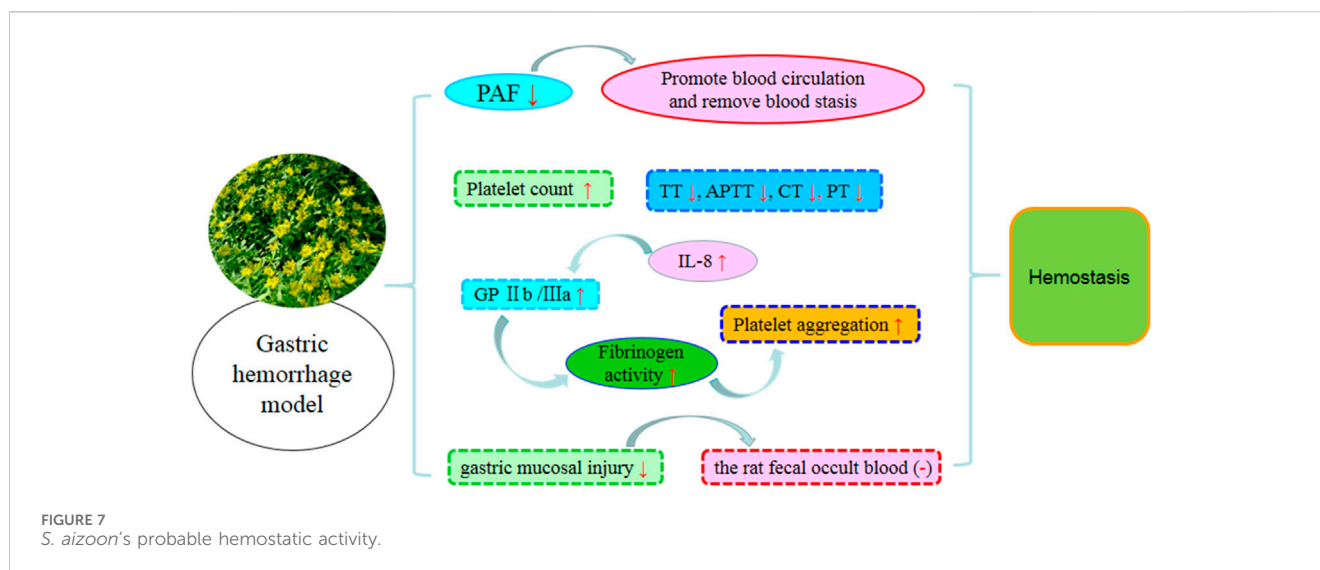
and intraperitoneal injection in mice of *S. aizoon* syrup, the blood coagulation time and bleeding time were decreased (Chinese Academy of Medical Sciences, 1972). The probable hemostatic mechanism is shown in Figure 7.

## 7.4 Antimicrobial activity

The crude extracts from *S. aizoon* have antimicrobial activity. According to transcriptome and RNA sequencing analyses, the ethanol extracts extracted from *S. aizoon* had significant antimicrobial activities against *B. cinerea* (Wang K. et al., 2022), *Aeromonas* (Xu et al., 2019), postharvest citrus blue mold (Luo

et al., 2020), *Shewanella putrefaciens* (Wang et al., 2020), and *Pseudomonas fragi* (Wang H. X. et al., 2022). Studies revealed that alcohol extracts had a good inhibitory ability against 20 strains of multidrug-resistant *Pseudomonas aeruginosa* (MIC50 value = 0.125 g/mL) (Zhang et al., 2012; Wang H. et al., 2023), *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Micrococcus* (MIC value = 0.125 g/mL). However, the inhibitory impact on three types of fungus, including *Candida tropicalis*, *Candida parapsilosis*, and *Candida albicans*, was very poor, with MIC values above 0.5 g/mL (Zhang et al., 2011).

Furthermore, monomer metabolites isolated from *S. aizoon* also have antimicrobial activity. Xu et al. (2015) revealed that herbacetin-3-O-α-L-rhamnopyranosyl-8-O-α-D-lyxopyranoside (**28**), myricetin-3-O-β-D-glucopyranoside (**12**), and gossypetin-3-O-β-D-

glucopyranosyl-8-O-β-D-xylopyranoside (**31**) exhibited more potency against Gram-positive than against Gram-negative bacteria. *S. aizoon*'s probable antimicrobial actions are shown in Figure 8.

## 7.5 Sedative and hypnotic effects

Traditional Chinese medicine and its preparations are commonly used to treat sleeplessness, agitation, and other symptoms. They offer the benefits of safety and dependability, as well as fewer toxicity and side effects, as compared to Western medication with sedative and hypnotic properties. Using the mouse model, Guo et al. (2009) showed that the water and alcohol extracts have tranquilizing mind and the calming effects. Later, they also found that the ethyl acetate and butanol extracts could effectively lower the autonomic activity in mice, lengthen sleeping duration in mice, and increase the number of sleeping mice (Guo et al., 2010).

Additionally, the *S. aizoon*'s prescription or in combination with other drugs also possess sedative and hypnotic properties, which are often used to treat sleeplessness, restlessness, and other disorders. For instance, Yangxincao Anshen Granules made with *S. aizoon* (12, 6 g/kg/d) significantly reduced the spontaneous movements of mice, and the granules, in conjunction with pentobarbital, extended the duration of their sleep, providing good sedative and hypnotic effects without negative side effects (Zhang R. Z. et al., 2015). Similar results have been recorded for the combination between *S. aizoon* and *Semen ziziphus spinosa* (Zhang L. et al., 2015).

## 7.6 Anti-cancer activity

*S. aizoon*'s active metabolites and crude extracts with anti-cancer potential have piqued the interests of researchers in recent years. The ethanol extracts isolated from *S. aizoon* (50, 100, and 200 μg/mL) could lower the survival rate of human liver cancer cells HepG2 and inhibit human hepatocarcinoma proliferation by 11.15%, 41.96%, and 52.04%, respectively. With the increase in concentration, the inhibition rate of liver cancer cells increased, showing a certain dose–effect relationship (Wang et al., 2013). The aqueous extracts of *S. aizoon* [equivalent to adding 15.9 mg raw drug, containing 31.7 μg gallic acid (**60**)] could destroy the phospholipid-dominated structures and block nucleic acid synthesis and metabolism, which caused the death of cancer cells, and the killing effect was improved when the drug treatment period was extended (Fu et al., 2008).

Among the active metabolites tested, myricetin-3-O-D-glucopyranoside (**12**) obtained from the aerial portion of *S. aizoon* exhibited an effect on cell proliferation against HepG2, MCF-7, and A549 tumor cells, with IC50 values of 46.30, 75.27, and 49.76 mol/L, respectively (Xu et al., 2015). Li et al. (2017) found that 5a-(3,4-dihydroxyphenyl)-1,3,8,10,10b-pentahydroxy-9-(4-hydroxybenzoyl)-5a,10b-dihydro-11H-benzofuro chromen-11-one, an iriflophene unit, and a quercetin unit connecting via a furan ring (**44**) and 1,8,10,10b-tetrahydroxy-5a-(4-hydroxy-3-methoxyphenyl)-9-(4-hydroxybenzoyl)-3-methoxy-5a,10b-dihydro-11H-benzofuro[2,3-b]chromen-11-one, an iriflophene unit, and a rhamnazin unit connecting via a furan ring (**47**) isolated from the roots of *S. aizoon* exhibited cytotoxic activities against BXPC-3,

A549, and MCF-7 tumor cell lines, with IC50 ranging from 24.84 to 37.22 μmol/L. *S. aizoon*'s probable anti-cancer actions are shown in Figure 9.

## 7.7 Anti-inflammatory effect

In Northeast Asia, *S. aizoon* has been used as a traditional medicine to treat inflammatory illnesses. Several extracts (PE, EtOAc, and $H_2O$) of *S. aizoon* were administered to LPS-stimulated RAW 264.7 cells to investigate anti-inflammatory activities. The phenolic and flavonoid-rich EtOAc extracts reduced NO, TNF-α, and IL-6 production induced by LPS (Lin et al., 2015a). In a study by Kim et al. (2004), methanol extracts of *S. kamtschaticum* Fischer showed a significant inhibitory effect in the inflammation models of mouse ear edema (50–400 mg/kg for 3 days) and rat paw edema (400–800 mg/kg for 3 days) induced by croton oil and multiple phorbol ester. The cyclooxygenase-2 expression was downregulated. Possible mechanisms of action are given in Figure 10.
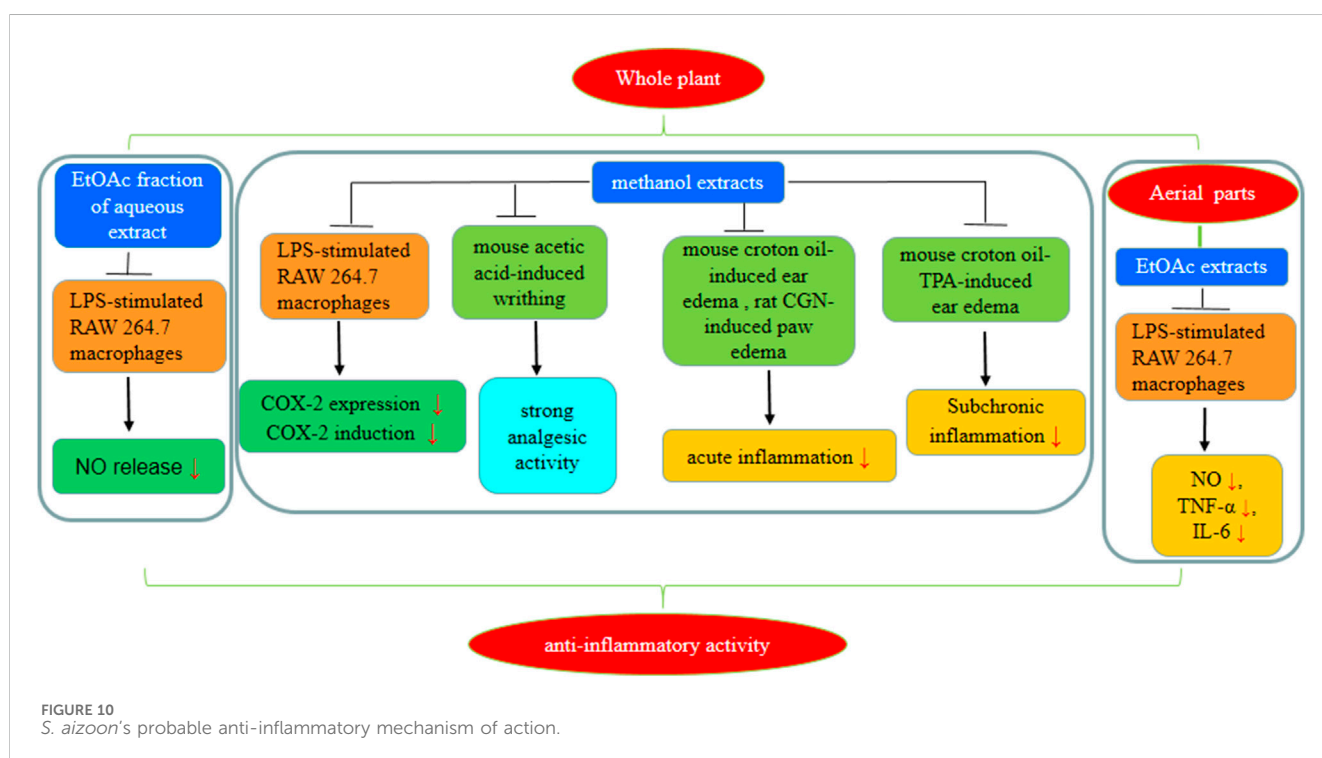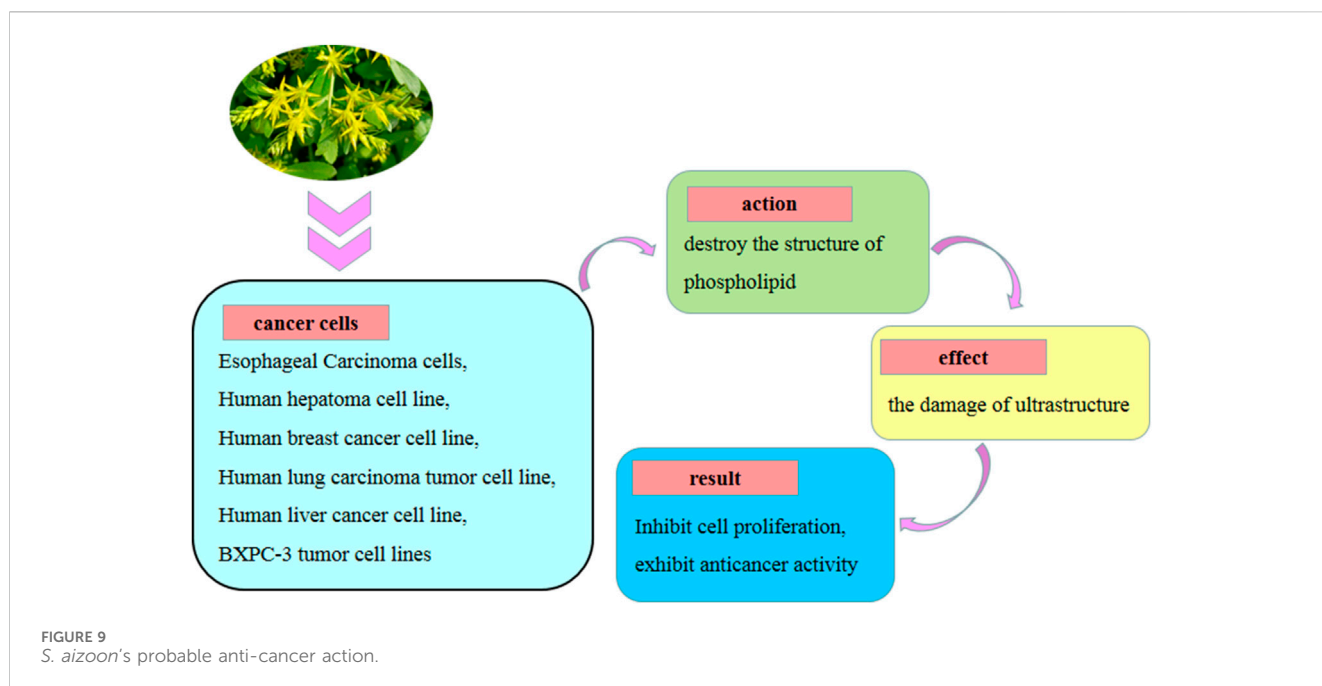
## 7.8 Cardioprotective effects

*S. aizoon* lowered blood pressure, serum CK activity, and AT1 protein expression, reversed myocardial remodeling, and increased AT2 and catalase protein expression (Han et al., 2022). Chen (2000) showed that fresh *S. aizoon* grass could help stroke victims regain consciousness. It is thought that this herb has evident effects in improving blood circulation, reducing blood stasis, and decreasing blood pressure. Using the method of network pharmacology and molecular docking, studies found that *S. aizoon* had the effect of treating atherosclerosis and coronary heart disease (Zhu et al., 2022, 2023).

Interestingly, the extract of *S. aizoon* increased cardiac activity and decreased amphetamine toxicity (Zheng, 1975). According to the study of Wang et al. (2013), *S. aizoon* had the ability to regulating blood lipid levels and could dramatically lower the mice's liver index and fat coefficient. Additionally, when hyperlipidemia rats were treated with Yangxincao capsules (derived from whole grass extract), the serum levels of TC, TG, and LDL-C were decreased, while HDL-c and its subcomponents (HDL-c, HDL-3-C, and HDL-C/TC) were increased, implying that the mechanism of lipid regulation of *S. aizoon* was related to the enhancement of the activities of LPL, LCAT, and HDL2-C (Wu et al., 2006).

## 7.9 Other activities

In T1MD mice, it has been shown that *S. aizoon* extract has the ability to enhance glucolipid metabolism and organ coefficient and decrease liver tissue damage (Qi et al., 2022). In addition, polysaccharides from *S. aizoon* have an immune-stimulating effect by increasing the thymus index, spleen index, T- and B-lymphocyte transformation proliferation, and NK cell activity of mice, as well as enhancing the percentage values of CD3^{+}, CD4^{+}, and CD19^{+} and the percentage values of CD4+/CD8+ in the

FIGURE 9
*S. aizoon*'s probable anti-cancer action.



FIGURE 10
*S. aizoon*'s probable anti-inflammatory mechanism of action.

peripheral blood. Such effect was associated with the increased secretion of IL-2 and IFN-γ(Huang, 2019).

## 8 Acute toxicity

A previous study showed that excessive consumption may cause small hepatic vein occlusion disease with upper quadrant abdominal

pain, hepatomegaly, liver dysfunction, and ascites as the main symptoms (Wu et al., 2008; Shao et al., 2015).

## 9 Quality control

The quality of traditional Chinese medicine is the basis for ensuring the stability of its efficacy and the safety of its application,

and its standardization and modernization are the important prerequisites for promoting Chinese medicine toward internationalization. In order to better identify the plant, Scholars (Han, 2008) have controlled the quality of *S. aizoon* from four aspects: morphology, microscopy, TLC, and RAPD. It is required that the water content shall not exceed 10.53%, the ash content shall not exceed 14.70%, and the leaching content shall not be less than 32.57% (Wei et al., 2020). The linear ranges of quercitroside, quercetin, and kaempferol were 0.0029 ~ 0.183, 0.0016 ~ 0.1020, and 0.0045 ~ 0.260 µg/µL, respectively (He and Du, 2016), and those of luteolin and isorhamnetin were 1.12 ~ 112.00 and 0.98 ~ 97.60 µg/mL (Lin et al., 2013), respectively. However, these methods may not be sufficient to evaluate the quality of *S. aizoon*.

Traditional Chinese medicine (TCM) fingerprints can comprehensively and quantitatively reflect the chemical information contained in TCM and is an effective means of quality control of TCM. Lin et al. (2015b) used 11 standards to analyze the phytochemical profiles of the active extracts by HPLC fingerprints. Yang et al. (2023) established the HPLC-ECD fingerprint spectra of *S. aizoon* from different origins and identified 12 metabolites.

## 10 Conclusion and future perspectives

This review provides comprehensive and detailed information about the history, traditional uses, botany, phytochemistry, pharmacological activities, and acute toxicity of *S. aizoon*. So far, more than 200 metabolites have been identified with a variety of pharmacological activities. These modern pharmacological studies supported most traditional uses of *S. aizoon* as folk medicine. However, gaps still exist in the systematic study of *S. aizoon*.

First, *S. aizoon* has many nicknames, which results in being mixed with other herbs. Therefore, molecular biological studies are required to screen out the reference genes for better identification of *S. aizoon*.

Second, the pharmacological potential of *S. aizoon* has not yet been fully discovered, which may be further investigated by a combination of *in vitro* and *in vivo* bioactivity assays, metabolomics, network pharmacology, and *in silico* bioactivity prediction methods. In addition, the therapeutic potential of *S. aizoon* and its bioactive metabolites, safety, efficacy, and potential mechanism of action require further preclinical and clinical studies to validate for future clinical applications.

Third, *S. aizoon* is widely popular in herbal healthcare as a commonly used medicinal and edible substance and is especially used in immunomodulation and blood lipid regulation. Nevertheless, the use of *S. aizoon* in combination with other herbs in healthcare products should be strengthened, and studies on improving memory and promoting digestion may be conducted.

Fourth, the spectrum–efficacy relationship of *S. aizoon* in immunomodulation and anti-inflammatory therapy should be further investigated in order to better uncover its active metabolites.

## Author contributions

B-LW: conceptualization, funding acquisition, methodology, and writing–original draft. Z-KG: writing–review and editing, formal analysis and validation. J-RQ: writing–review and editing, formal analysis and validation. S-QL: data curation, investigation, visualization, and writing–original draft. X-CH: funding acquisition and writing–review and editing. Y-HZ: writing–review and editing and visualization.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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# Glossary

| | |
|---|---|
| ABTS | 2, 2′-Azinobis-(3-ethylbenzothiazoline-6-sulfonate) |
| AGG | Abrus agglutinin |
| APTT | Activated partial thromboplastin time |
| BXPC-3 | Human pancreatic adenocarcinoma cells |
| CAT | catalase |
| CNKI | China National Knowledge Infrastructure |
| CT | Coagulation time |
| DPPH | 2, 2-Diphenyl-1-picrylhydrazyl |
| EtOAc | Ethyl acetate |
| FBG | Fasting blood glucose |
| GP llb/llla | Platelet membrane glycoprotein |
| HepG2 | Human hepatoma cell line |
| H/R | Hypoxia/reoxygenation |
| HSQC | Heteronuclear singular quantum correlation |
| IL-1β | Interleukin 1β |
| IR | Infrared spectroscopy |
| LDH | Lactate dehydrogenase |
| LPS | Lipopolysaccharide |
| MAPK | Mitogen-activated protein kinase |
| MDA | Malondialdehyde |
| MTD | Maximum tolerance dose |
| NMR | Nuclear magnetic resonance |
| PC12 | Adrenal pheochromocytoma cell line |
| *Pseud. aeruginosa* | *Pseudomonas aeruginosa* |
| RAPD | Random amplified polymorphic DNA |
| ROS | Reactive oxygen species |
| SOD | Superoxide dismutase |
| STz | Streptozotocin |
| TCM | Traditional Chinese medicine |
| TG | Triglyceride |
| TNF-α | Tumor necrosis factor-α |
| T-SOD | Total superoxide dismutase |
| UV | Ultraviolet and visible spectrum |
| Ac | Acetate |
| Ara | Arabinopyranoside |
| A549 | Human lung carcinoma |
| BUN | Blood urea nitrogen |
| CD | Circular dichroic |
| CGN | λ-Carrageenan |
| DEGS | Differentially expressed genes |

| | |
|---|---|
| E.coli | *Escherichia coli* |
| ET-1 | Endothelin 1 |
| Glu | Glucopyranoside |
| GSH-Px | Glutathione peroxidase |
| HMBC | 1H-detected heteronuclear multiple-bond correlation |
| HRESIMS | High-resolution electrospray ionization mass spectroscopy |
| IC50 | 50% inhibitory concentration |
| IL-6 | Interleukin 6 |
| LAC | Lactic acid |
| LD50 | Semi-lethal dosage |
| MAP | Mean arterial pressure |
| MCF-7 | Human breast cancer |
| MDRPA | Multidrug-resistant *pseudomonas aeruginosa* |
| MTT | 3-(4,5-Dimethylthiazol-2yl) −2,5-diphenyltetrazolium bromide |
| OGTT | Oral glucose tolerance test |
| POD | Peroxidase |
| PT | Prothrombin time |
| Rha | Rhamnopyranosyl |
| SBP | Systolic blood pressure |
| Staphy.Auren | *Staphylococcus aureus* |
| TC | Total cholesterol |
| T1DM | Type 1 diabetes mellitus |
| TLC | Thin-layer chromatography |
| TPA | 12-O-tetradecanoylphorbol 13-acetate |
| TT | Thrombin time |
| Xyl | Xylopyranoside |