Arabian Journal of Chemistry (2023) 16, 104936

King Saud University

Arabian Journal of Chemistry

www.ksu.edu.sa
www.sciencedirect.com

REVIEW ARTICLE

The potential of *Amomum tsao-ko* as a traditional Chinese medicine: Traditional clinical applications, phytochemistry and pharmacological properties

Gang He [a,b], **Shao-bing Yang** [a,*], **Yuan-zhong Wang** [a,*]

[a] *Medicinal Plants Research Institute, Yunnan Academy of Agricultural Sciences, Kunming 650200, China*
[b] *College of Food Science and Technology, Yunnan Agricultural University, Kunming 650201 China*

Received 3 November 2022; accepted 23 April 2023
Available online 2 May 2023

KEYWORDS

Amomum tsao-ko;
Chinese herbal medicine;
Chemical compounds;
Physiological characteristics;
Review

Abstract In Southeast Asia, *Amomum tsao-ko*(*A. tsao-ko*) is a well-known plant spice that has both medicinal and edible value. *A.tsao-ko* was mainly used in the past for flavoring and aroma enhancement in cooking. It is also a medicinal plant used in folklore to treat diseases and is widely used in the therapeutic system. In China, *A. tsao-ko* is often used as a treatment or adjunct to the treatment of malaria, gastrointestinal disorders, epilepsy and cholera. This review describes in detail the traditional and folkloric uses, botanical studies, phytochemical components, and pharmacological activities of *A. tsao-ko*, elucidates its medicinal value as a traditional herbal medicine, and analyzes its potential for clinical applications. To provide reference for the comprehensive development and exploitation of *A. tsao-ko* in the fields of functional food, medicine and cosmetics. The available information about *A. tsao-ko* was collected through Web of Science, Google Scholar, PubMed, Baidu Scholar, Science Direct, China Knowledge Infrastructure (CNKI), and Springer Search. The keywords used included *A. tsao-ko*, essential oil, secondary metabolites, chemical composition, biological activity, pharmacology, traditional medicinal use, safety, and other related words. The literature of *A. tsao-ko* traditional and folk uses was retrieved from CNKI and Duxiu Search (https://www.duxiu.com/). The botany research information of *A. tsao-ko* was obtained through the Plant Plus of China website (https://www.iplant.cn). The economic value of *A.tsao-ko* can be obtained from Chinese herbal medicine industry information portal (https://www.zyctd.com/). So far, more than 493 chemical components have been isolated from *A. tsao-ko*. It possesses a variety of functions to maintain human health and protect the body from external influence, including regulating gastrointestinal function, antibacterial, anti-inflammatory, anti-tumor, regulating metabolic syndrome, and neuroprotection. In addition, *A. tsao-ko* is also an important cash crop in some

* Corresponding authors at: Medicinal Plants Research Institute, Yunnan Academy of Agricultural Sciences, Kunming 650200, China.
E-mail addresses: ysb9-116@163.com (S.-b. Yang), boletus@126.com (Y.-z. Wang).
Peer review under responsibility of King Saud University.

ELSEVIER | Production and hosting by Elsevier

https://doi.org/10.1016/j.arabjc.2023.104936
1878-5352

areas, including southwest China, Vietnam, and northern Laos. Future research should focus on exploring the mechanisms between the single chemical constituents in *A. tsao-ko* and their pharmacological activities, as well as the relationship between their biological activities and medicinal clinical research.

1. Introduction

Chinese herbal medicine (CHM) has received more and more attention in the prevention and treatment of chronic diseases because of its non-toxicity or low-toxicity. Therefore, with the development of modern pharmacology, exploring reliable natural medicines instead of chemical medicines to treat diseases has become the main direction of people's research on medicinal plants. The extraction of disease-fighting compounds from herbs has become a new direction for novel drug research (Hasan et al., 2015; Xin et al.,2014; Ran et al., 2014), it is also used as an important route for the synthesis of chemical substances in the pharmaceutical process (Dang et al., 2014). In previous studies, spices have been widely studied by researchers because they were rich in natural medicinal compounds, such as *Illicium verum* Hook. f., *Alpinia galanga* (Linn.) Willd., *Angelica dahurica* (Fisch. ex Hoffm.) (Bai et al., 2016; Muhsinah et al., 2022; Zhou et al., 2021).

Amomum tsao-ko Crevost et Lemaire (*A. tsao-ko*) is a perennial herb belonging to Zingiberaceae. Based on a novel multi-marker phylogenetic framework using matK and nrITS, new genera Lanxangia was described (Boer et al., 2018). *A. tsao-ko* got a new name *Lanxangia tsaoko* (Li et al., 2021;Ranavat et al., 2021). In this review, *A. tsao-ko* still follow the Chinese Pharmacopoeia (2020). It is mainly distributed in various countries in southeast Asia, such as China and Vietnam. Among them, China is the main producing country, especially in Yunnan province, where the planting area has reached more than 90% of the national planting area (Ma et al., 2021). According to related reports, the *A. tsao-ko* was first recorded in the "Taiping Huimin Heji Bureau Prescription" in the Song Dynasty was used to treat malaria, this is the earliest recorded medicinal use found so far (Qin et al., 2021). In the process of treating diseases, *A. tsao-ko* was often matched with other CHMs, such as *Anemarrhena asphodeloides* Bunge, *Dichroa febrifuga* Lour, *Magnolia officinalis* Rehd. et Wil. These traditional prescriptions have good efficacy and sufficient clinical experience. In the development of modern pharmacology, these classical prescriptions have also been studied and great results have been achieved. For example, Tsao-ko Anemarrhenae Decoction with improved dosage can effectively assist in the treatment of epilepsy and chronic renal failure (Gao et al., 2018; Sun and Fu, 2015; Zhang et al., 2002; Wang et al., 2017); Da Yuan yin is a traditional formula with the function of clearing heat and detoxifying toxins, molecular docking results showed that Da Yuan yin, with *A. tsao-ko* as the main component, has the potential to treat Corona Virus Disease (COVID-19) (Ding et al., 2020; Zong et al., 2020). A growing body of pharmacological and physiological investigations has demonstrated that *A. tsao-ko* has regulating gastrointestinal function, antioxidant (Cui et al., 2017;), anti-inflammatory (Hong et al., 2021b; Wang et al., 2021b), antibacterial (Tang et al., 2020), and antitumor (Chen et al., 2020), and so on. *A. tsao-ko* could also treat or assist in the treatment of metabolic syndrome in the human body, including diabetes (He et al., 2021a; He et al., 2021b), hyperlipidemia (Shim et al., 2021), hyperglycemia and obesity (Hong et al., 2021a). In addition, the chemical components of *A. tsao-ko* have been studied to some extent, especially with regard to the relationship between chemical composition and pharmacological effects. At present, more than 490 chemical components have been isolated from *A. tsao-ko* alone. The most extensive research on volatile oil components has confirmed the pharmacological effects of volatile oil, and the 2020 edition of the Chinese Pharmacopoeia stipulates that the volatile oil content of *A. tsao-ko* seed clusters must be higher than 1.4% (ml/g) for inclusion in medicine. At the same time, *A. tsao-ko* non-volatile components and their pharmacological activities are being explored, such as polyphenols and flavonoids (Liu et al., 2021;Zhang et al., 2021). It is noteworthy that indenoids are chemical constituents specific to *A. tsao-ko* and can be used as its quality markers. After comprehensive phytochemical and pharmacological analysis, both the crude extract and purified compounds of *A. tsao-ko* have certain pharmacological effects (He et al., 2020b; He et al., 2021b; Zhang et al., 2021). In recent years, several novel chemical components have been isolated from *A. tsao-ko*, including Diarylheptanoids, Flavanol-fatty alcohol hybrids, and Flavanol-menthane conjugates. They have been shown to have potential antidiabetic activity, further providing a new direction for the pharmacological study of *A. tsao-ko*. The above study shows that *A. tsao-ko* is a CHM with outstanding medicinal value. Unfortunately, even though researchers have confirmed the medicinal value of *A. tsao-ko*, the number of available precursor molecules and herbal preparations is very small, and many of the findings have not yet been applied to real life. In addition, *A. tsao-ko* is an important cash crop that brings high economic benefits to the local population in southwestern China, as well as in countries such as Vietnam and Myanmar (Liu et al., 2021).

The available information about *A. tsao-ko* was collected through Web of Science, Google Scholar, PubMed, Baidu Scholar, Science Direct, China Knowledge Infrastructure (CNKI), and Springer Search. The keywords used included *A. tsao-ko*, *A. tsao-ko* essential oil, secondary metabolites, chemical composition, biological activity, pharmacology, traditional medicinal use, safety, and other related words. The literature of *A. tsao-ko* traditional and folk uses was retrieved from CNKI and Duxiu Search (https://www.duxiu.com/). The molecular structures of all compounds shown in the text were generated by ChemBioDraw Ultra 14.0. The botany research information of *A. tsao-ko* was obtained through the Plant Plus of China website (https://www.iplant.cn). The economic value of *A.tsao-ko* can be obtained from Chinese herbal medicine industry information portal (https://www.zyctd.com/).

In recent years, the pharmacology of *A. tsao-ko* has been extensively studied by the scientific community. However, there is a lack of systematic compilation of available data on their phytochemical compounds and pharmacological activities to provide a complete overview of their medicinal properties. In this context, the review summarized the traditional uses, distributions, phytochemical compounds, pharmacological properties, geographic traceability, and species identification technology of the botanical drugs, to guide readers to have a comprehensive understanding of this medicinal and food homology plant.

2. Botanical studies

According to Flora of China (https://www.iplant.cn/frps), *A. tsao-ko* is a perennial herb with tufted stems, which belongs to the ginger cardamom genus. The tree can be up to 3 m tall, the whole plant will emit a spicy smell, and the underground part is similar to ginger; Its leaves are green, Surface smooth, leaf apex is slightly sharp and oval-shaped, approximately 40–70 cm in length and about 10–12 cm in width (Fig. 1 **I**). Its ligule is entire, apically obtuse, generally 0.8–1.2 cm long; yel-

Fig. 1 *A. tsao-ko*: **A:** Harvesting; **B:** Fresh fruit; **C:** Different fruit shapes; **D:** Fruit ear; **E:** Growth environment; **F:** Flower; **G:** Dry naturally; **H:** Dried fruit; **I:** Leaves.

low or pale-yellow flowers serried inserted on the thick rachis, with 5–30 flowers per inflorescence, pedicels 10 cm or longer, surrounded by scales (Fig. 1 **F**), usually blooms from April to June; Its fruits are gray-brown or red-brown, oval-shaped, densely packed together when fresh, there are obvious longitudinal groove and prism, the top with a protuberant base column, was round, the base with fruit peduncle or fruit peduncle mark (Fig. 1 **D and E**). In general, *A. tsao-ko* has round, fusiform, ellipsoidal and conical fruit shapes, and there are studies that use fruit shape as a basis for classifying varieties . The shape of *A. tsao-ko* correlates with its chemical characteristics, with the most significant variation in volatile oil content, particularly in the rounded *A. tsao-ko*, which has the highest volatile oil content (Ma and Zhang et al., 2008). It has tough skin, removing skin, white or yellowish-brown septum in the middle, and the seeds are conical polyhedral, reddish-brown, and covered with grayish-white membranous, its fruiting period is generally from September to December (Fig. 1 **C**). The dried fruit is roughly 2–5 cm in length, the pericarps of which are grayish-brown to brown with longitudinal furrows and ribs, and is accompanied by a unique fragrance (Fig. 1 **G and H**). In conclusion, *A. tsao-ko* has very specific characteristics, with unique macroscopic morphological features and microscopic features of both seeds and fruits, so it can be identified by observing the characteristics of the seeds and fruits. According to related reports, *A. tsao-ko* has unique distribution characteristics, it is mainly distributed in high altitude areas from 22°71′11″ to 27°87′53″ north latitude, 97°90′86″ ~ 105°63′33″ east longitude, including southwestern China, Vietnam, northern Laos, Japan, and south Korea. Fig. 2 shows the main distribution areas of *A. tsao-ko* in China, with the largest area under cultivation in Yunnan province (Yang et al., 2017, Liu et al., 2019; Ma et al., 2021). Elevation is a definite influence on the yield of *A. tsao-ko*, when *A. tsao-ko* are transplanted from a low-latitude or low-altitude growth environment to a high-latitude or high-altitude growth environment, the number of flowers per inflorescence will increase, and the fruit rate will decrease (Yang et al., 2014). Therefore, in the process of cultivation and introduction of *A. tsao-ko*, a comprehensive consideration of its species and suitable habitat is required.

3. Traditional clinical applications

According to the theory of traditional Chinese medicine (TCM), human health is related to the balance of yin and yang. Once the yin and yang are imbalanced in the human body, many diseases will occur. At this time, TCM will treat diseases by adjusting the balance between yin and yang for each disease. TCM has many medicinal features, including wide efficacy, safe use, and sufficient clinical experience (**Table S1**). The history of *A. tsao-ko* used as medicine was first recorded in "Taiping Huimin Heji Bureau Prescription", called "Cao Guo". *A. tsao-ko*, *Amomum Roxb*, and *Alpinia katsumadai Hayata* are divided into one category by Shizhen Li in the masterpiece of "Ben Cao Gang Mu", and proposed the effect of "Warming spleen and stomach, dispersing cold and heat". After textual research, the efficacy of *A. tsao-ko* is recorded in "Bao Qing Ben Cao Zhe Zhong", including non-

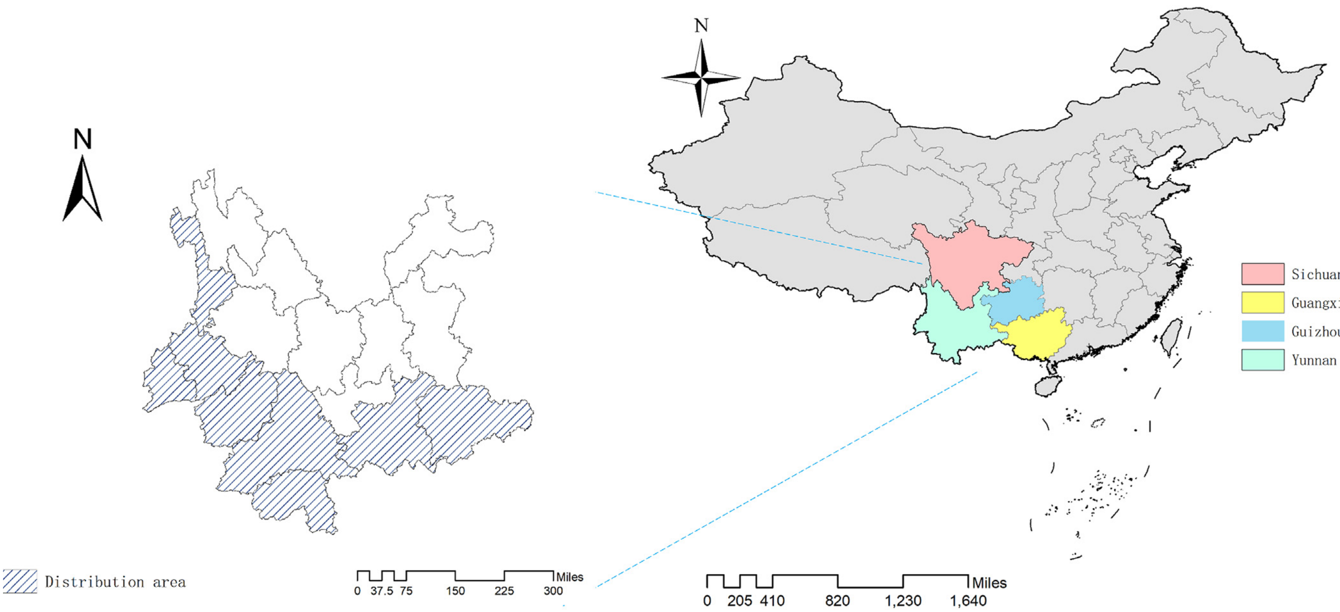


Fig. 2 Main distribution of *A. tsao-ko* in China.

toxic, warming the middle, remove the malign qi, stop vomiting, treatment of cholera, treatment of alcohol poisoning, warming spleen and stomach. According to "Yin Shan Zheng Yao", *A. tsao-ko* has the effects of treating heart and abdominal pain, stopping vomiting, lowering qi. Tsaoko-Anemarrhenae decoction from "Wen Bing Tiao Bian" is obtained by a decoction of *A. tsao-ko*, *Anemarrhena asphodeloides Bunge,* and *Pinellia ternata*. It is used for the treatment of malaria, clearing heat and dampness, eliminating turbidity, and regulating qi. In addition, the efficacy of *A. tsao-ko* has been recorded in Chinese classics such as "Ben Cao Bei Yao", "Ben Cao Qiu Zhen" and "Ben Cao Co Xin" in Qing Dynasty, and mainly warming the middle, removing food stagnation, prevent the attack of malaria, phlegm-resolving, and so on. In Chinese Pharmacopoeia (Commission, 2020) documented, *A. tsao-ko* is pungent, warm, returning to the spleen and stomach meridian. It has the effects of clearing heat and removing dampness, preventing the attack of malaria, expelling-phlegm, etc. And it can treat syndrome or pattern of accumulation of cold-dampness, flatulence in the lower abdomen, vomiting, malaria causes chills and fever, pestilence causes fever. In addition, *A. tsao-ko* is also very popular among Chinese folk. Research has found that a total of 10 ethnic minorities use *A. tsao-ko* to treat diseases (**Table S2**), the fruits of *A. tsao-ko* are the main medicinal parts, other sites are not commonly used medicinally. There are many prescriptions about *A. tsao-ko* with significant medicinal effects.

4. Clinical applications

Classical prescriptions have been passed down in China for thousands of years and have been continuously improved and verified. They have the characteristics of safety, reliability, and rich clinical experience (Wang et al., 2023). Compared with laboratory studies with less clinical time, it has a more reliable basis for treatment. Studies have shown that many classical prescriptions can provide ideas for modern pharmacological research (Zhao et al., 2023). For example, Tsaoko-Anemarrhenae Decoction, which is composed of eight kinds of CHMs such as *A. tsao-ko* and *Anemarrhena asphodeloides*, etc., has a good treatment for epilepsy. Moreover, it can block abnormal cortical discharge, thereby achieving anti-epileptic effects (Gan, 2004; Gao et al., 2018; Zhang et al., 2002). In addition, Shao Chaodi used this prescription to treat chronic renal failure, and the effect was remarkable (Wang et al., 2017). Shipiyin, is composed of CHMs such as *A. tsao-ko*, *Atractylodes macrocephala,* etc. In He Dongmei's clinical study, 86 patients with intractable diarrhea were divided into a treatment group (treated with Shipiyin) and a control group (treated with Sishen) pill treatment, the results showed that the effective rate of the treatment group was 96.4%, and the total effective rate of the control group was 70%. Shipiyin had a more significant clinical effect on refractory diarrhea. In addition, Shipiyin can improve heart function by reducing serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) and Caspase-3 (CASP3) protein expression in heart failure model rats, and inhibiting cardiomyocyte apoptosis in heart failure rat models, thereby delaying heart failure (Lei et al., 2021). Shipiyin combined with diosmin can better improve the clinical symptoms, which provides a new clinical program for the treatment of lymphedema with integrated Chinese and western medicine after breast cancer surgery (Hu et al., 2021). Da-Yuan-Yin is composed of 11 CHMs such as *Houpoea officinalis* and *A. tsao-ko,* and so on. Liang Qiaoqiu's clinical studies have confirmed that it has the effect of adjuvant treatment of bronchitis. Compared with conventional treatment, Da-Yuan-Yin is added to the conventional treatment, and the cure rate has increased from 64.5% to 87.1%. This prescription has also achieved good curative effects in the treatment of COVID-19. Its mechanism may be through the combination with angiotensin-converting enzyme II (ACE2) to act on targets such as prostaglandin-endoperoxide synthase 2 (PTGS2), heat shock protein 90 alpha (HSP90AA1), and estrogen receptor 1 (ESR1) to regulate multiple signals access, which may have a therapeutic effect on COVID-19 (Zong et al., 2020). In summary, the improvement of traditional medicinal methods can lead to effective therapeutic results and is a new pathway for the treatment or adjunctive treatment of modern diseases. For the industry of drug development, these methods can provide new ideas for the development of Chinese patent drug.

5. Chemical compounds

With the development of modern pharmacology, the exploration of natural medicines to replace the original chemical agents to prevent and treat diseases has attracted more and more attention from researchers. What exciting is that there are abundant natural chemical resources in natural plants (Wu et al., 2012). *A. tsao-ko* is not only seasoning for cooking, but also a CHM with outstanding medicinal value. As we all know, chemical compounds are the material basis of CHM in the treatment of diseases. The research on the chemical component of *A. tsao-ko* could be traced back to the middle of the 20th century. Japanese researchers isolated and identified 1,8-citric acid and geranioic acid from AEO (Li et al., 1975). As shown in Table S3 and Fig. 3, a total of 493 compounds that have been isolated from *A. tsao-ko* were reviewed, this study subdivides them into 20 categories, and their structural formulae are shown in Tables 1-9. The effect of drying temperature on the quality of *A. tsao-ko* is greater and is mainly related to the changes in the volatile components of *A. tsao-ko*. Under high temperature drying (85○ C and 100○ C), *A. tsao-ko* is rich in monoterpenes such as α-thujene, α-pinene, terpinolene, neral, 1,8-cineole, and so on (Wang et al., 2021a). Many studies have shown that these compounds have antioxidant, anticancer, sedative, anti-inflammatory, and antibacterial properties (Caceres et al., 2017; Ito and Ito, 2013; Melo Júnior et al., 2017; Ruberto and Baratta, 2000). The content of (E)-2 unsaturated aldehydes is relatively high when dried at relatively low temperatures (25 °C, 40 °C, 55 °C, 70 °C), this chemical compound is closely related to the antibacterial activity (Ma et al., 2019). The content of such compounds decreases rapidly when the drying temperature is greater than 70 °C (Wang et al., 2021a).

5.1. AEO and its volatile compounds

Since the Middle Ages, essential oil (EO) has been widely used in agriculture, food seasoning, cosmetics, and fragrance industries. With the development of modern pharmacology, EOs have also been widely used in the pharmaceutical and functional food industries. In nature, EOs have the function of plant protection, reducing the appetite of herbivores by scent to protect plant survival. In addition, EOs can attract animals and insects to pollinate plants and spread seeds, or repel unfriendly organisms that are harmful to plants (Bakkali et al., 2008). EOs are also often used as bacteriostatic agents, and many studies have collectively showed that their bacteriostatic function is by affecting the normal function of cell membranes, disrupting the stability of the lipid layer, affecting cellular energy metabolism and the reductase system (Da Costa Lima and de Souza, 2021; Rossi et al., 2022). At present, many volatile oil compounds have been isolated from *A. tsao-ko*, mainly including monoterpenes (1–34), oxygenated monoterpenes (35–95), sesquiterpenes (96–116), oxygenated sesquiterpenes (117–127), diterpenoids (128–131), aromatics (132–156), aliphatics (157–248), and ketones (249–264). Among them 1,8-cineole (70), α-citral (93), α-pinene (2), β-pinene (3), limonene (18), decanal (166), linalool (40), α-terpineol (41), geraniol (42), nerolidol (97) are the main chemical compounds.

5.2. Phenolics

Phenolics are important biologically active compounds, characterized by a phenolic structure (containing one or more

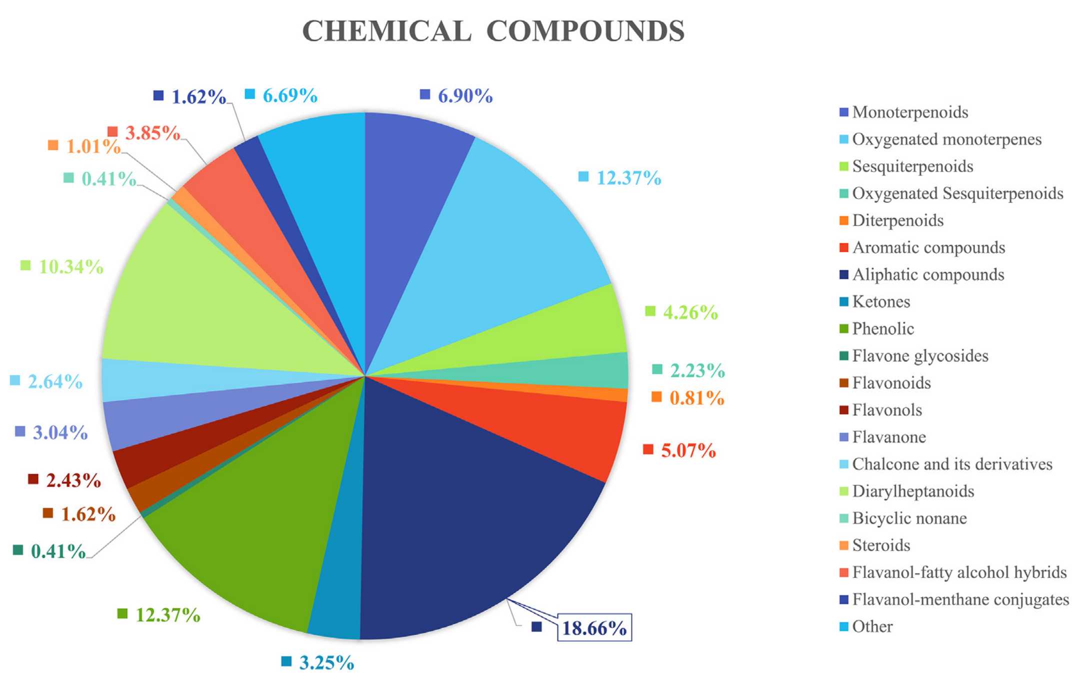


Fig. 3 Compounds and proportion of chemical compounds in *A. tsao-ko*.

Table 1 Structure of terpenoids in *A. tsao-ko*.

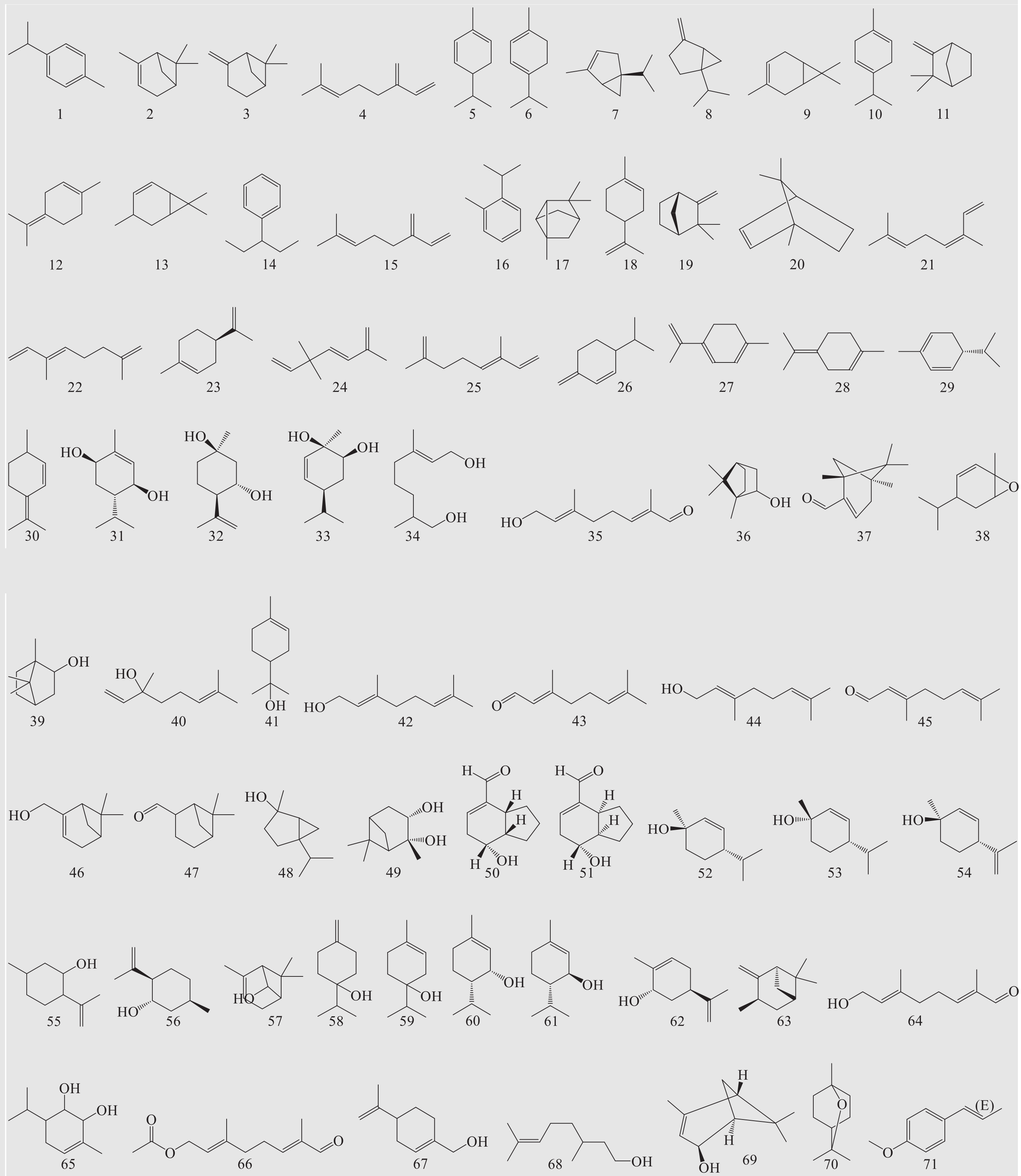
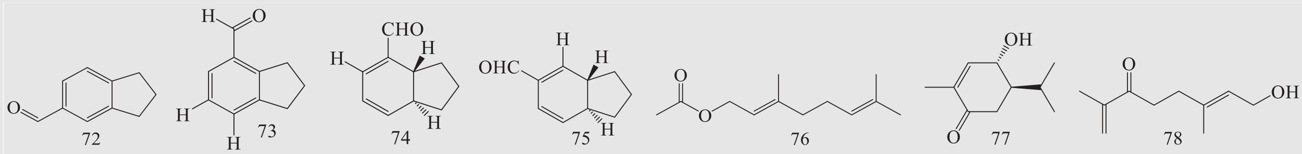
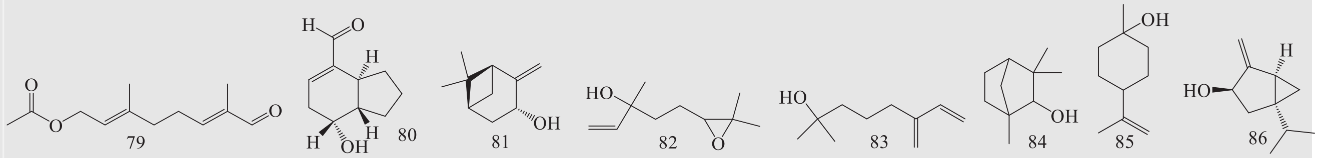


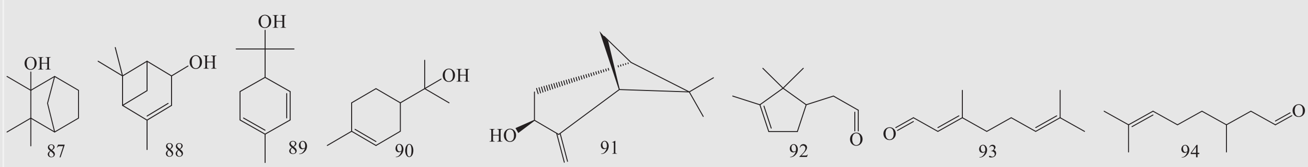
Table 1 (*continued*)



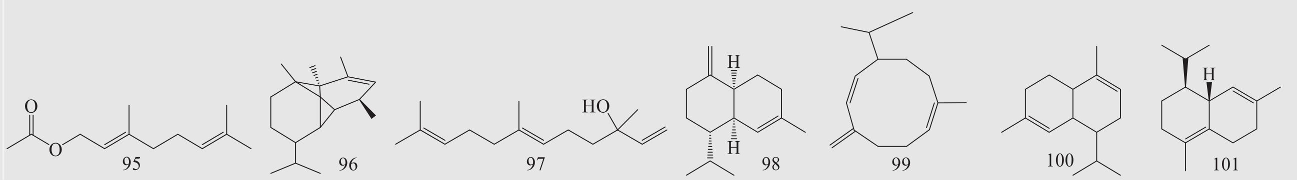
72 73 74 75 76 77 78



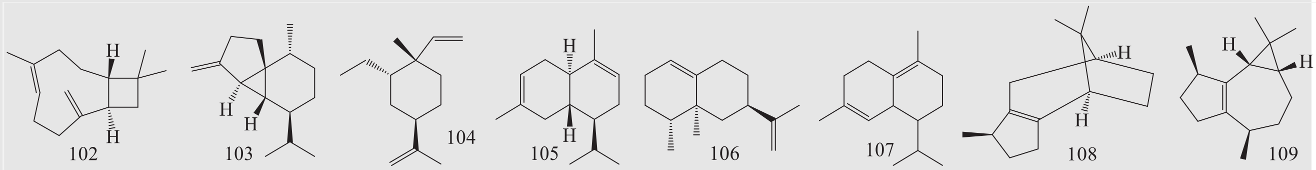
79 80 81 82 83 84 85 86



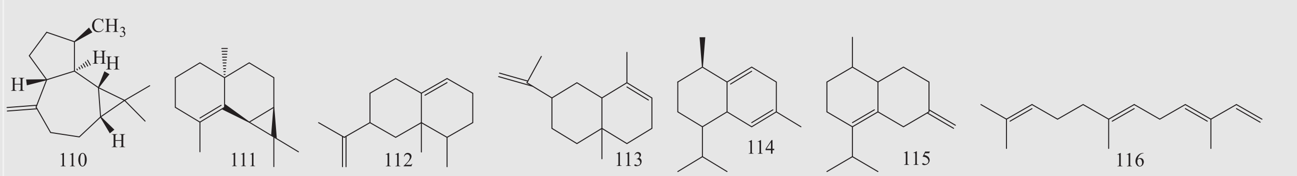
87 88 89 90 91 92 93 94



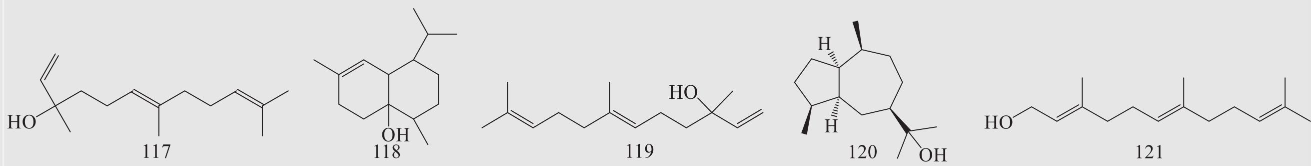
95 96 97 98 99 100 101



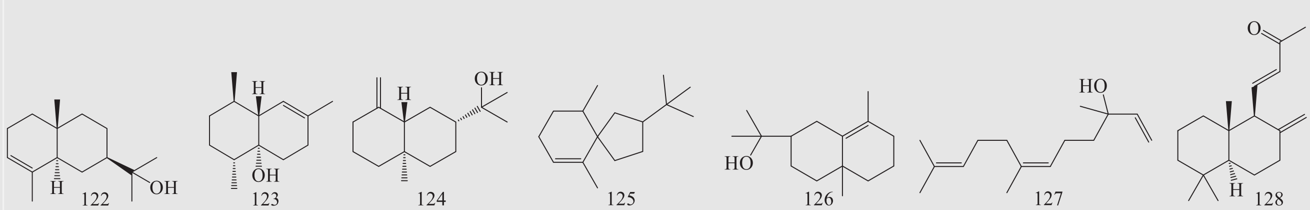
102 103 104 105 106 107 108 109



110 111 112 113 114 115 116



117 118 119 120 121



122 123 124 125 126 127 128

(*continued on next page*)

Table 1 (*continued*)

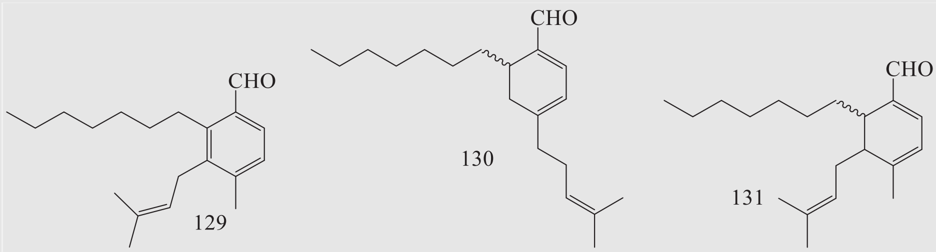
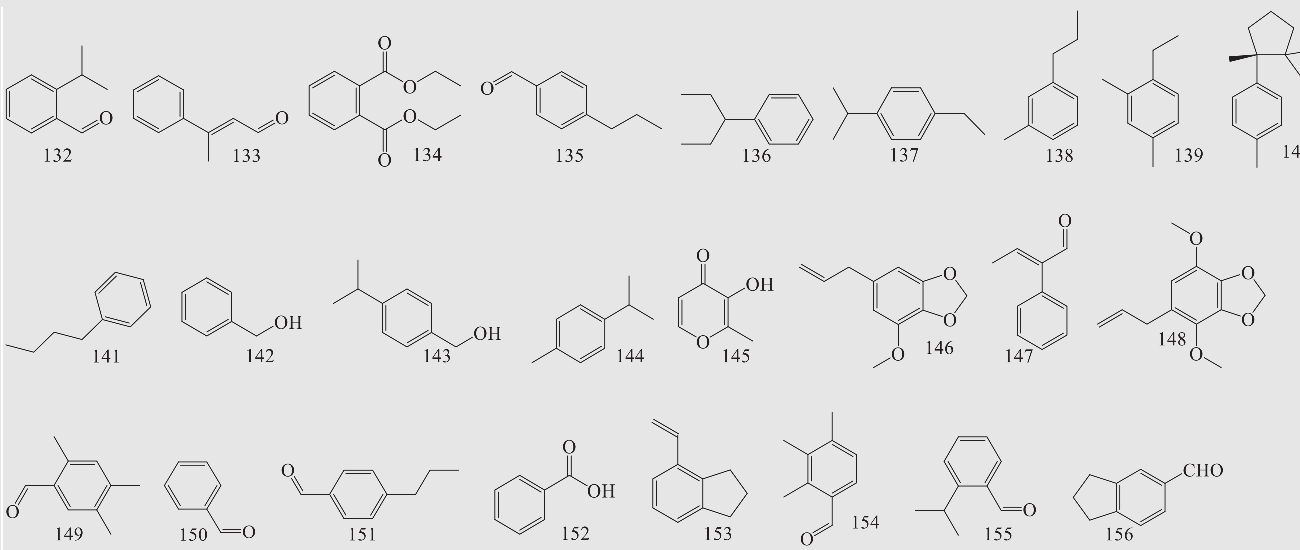


Table 2 Structure of aromatic compounds in *A. tsao-ko*.



hydroxyl groups on an aromatic ring), which can be divided into different groups according to the number of phenolic rings in the structure and the bonding elements between phenolic rings (Scalbert et al., 2005). It was of great significance in plant physiology and protection of plants from external aggression. At the same time, it also imparts a variety of biological activities to plants (Denny, 2007). The biological activity of phenolic compounds appears to be related to the presence and number of hydroxyl groups. Among them, the conjugation and resonance relationship had a great correlation with its antioxidant activity (Leopoldini et al., 2004). In recent years, a large number of phenolic compounds from *A. tsao-ko* were obtained by various extraction techniques (Li et al., 2017a; Shi et al., 2021;Wang et al., 2009).

5.3. Contains the chemical components of C6-C3-C6

Flavones are secondary metabolites which are widely present in plants and possess C6-C3-C6 as the basic carbon framework. It is extensively reported for exhibiting various biological properties. In recent years, researchers have isolated a large number of flavonoids from *A. tsao-ko* (Zhang et al., 2021; Kim et al., 2019a). Flavonoids are classified into various sub groups according to the substitution pattern of ring C. The oxidation state of the heterocyclic ring as well as the position of B ring are important in the classification as flavone glycosides (326–327), flavonoids (328–335), flavonoid (336–347), flavanone (348–362), chalcone and its derivatives (363–375).

5.4. Diarylheptanoids

Diarylheptanoids are an important bioactive compound in *A. tsao-ko* with a 2,6-epoxy pyran ring structure that inhibits α-glucosidase activity and has potential as a new antidiabetic drug candidate. 11 new and 13 known diarylheptanoids were isolated from the active part of *A. tsao-ko* under the guidance of bioassay. The enzyme kinetic study suggested that diarylheptanoids as the active constituents of *A. tsao-ko* with α-glucosidase inhibitory effects (He et al., 2020a). Thirteen new and four known 2,6-epoxydiarylheptanes were also isolated successively from *A. tsao-ko*, and 2,6-epoxydiarylheptane-like compounds were proposed as new antidiabetic drug candidates (He et al., 2020b).

5.5. Bicyclic nonane and steroids

Bicyclic nonane is a unique chemical in *A.tsao-ko*, a class of compounds with a bicyclic parent nucleus formed by a hexane ring and a pentane ring as the basic framework. One study isolated two bicyclic nonane from A. tsao-ko, both of which have inhibited LPS-induced NO production in BV2 microglial cells and are potential anti-inflammatory substances (Lee et al., 2008). Steroids are a class of compounds with the basic backbone structure of cyclopentane polyhydrophenanthrene as the parent nucleus, which usually bears two angular methyl groups and a side chain or oxygen-containing group containing a different number of carbon atoms. Qiu et al. (2012) analyzed and identified the active ingredients of *A. tsao-ko* by ultrasonic extraction combined with combined gas chromatography-mass spectrometry, and proved that *A. tsao-ko* contained steroidal compounds such as Stigmasterol and γ-Sitosterol. In addition, based on spectroscopic methods including MS, H-NMR, C-NMR, DEPT135, and HMQC spectroscopy, two more steroid compounds were isolated from *A. tsao-ko* (Zhang et al., 2014).

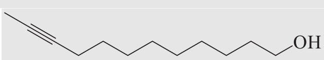
5.6. Flavanol-fatty alcohol hybrids and flavanol-menthane conjugates

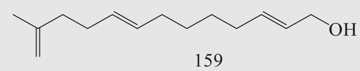
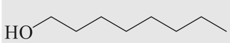
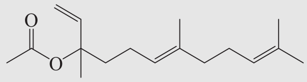
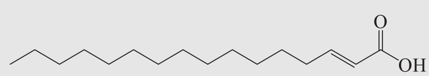
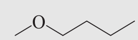
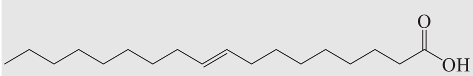
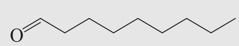
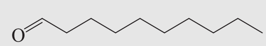
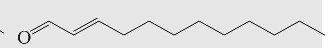
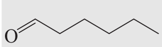
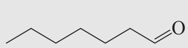
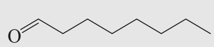
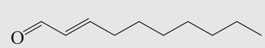
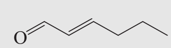
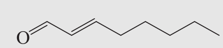
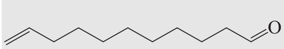
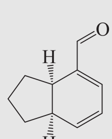
19 new flavanol-fatty alcohol mixtures were isolated from *A. tsao-ko* for the first time and were named tsaokoflavanols A-S (434–452), *in vivo* experiments showed significant α-glucosidase and PTP1B inhibitory activities (He et al., 2020a). The following year, eight more rare flavanol-menthane-conjugates were isolated from *A. tsao-ko* and were named amomutsaokins A-H (453–460). It is interesting to note that compounds 453–456 are formed due to flavanol-menthane conjugates with the menthane part linked at the C-6 position of flavanol. Pharmacological studies have shown their inhibitory effect on three diabetes-related proteins (PTP1B, TCPTP and α--glucosidase) (He et al., 2021b).

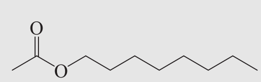
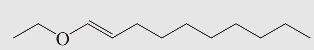
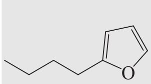
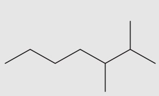
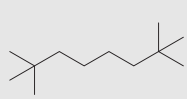
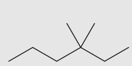
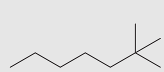
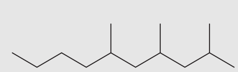
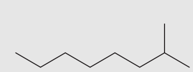
5.7. Other compounds

According to the systematic pre-test study of phytochemical composition, *A. tsao-ko* also contains sugars, proteins, tannins, saponins, anthraquinones, coumarins, lactones, cardiac glycosides, steroids, oils, and anthocyanins in a variety of chemical compounds (Liu et al., 2011). According to research reports, *A. tsao-ko* is also rich in amino acids and mineral nutrients. An automatic amino acid analyzer was used to

Table 3 Structure of aliphatic compounds in *A. tsao-ko*.

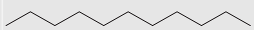

157

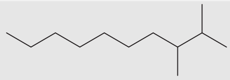
158

159

160

161

162

164

163

165

166

167

168

169

170

171

172

173

174

175

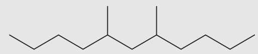
176

177

178

179

180

181

182

183

184

186

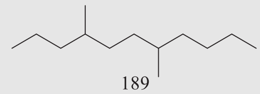
(*continued on next page*)

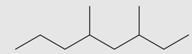
Table 3 (*continued*)

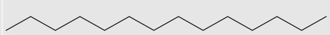

185

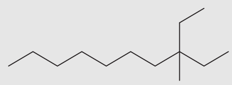

187

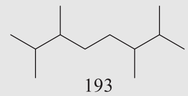

188

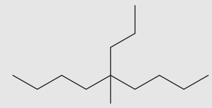

189

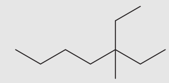

190

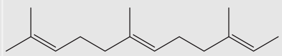

191

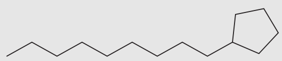

192

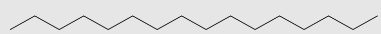

193

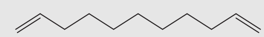

194

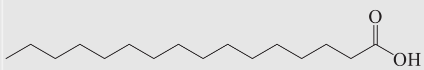

195

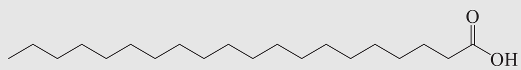

196

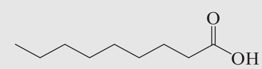

197

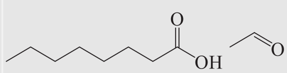

198

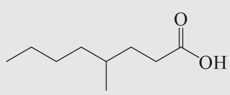

199

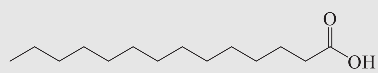

200

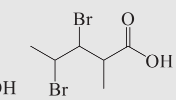

201

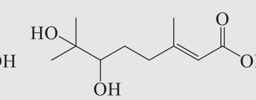

202

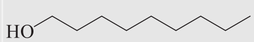

203

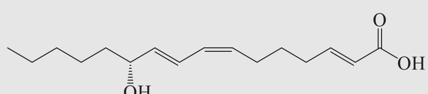

204

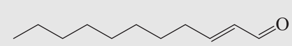

205


206


207


208


209


210

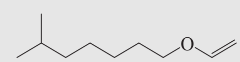

211

Table 3 (*continued*)

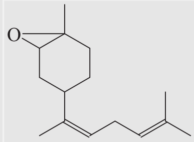
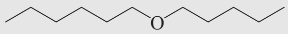
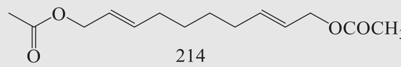
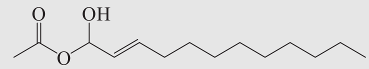
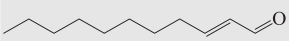
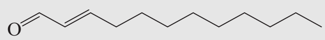
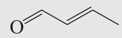
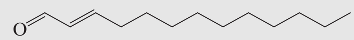
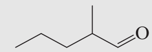
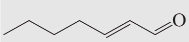
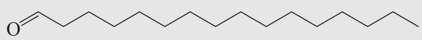
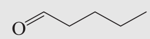
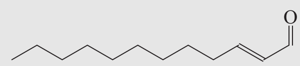
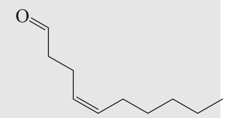
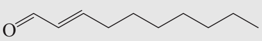
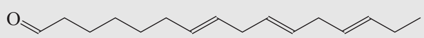
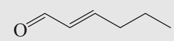
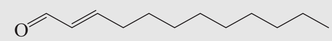
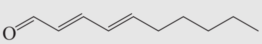
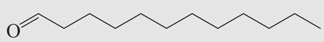
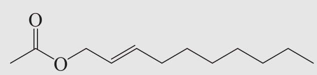
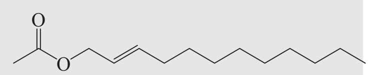
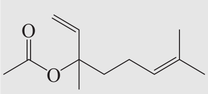
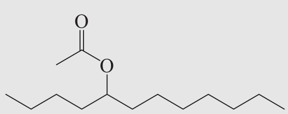
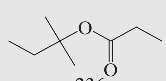
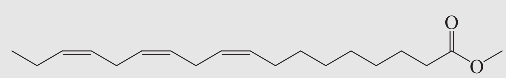
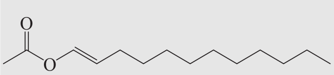
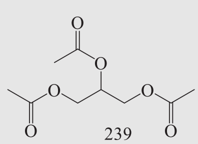
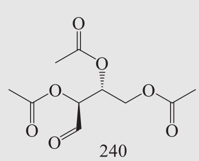
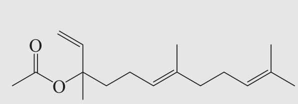
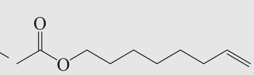
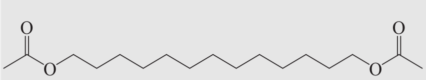
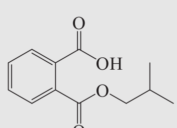
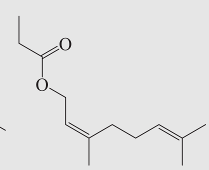
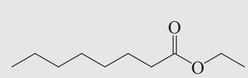
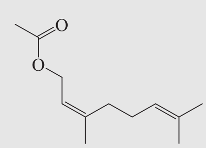
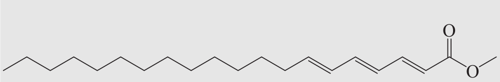
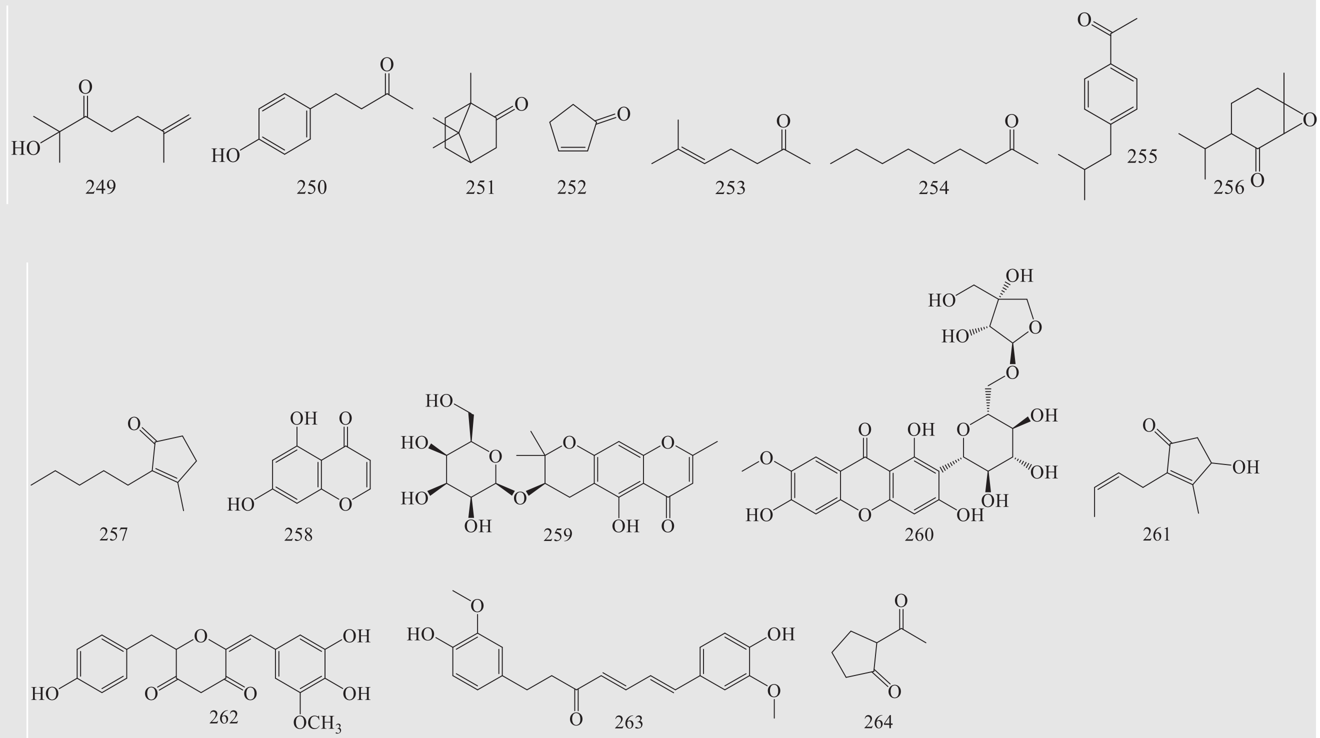

212

213

214

215

216

217

218

219

220

221

222

223

224

225

226

227

228

229

230

231

232

233

234

235

236

237

238

239

240

241

242

243

244

246

247

248

245

Table 4 Structure of ketones in *A. tsao-ko*.



determine the content of 17 amino acids in *A. tsao-ko*, and the ICP method was used to determine the content of 9 mineral nutrients. It was found that the highest amino acid content was cereals and up to 3.01 g·kg^{-1}; Manganese content of the five trace elements was the highest and up to 822 mg·kg^{-1} (Pu et al., 2015).

6. Pharmacological properties

In Asia, *A. tsao-ko* has long been used as a spice or seasoning in food, has a long history of use and has played an important role in human civilization and national history. In China, *A. tsao-ko* is also a traditional Chinese medicinal material that can treat diseases, as documented in the Chinese Pharmacopoeia (2020). Modern pharmacological studies have proved that it can regulate gastrointestinal function, antibacterial (Liu et al., 2018; Shim et al., 2021), insecticidal (Wang et al., 2014), antioxidant (Cui et al., 2017), anti-inflammatory (Lee et al., 2019), neuroprotective (Zhang et al., 2016), anti-tumor (Zhang et al., 2015), anti-diabetes (Saeedi et al., 2019) and other activities (Fig. 4 **and Table S4**).

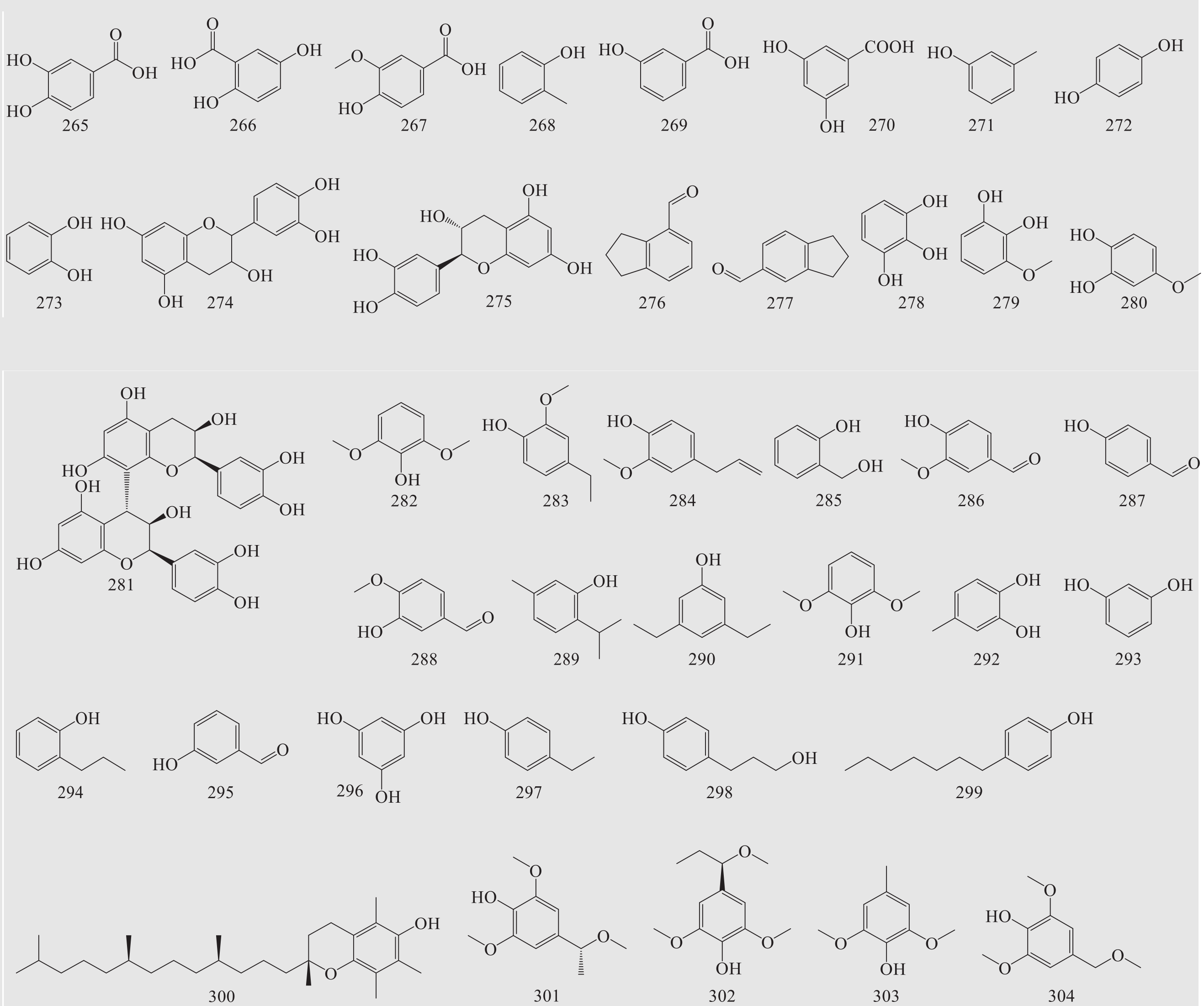
6.1. Regulate metabolic syndrome

Metabolic syndrome (MS) is one of the major medical and public health problems in the world. The main symptoms include complex metabolic disorders such as obesity, hyperglycemia, hypertension, and hyperlipidemia (Liu et al., 2023). Studies have shown that the active substances in CHM can reduce inflammation, resist oxidative stress, inhibit α-amylase and α-glucosidase, regulate intestinal flora, and inhibit the differentiation of preadipocytes (Li et al., 2023). *A. tsao-ko* as TCM, has the effect of regulating human metabolic syndrome. A large number of studies have shown that AEO, polyphenols, and flavonoids of *A. tsao-ko* are effective factors for regulating metabolism (He et al., 2021a, He et al., 2021b). This review summarises the research status of *A. tsao-ko* in regulating blood sugar and blood lipids, treating diabetes, and cardiovascular diseases (Fig. 5). In the future, it can be further studied for its potential medicinal value in other types of diseases, and promote the development of TCM health industry.

6.1.1. Anti-diabetes

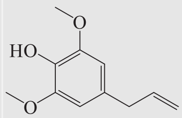
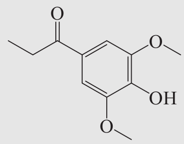
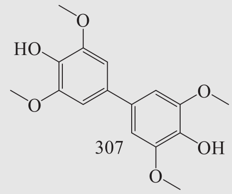
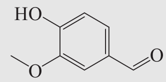
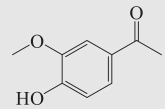
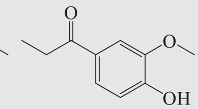
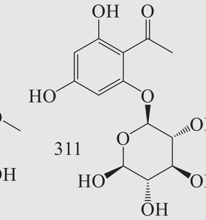
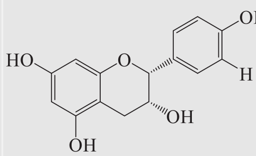
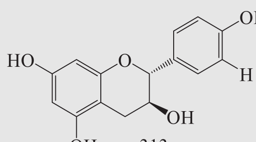
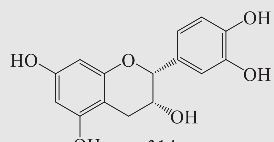
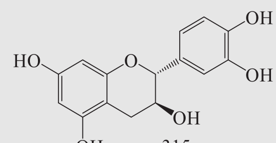
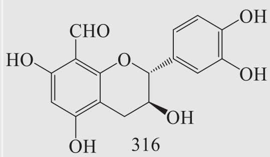
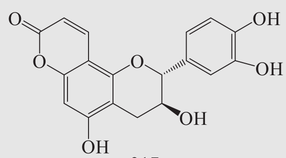
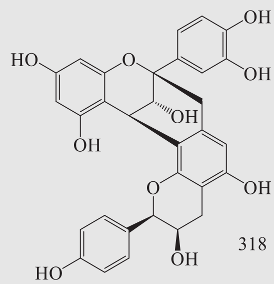
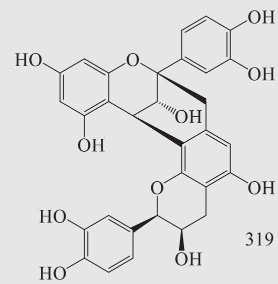
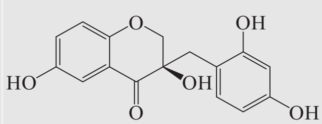
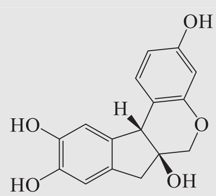
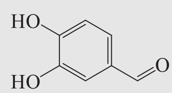
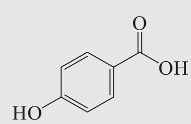
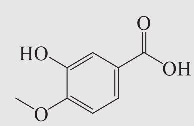
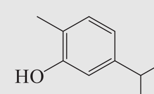
According to the International Diabetes Federation Diabetes Atlas, 9th edition: in the absence of effective control measures, the number of people with diabetes is expected to reach 578 million in 2030 (Saeedi et al., 2019). In the human body, α-amylase and α-glucosidase are the key enzymes for digesting and absorbing carbohydrates. Inhibiting their activity will delay the absorption of carbohydrates and increase in blood glucose levels after meals. At present, there are two main methods of lowering blood sugar, insulin injection, and oral hypoglycemic drugs, and they have good clinical effects. However, it was a pity that these clinical drugs will cause adverse side effects for the human body during the treatment process, which are very painful for the patients. *A. tsao-ko* contains biologically active substances that can lower blood sugar. In countries such as India, Pakistan, and China, *Amomum subulatum Roxb* and *A. tsao-ko* is considered to be effective drug for treating diabetes (Hussain et al., 2018). The water extracts (v/v) of *Amomum subulatum* Roxb and *A. tsao-ko* (seed and peel) have significant inhibitory activity on α-amylase and α-glucosidase. At the concentration of 4.0 mg/mL, the seed extracts of *A. tsao-ko* extracts were relatively analogous to acarbose activity that exhibited maximum α-amylase and α-glucosidase inhibitory activity of 83.9% and 54% respectively. *In vivo*, polar fractions of *A. tsao-ko* have anti-oxidative and hypoglycemic activity in mice, this component could be epicatechin (Yu et al., 2010). In addition, under the guidance of LCMS and bioassay, two complicated flavanol-monoterpenoid hybrids (Compounds 453 and 457) were isolated from *A. tsao-ko*, with strong α-glucosidase inhibitory activity, with IC_{50} values of 18.8 and 38.6 μmol/L (acarbose, IC_{50} = 213 μmol/L), which can be used as an anti-diabetic natural compound. They have selective inhibitory effect on PTP1B (IC_{50}: 201.45 ~ 317.51 gm.), and an inhibitory effect on the chemical component of α-glucosidase (IC_{50}: 3.73 ~ 76. 23 μm) (He et al., 2021a). Docking simulation proved the importance of the hemiacetal hydroxy, the orientation of 3,4-dihydroxyphenyl, and the length of alkyl in binding with α-glucosidase and PTP1B (He et al., 2020a). *In vitro*, the IC_{50} values of α-amylase and α-glucosidase were 14.23 and 1.76 mg/mL. *In vivo*, a high-fat diet and streptozotocin combined to induce type 2 diabetes model in rats were established,

Table 5 Structure of polyphenols in *A. tsao-ko*.



(*continued on next page*)

Table 5 (*continued*)

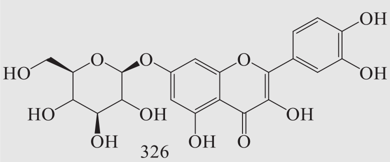

305

306

307

308

309

310

311

312

313

314

315

316

317

318

319

320

321

322

323

324

325

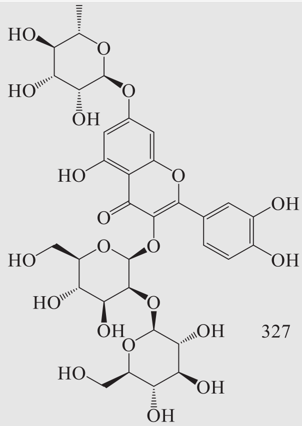
and the model was used for 6 weeks with *A. tsao-ko* extracts After treatment, it was found that the fruit extract can significantly improve the impaired glucose tolerance, and reduce the levels of fasting blood glucose, insulin, malondialdehyde, and increase the level of superoxide dismutase. Combined with histopathological findings, the findings suggest that *A. tsao-ko* extract retains the structure and function of the pancreas, and exhibits good anti-diabetic activity both *in vivo* and *in vitro* (Zhang et al., 2021). Methanol extracts of *A. tsao-ko* could obviously inhibit α-glucosidase activity and improve glucose tolerance in mice (Xie et al., 2021). Although most of the pharmacological activities of *A. tsao-ko* are obtained through *in vitro* experiments, these valuable research results provide some evidence for clarifying the therapeutic mechanism of *A. tsao-ko*. It can be used as a potential medicinal resource, such as functional food to reduce blood glucose and lipid levels or as a new candidate drug for anti-diabetes.

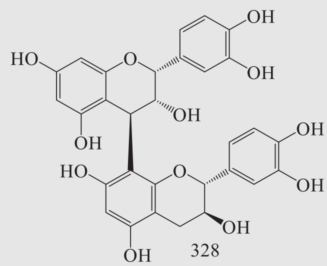
6.1.2. Anti-obesity and hypolipidemic activity

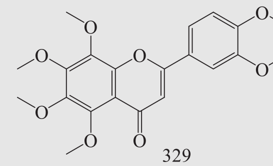
According to statistics, up to now, the incidence of dyslipidemia in Chinese adults has exceeded 25%. Hyperlipidemia is mainly divided into two types: Primary and secondary. The former is mainly caused by genetic factors and dietary habits; the latter is mainly caused by other intermediate primary diseases, such as diabetes and obesity (Nanayakkara et al., 2021). At present, the drugs for the treatment of hyperlipidemia are mainly statins, including simvastatin. However, long-term use of these drugs can cause many side effects, such as myalgia and liver damage. In recent years, some studies have found that *A. tsao-ko* has bioactive compounds that can improve hyperlipidemia, which provides a research idea for the development of new hypolipidemic drugs. *A. tsao-ko* has the effect of inhibiting the activity of lipase, the inhibitory effect of (2E,7Z) -tetradeca-2,7-dienoic acid and (E)-tetradec-2-enoic acid on lipase were compared with that of Orlistat.

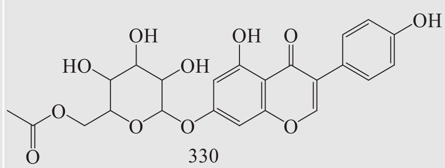
Table 6 Structure of flavone and diarylheptanoids in *A. tsao-ko*.

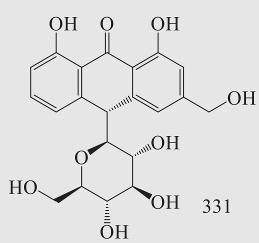

326

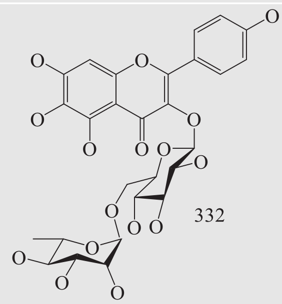

327

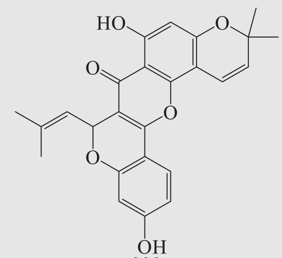

328

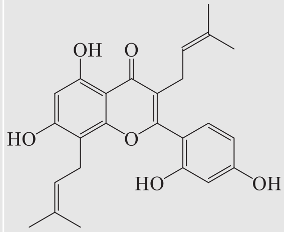

329

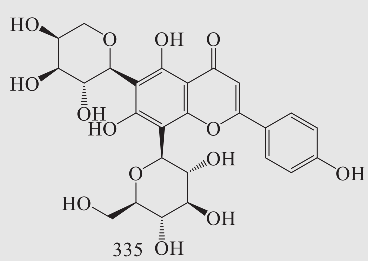

330

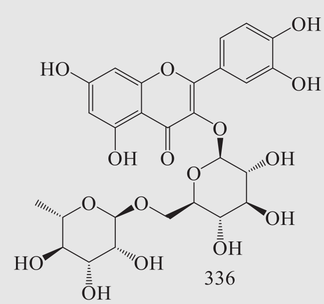

331

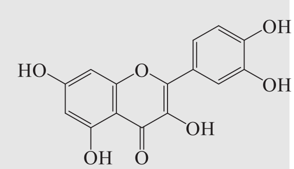

332

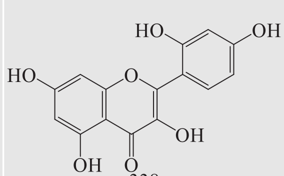

333

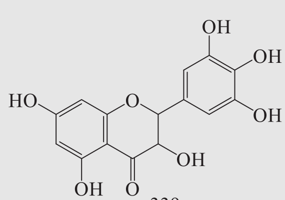

334

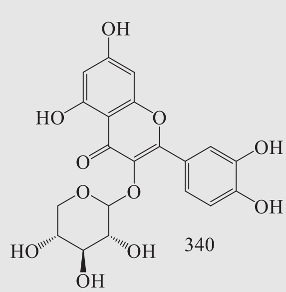

335

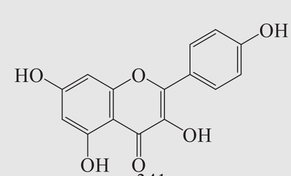

336


337


338

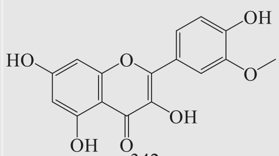

339


340

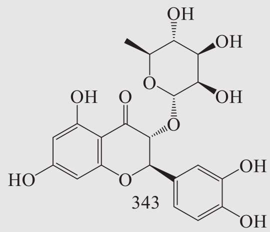

341

(*continued on next page*)

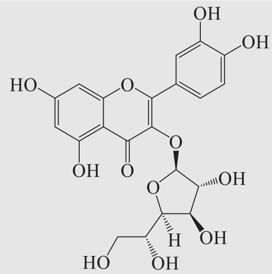
Table 6 (*continued*)



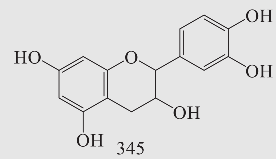
342



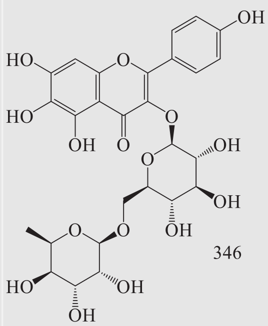
343



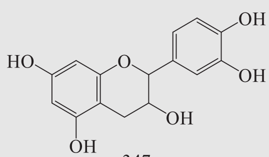
344



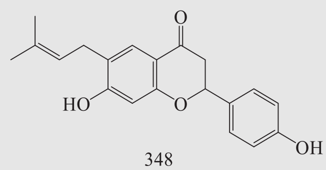
345



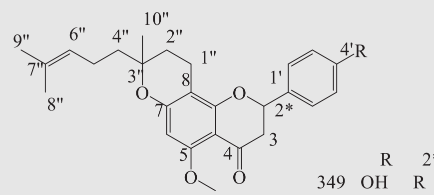
346



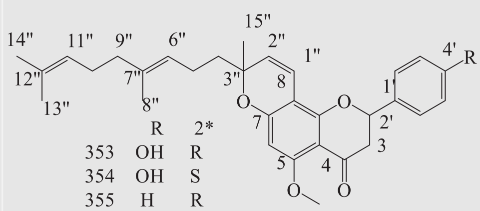
347



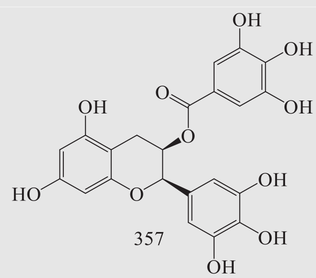
348



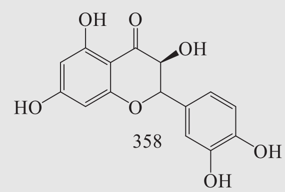
	R	2*
349	OH	R
350	OH	S
351	H	R
352	H	S



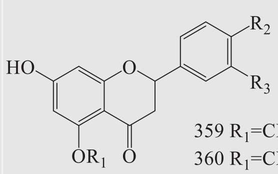
	R	2*
353	OH	R
354	OH	S
355	H	R
356	H	S



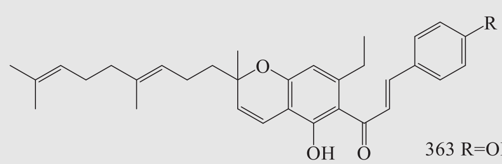
357



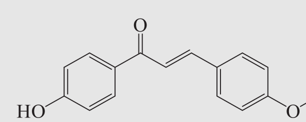
358



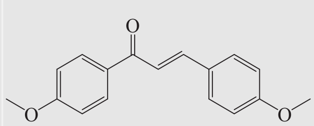
359 R_1=CH_3,R_2=H,R_3=H
360 R_1=CH_3,R_2=OH,R_3=H
361 R_1=H,R_2=OH,R_3=H
362 R_1=H,R_2=OCH_3,R_3=OH



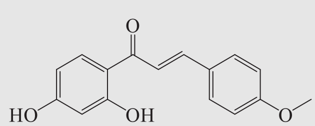
363 R=OH
364 R=H



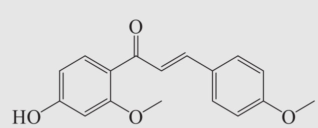
365



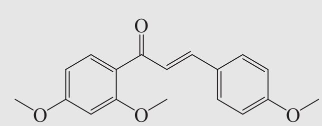
366



367

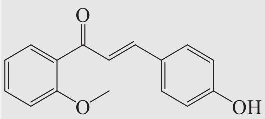


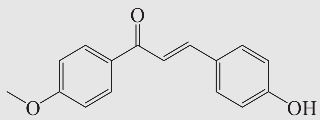
368

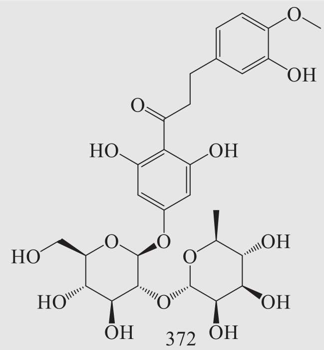


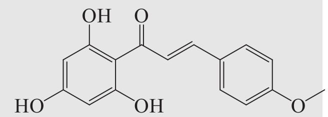
369

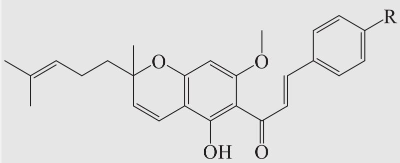
Table 6 (*continued*)

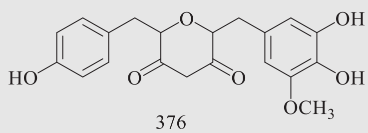

370

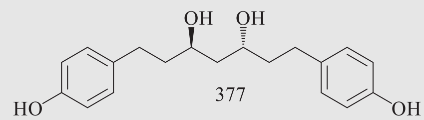

371

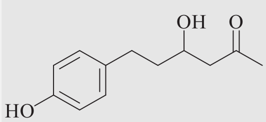

372

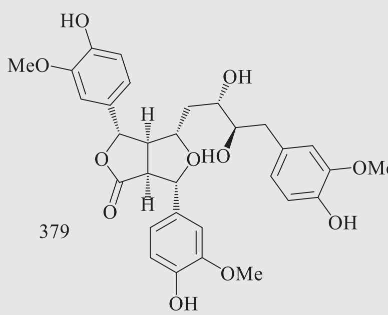

373

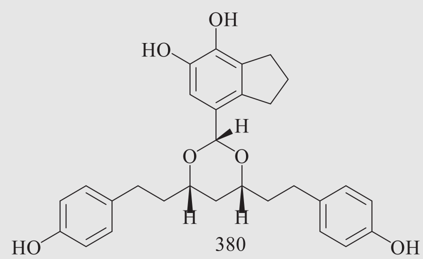

374 R=H
375 R=OH


376


377

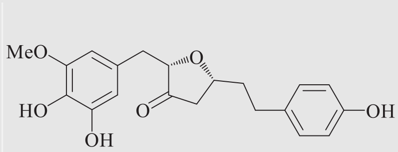

378

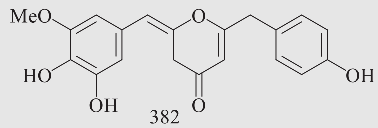

379

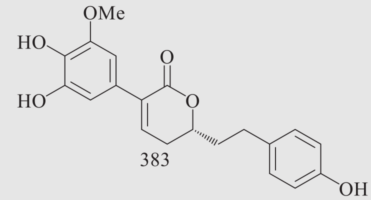

380

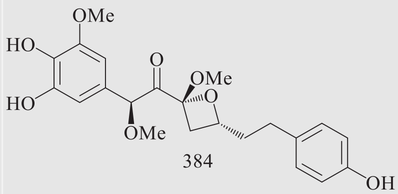
(*continued on next page*)

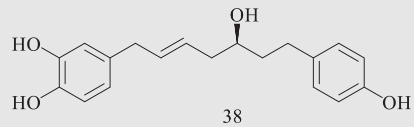
Table 6 (*continued*)

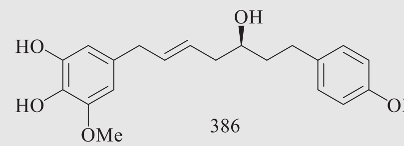

381

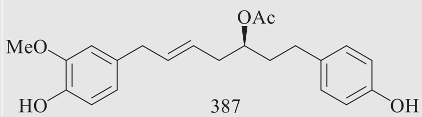

382

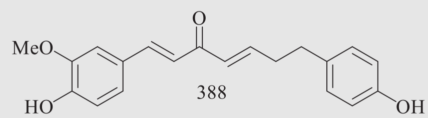

383

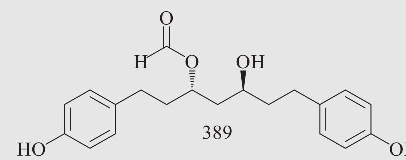

384

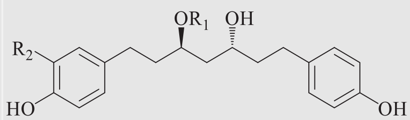

38
5

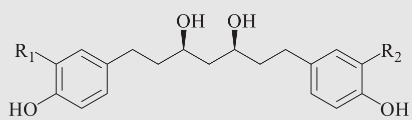

386

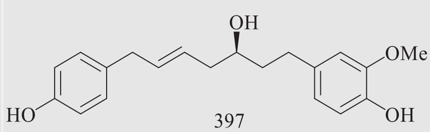

387

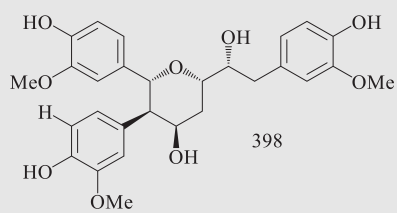

388

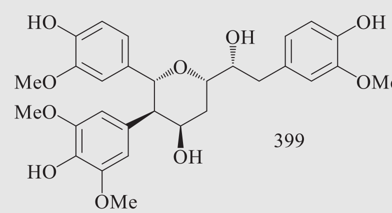

389

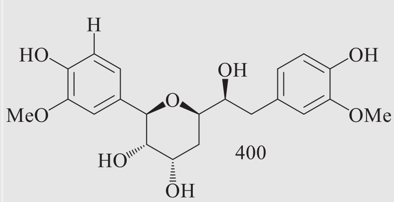

390 R_1=H,R_2=H
391 R_1=Ac,R_2=H
392 R_1=H,R_2=OH
393 R_1=H,R_2=OMe

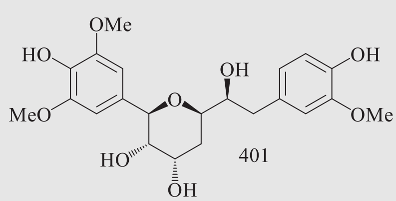

394R_1=OH,R_2=H
395R_1=OMe,R_2=H
396R_1=OMe,R_2=OH

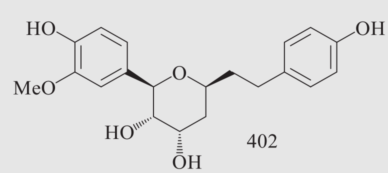

397

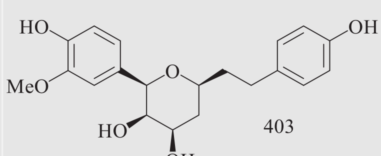

398

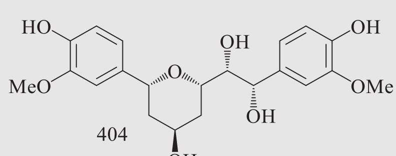

399

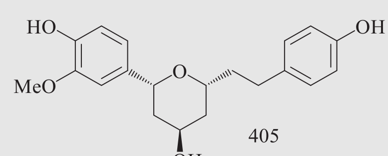

400

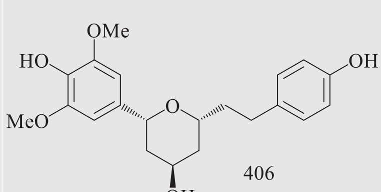

401

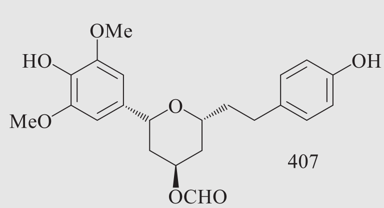

402


403


404


405


406


407

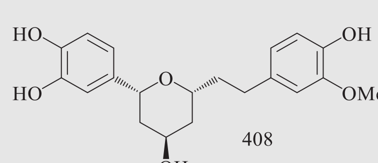
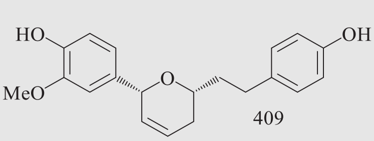
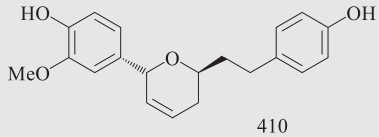
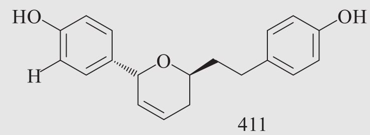
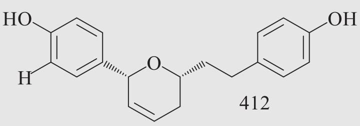

408

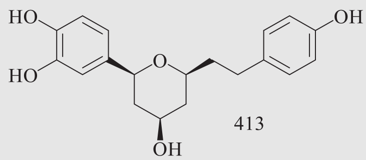
Table 6 (*continued*)

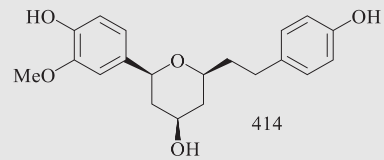

409

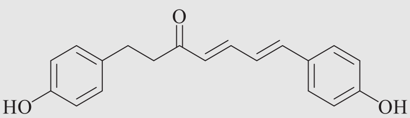

410

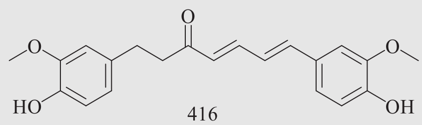

411

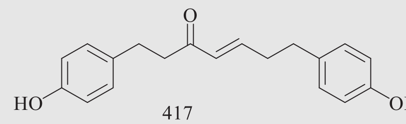

412

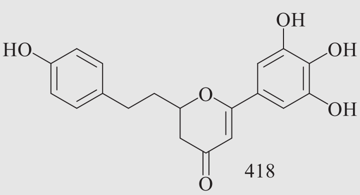

413

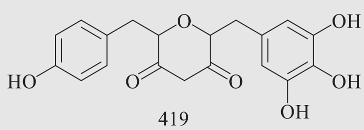

414

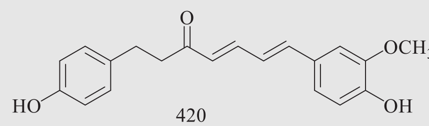

415

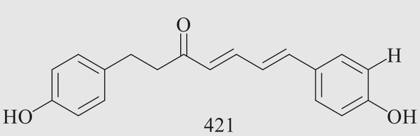

416

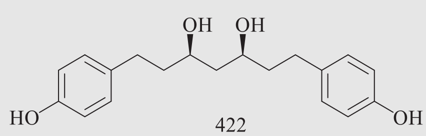

417

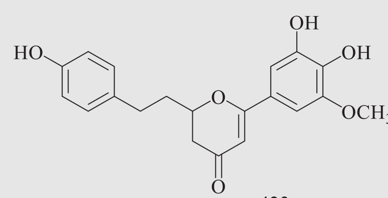

418

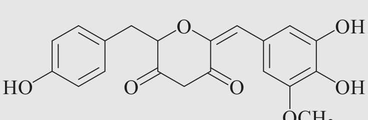

419

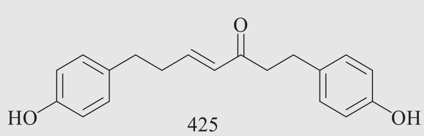

420

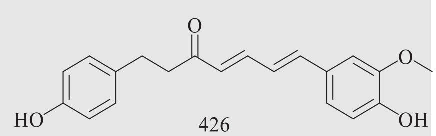

421


422


423


424


425


426

The concentration was 50 μg/mL, the lipase inhibition effect of two compounds were better than Orlistat (Liu et al., 2018). Ethanol extract of *A. tsao-ko* (EAT) can improve obesity and hyperlipidemia in C57BL/6 mice with a high carbohydrate diet. Histological analysis showed that the mice taking EAT orally for 84 days lost weight, and EAT improved plasma cholesterol, triglyceride, and other indicators of the mice. The contents of TC and TG, as well as lipid droplets of HCD-induced hepatic accumulation in the liver tissue, were suppressed by EAT (Park et al., 2021). Studies have also shown that EAT can improve obesity caused by menopause (Ghani et al., 2020). Menopause is the natural cessation of menstruation due to the loss of ovarian function, which can lead to serious physiological complications, such as obesity. Menopause will cause a decrease in estrogen, which will increase glucose intolerance, insulin resistance, and redistribution of fat into the abdominal cavity, which will lead to obesity and related metabolic syndrome in women. Shim et al. (2021) found that EAT significantly decreased OVX-induced body weight gain and fat accumulation, significantly prevented OVX-induced deterioration of bone mineral density and microstructure of trabecular tissues, and significantly inhibited osteoclast differentiation by downregulating NF-κB/Fos/NFAT c1 signaling in osteoclasts. It can be seen that *A.*

tsao-ko can be used as a raw material for the development of effective natural fat inhibitors. In addition, Compounds 237, 117, 273, and 311 can inhibit the differentiation of 3 T3-L1 cells in a concentration-dependent manner, and the percentage of differentiated cells is lower at higher concentrations. Among them, compounds 237 and 273 have strong anti-lipid activity, but their specific mechanisms of action are not clear (Hong et al., 2021b).

6.1.3. Anti-cardiovascular disease

Cardiovascular diseases, a list of cardiovascular diseases related to the heart or blood vessels, mainly including stroke and ischemic heart disease, are among the top 10 causes of death in humans and a leading cause of disability (Hsu et al., 2021). Hypercholesterolemia is also one of the main risk factors for cardiovascular diseases. It has been reported that improving blood HDL-C levels or reducing blood TC and LDL-C levels can effectively prevent cardiovascular diseases (Bianconi et al., 2021). The risks of cardiovascular disease can be reduced by changing environmental risk factors, such as diet and regulating the component of intestinal flora to prevent (Hsu et al., 2021). Targeted therapy of intestinal microorganisms plays an important role in the prevention and treatment of cardiovascular diseases. Gut microbiota may directly or indirectly affect the risks of cardiovascular disease, and that gut microbiota in early life is associated with cardiovascular disease later part of life (Zhao et al., 2021). The polyphenolic extracts and volatile oil in *A. tsao-ko* have the activities of regulating the mRNA and protein expressions of enzymes and transporters of cholesterol absorption and metabolism. It can effectively improve cholesterol plasma TC concentrations and atherosclerosis in hamsters fed with a 0.1% cholesterol diet. In addition, the polyphenolic extracts and volatile oil in *A. tsao-ko* restore the deteriorating intestinal microbiota and promote the growth of Ruminococcus-2 by inhibiting the growth of *Allobaculum* and *Desulfovibrio* (Liu et al., 2021).

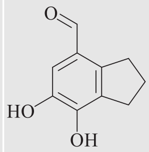
6.2. Anti-cancer

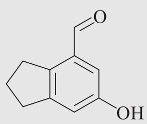
A study found that the methanolic extract of *A. tsao-ko* has cytotoxic activity, and diarylheptane compound 421 can be separated through the guidance of biological activity. Compound 421 had cytotoxicity against lung cancer A549 (IC_{50} = 4.9 μg/mL) and melanoma SK-Mel-2 cells (IC_{50} = 11.4 μg/mL), comparable to cisplatin (IC_{50} = 7.4 and 10.0 μg/mL) (Moon et al., 2005). Furthermore, Yang et al. (2010) use of MTT method to study the AEO and its main bioactive substances (42 and 70) on human tumor cell lines (HepG2, Bel7402, Hela, A549, SGC-7901) and normal human cell lines (HL-7702, HUVEC) toxicity. By comparing with the anti-tumor drug mitomycin, it was found that the IC_{50} value of AEO on all cancer cell lines was higher than that of mitomycin. AEO was less sensitive to the cytotoxicity of human normal cell lines HL-7702 (IC_{50}: 163.91 ± 5.11 ~ 272.41 ± 0.97 μg/mL) and HUVEC (IC_{50}: 2.54 ± 0.13 ~ 16.04 ± 0.04 μg/mL) (Yang et al., 2010). In addition, there are research reports, which use the MTT method to determine the chemical compounds in *A. tsao-ko* antiproliferative activities against HepG-2, SMMC-7721, Hela, and A549 human cancer cell lines. *A. tsao-ko* also has strong anti-tumor activity against HepG-2, SMMC-7721, Hela, and A549 cell lines (Zhang et al., 2015). Zhang and Yang (2015) established the H_{22} tumor-bearing mice model to study the inhibitory effect of AEO on tumor cell growth. AEO could inhibit the proliferation of 6-10B cells in a dose-dependent manner, and its IC_{50} for 24 h was 0.14 mg/mL. AEO can induce apoptosis by up-regulating the expression of Bax protein and down-regulating the expression of Bcl-2 protein, thereby achieving the effect of inhibiting the growth of tumor cells. Its pharmacological mechanism may be induced apoptosis of 6-10B cells through the mitochondrial apoptosis pathway, thereby exerting itself effectively (Gao et al., 2021). Moreover, EAT has been confirmed to have anti-ovarian cancer activity, and angiogenesis was a key factor in the growth of tumor cells (Pradeep et al., 2014). The inhibition rates of *A. tsao-ko* on SPHK1/2 enzyme activities were 59.75% and 22.75%, respectively, which could induce cell cycle arrest and apoptosis, exerting anticancer effects (Lee et al., 2019a). EAT did not influence vascular endothelial cells directly, but decreased IL-6 and VEGF secreted by ovarian cancer cells to inhibit angiogenesis through inhibition of p-STAT3 and NF-kB activation. And p-STAT3 and NF-kB could adjust each other and IL-6 and VEGF also mediates p-STAT3 and NF-kB too, which created a loop. EAT interrupted p-STAT3/NF-kB/IL-6 and VEGF loop through induced ER stress, achieving an anti-tumor effect (Chen et al., 2020).

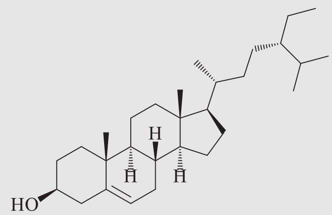
6.3. Anti-inflammation

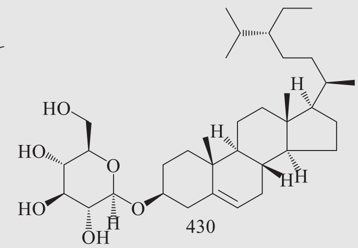
Inflammation is a harmful and irritating biological reaction triggered by the immune system due to pathogens, damaged cells, toxic compounds, and other factors, leading to acute or chronic inflammation in the body, which will cause pathological changes in the body (Chen et al., 2018; Medzhitov, 2010). Controlled inflammatory factors can be served as a defense mechanism for human health, but uncontrolled inflammatory factors can also lead to various inflammatory diseases in the human body (Zhou et al., 2016). In the studies of *A. tsao-ko*, researchers found that *A. tsao-ko* contains natural chemical compounds with good anti-inflammatory effects, including terpenoids and flavones. It has been reported that luteolin can induce the expression of OH-1 through Nrf_2 signaling to exert anti-inflammatory activity, thereby protecting body cells from various inflammatory factors (Akram et al., 2015). The extract and isolate of *A. tsao-ko* can effectively inhibit inductive nitric oxide synthase, it is of great significance for developing NO inhibitors to fight against inflammation (Mariotto et al., 2007). 2,8-decadiene-1,10-diol had anti-inflammatory activity in lipopolysaccharide-stimulated RAW 264.7 cells. 2,8-decadiene-1,10-diol can inhibit the production of NO by downregulating inducible NO synthase. Moreover, 2,8-decadiene-1,10-diol suppressed the production of pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α. 2,8-decadiene-1,10-diol can inhibitory the expression of inflammatory proteins by mediated through the inactivation of mitogen-activated protein kinases (MAPKs), mainly extracellular signal-regulated kinase, c-Jun-N-terminal kinase, and p^{38MAPK}, and inhibition of nuclear factor-κB (NF-κB) pathways including degradation of inhibitor of κB-α and nuclear localization of NF-κB (Kim et al., 2016). In LPS-induced RAW 264.7 macrophages, the methanol extract

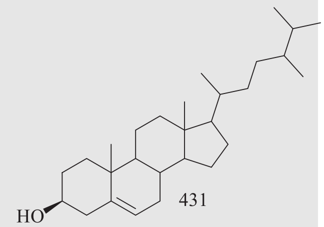
Table 7 Structure of bicyclic nonane and steroids in *A. tsao-ko*.

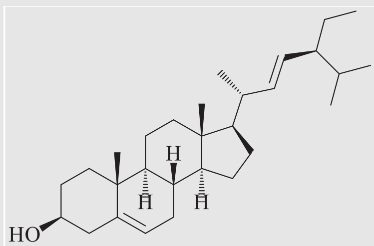

427

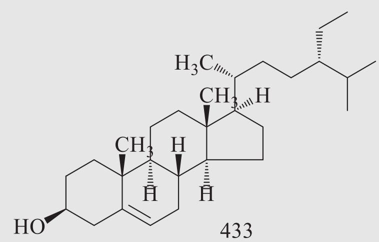

428


429


430


431


432


433

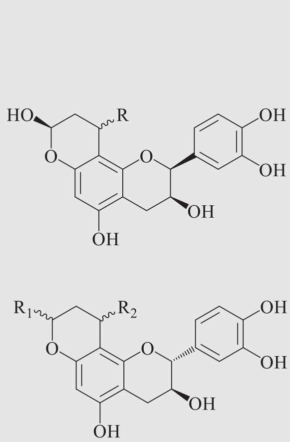
of *A. tsao-ko* reduced the production of NO by inhibiting inducible NO synthase (iNOS) expression, and increased heme oxygenase-1 (HO-1) expression at the protein and mRNA levels (Shin et al., 2015). Compound 33 can inhibit the excessive production of NO-induced by lipopolysaccharide, thus achieving the purpose of inhibiting the expression of pro-inflammatory cytokines (Hong et al., 2021b). Compounds 373, 374, and 375 were obtained from *A. tsao-ko*, with a chalcone skeleton, which showed obviously inhibitory effects on the NO production with IC_{50} values up to 22.5 μm (Kim et al., 2019b). In addition, compound 33 with the anti-inflammatory effect was exerted by inhibiting the NO production via down-regulation of iNOS in LPS-stimulated RAW264.7 cells (Hong et al., 2021b).

6.4. Anti-bacterial

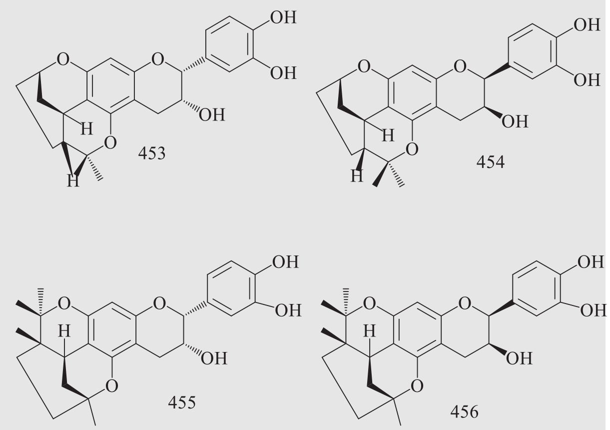
At present, bacterial infection was the main source of infectious diseases. Bacteria have certain drug resistance, which may lead to the death of infected patients in severe cases (Stracy et al., 2022). The problem of bacterial resistance has become one of the major global health threats, so the development of new antibacterial agents has a very important role in medical research. The broad-spectrum inhibitory effect of *A. tsao-ko* on fungi, pathogenic bacteria, Gram-positive, Gram-negative bacteria, and *Trichomonas vaginalis*. The AEO exhibited moderate to potent broad-spectrum antimicrobial activity against 5 g-positive and 2 g-negative bacteria (MIC:2.94–5.86 mg/ml) (Cui et al., 2017). By intramuscular administration, AEO at the lowest effective dose of 0.92 g/kg/d protected mice from *S. aureus* or *E. coli* infection with a 100% survival rate (Dai et al., 2016a). The bacteriostatic mechanism of AEO to foodborne bacteria *Escherichia coli* may be through the change of permeability and integrity of cell membrane, resulting in leakage of nucleic acid and protein, MIC and MBC of 3.13 mg/mL and 6.25 mg/mL (Guo et al., 2017). In previous studied, compared with most of which exhibited intact genomic DNA, the cells cultured with AEO had numerous cells with condensed chromatin, significant nuclear fragmentation (Yang et al., 2010). *In vitro,* AEO had obvious anti-MRSA activity and had a synergistic effect and additive effect with other antibiotics, which can reverse the activity of MRSA against β-lactam antibiotics multidrug resistance. Xu et al. (2017) used the microfluidic method to determine the fractional inhibitory concentration (FIC) indexes of three kinds of β-lactam antibiotics (amoxicillin, cefalexin, and cefepime), AEO and three antibiotics synergy effects can reach 80%, and effectively enhances the therapeutic effect of antibiotics on MRSA. The extracts had anti-quorum (QS) sensing and anti-biofilm activities against gram-positive and gram-negative bacteria. Furthermore, the anti-QS activity of the *A. tsao-ko* extract (0.5–4 mg/ml) by using C. violaceum a biosensor strain and biofilm formation by crystal violate assay. It was found that minimum inhibitory concentration (MIC) for *Staphylococcus aureus* (Gram-positive), *Salmonella Typhimurium*, and *Pseudomonas aeruginosa* (Gram negative) were 1, and 2 mg/ml respectively (Rahman et al., 2017).

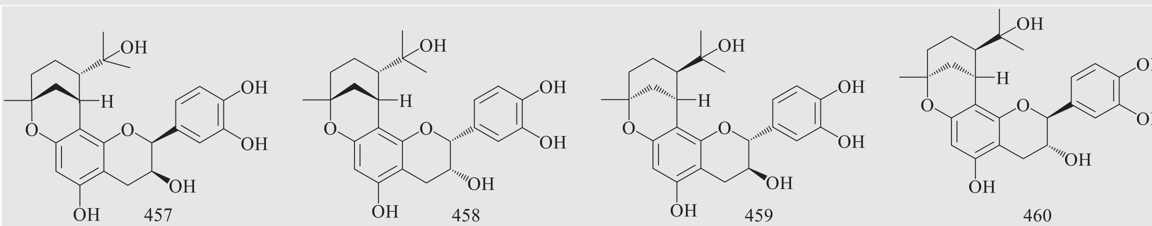
Trichomoniasis, caused by the flagellate protozoan *Trichomonas vaginalis*, is the most common non-viral sexually transmitted disease (STD) and is often treated with the drug 5-nitroimidazole. Over time, many strains of *Trichomonas vaginalis* have developed resistance to these therapeutic drugs (Osmari et al., 2020). Scientists found that AEO and compound 42, had a certain therapeutic effect on the strain. After the strain was treated with AEO and compound 42, the nuclear membrane was damaged, nuclei were dissolved, and the chromatin was accumulated; In the cytoplasm, numerous vacuoles appeared, rough endoplasmic reticulum dilated, the number of ribosomes was reduced, organelles disintegrated, the cell membrane was partially damaged, with cytoplasmic leakage, and

Table 8 Structure of flavanol-fatty alcohol hybrids and flavanol-menthane conjugates in *A. tsao-ko*.



434 R=α-pentyl
435 R=α-heptyl
436 R=β-heptyl
437 R=α-(E)-7-hydroxyhept-5-en-1-yl
438 R=α-(E)-7-acetoxyhept-5-en-1-yl
439 R=α-nonyl
440 R_1=α-OH, R_2=α-pentyl
441 R_1=α-OH, R_2=β-pentyl
442 R_1=β-OH, R_2=β-pentyl
443 R_1=α-OH, R_2=α-heptyl
444 R_1=α-OH, R_2=β-heptyl
445 R_1=β-OH, R_2=β-heptyl
446 R_1=β-OH, R_2=α-heptyl
447 R_1=α-OH, R_2=β-(E)-7-hydroxyhept-5-en-1-yl
448 R_1=β-OH, R_2=α-(E)-7-hydroxyhept-5-en-1-yl
449 R_1=α-OH, R_2=β-(E)-7-acetoxyhept-5-en-1-yl
450 R_1=β-OH, R_2=α-(E)-7-acetoxyhept-5-en-1-yl
451 R_1=α-OH, R_2=β-nonyl
452 R_1=β-OH, R_2=β-nonyl



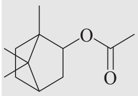
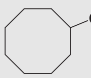
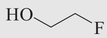
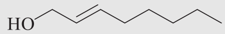
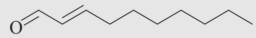
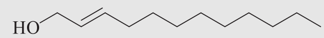
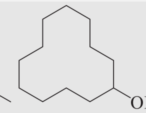


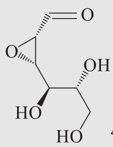
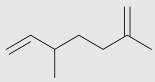
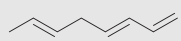
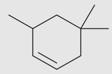
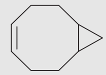
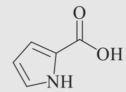
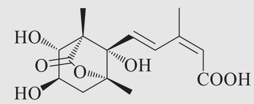
cell disintegration was observed (Dai et al., 2015a). Furthermore, food-borne pathogens are a large group of bacteria that affect human health. Among them, *Bacillus subtilis* and *Listeria monocytogenes* have a greater impact on human health. Studies have found that *A. tsao-ko* extract can destroy the cell wall, cell morphology, and cell integrity of the two bacteria, thereby inhibiting the growth of *Bacillus subtilis* and *Listeria monocytogenes* (Tang et al., 2020). According to reports, *A. tsao-ko* also has good anti-pneumococcal activity (inhibition rate greater than 99%). The researchers tested the extract and isolates of *A. tsao-ko* for inhibitory activity against pneumonia, the MIC was 50 μg/mL, equal to the chloramphenicol positive control (Liu et al., 2018c). According to previous studies, the mechanism of the antibacterial activity of *A. tsao-ko* can be summarized into the following two aspects: On the one hand, it acts on the biofilm system of microbial cells, resulting in the destruction of the membrane structure and the increase in membrane permeability, resulting in the leakage of intracellular ions and contents; On the other hand, it acts on the enzyme system of microbial biochemical reactions, and the enzyme system is destroyed, resulting in cell death, thereby exerting bacteriostatic activity (Álvarez-Martínez et al., 2021). The broad-spectrum antibacterial activity of *A. tsao-ko* against microorganisms, especially pathogenic bacteria, makes *A. tsao-ko* a potential natural resource for the development of bacteriostatic agents and antibiotics, which also gives a hint to the probable mechanism of its clinical application such as foodborne and infectious diseases.

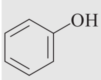
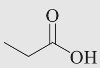
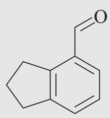
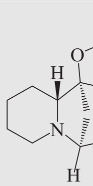
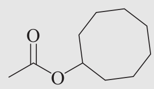
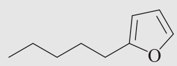
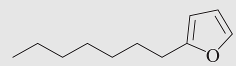
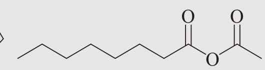
6.5. Antioxidation

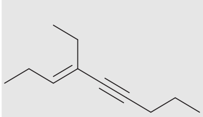
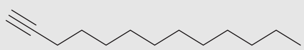
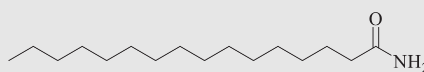
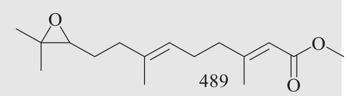
Numerous studies have shown that cancer, arteriosclerosis or other diseases, and aging are all related to the production of excess free radicals (Martemucci et al., 2022). Antioxidants can effectively remove the free radicals generated by the human body due to continuous contact with the outside world, thereby avoiding the harm free radicals brings to the human body to the greatest extent (Sharma et al., 2018). Therefore, antioxidation is an important step in preventing diseases and resisting aging, and one of the important directions for the development of health and skincare products. *A. tsao-ko* has a very strong antioxidant capacity, mainly fat-soluble ingredients, of which catechin and their derivatives had a similar free radical scavenging ability to vitamin C (Yan, 2014). There are reports that catechin and catechol derivatives showed strong activities in both the DPPH radical scavenging activity and antioxidant activity assays. The study also explained that the difference in radical scavenging ability of Protocatechuic acid (265) and Protocatechualdehyde (322) may be because carboxyl groups can form intermolecular hydrogen bonds, while aldehyde groups cannot. Because of this bonding, the electron-with-drawing capacity of compound 265 is decreased, which leads to the weakening of its activity toward DPPH free radicals (Martin et al., 2000). In addition, AEO and their natural compounds have been extensively studied due to their strong aroma and strong antioxidant capacity (Ni et al.,

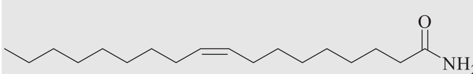
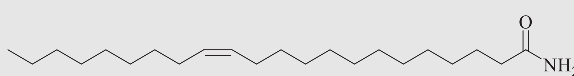
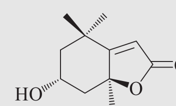
Table 9 Structure of other compounds in *A. tsao-ko*.

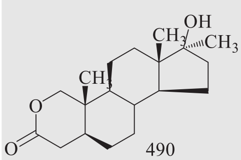
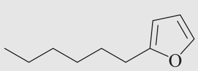
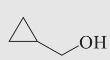
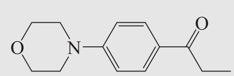

461

462

463

464

465

466

467


468

469

470

471

472

473

474

475


476


477

478

479

480

481

482


483

484

485

489


486

487

488


490

491

492

493

2021). There are reports that AEO obtained from *A. tsao-ko* can be explored as a potent natural antimicrobial and antioxidant preservative ingredient in food industry. The IC_{50} values of AEO determined by DPPH radical scavenging activity and β-carotene/linoleic acid bleaching assay were 5.27 and 0.63 mg/mL (Cui et al., 2017a). Ethanol (95%) extract and ethyl acetate extract of *A. tsao-ko* had significant DPPH free radical scavenging activity, and the compounds with antioxidant activity were mainly concentrated in ethyl acetate extract (Zhang et al., 2015). In addition, studies have shown that polyphenolic active substances isolated from *A. tsao-ko* have certain DPPH and ABTS free radical scavenging capabilities, with IC_{50} values of 42.46 μg/mL and 85.47 μg/mL, respectively. And the concentration of polyphenols was positively correlated with its antioxidant activity (Li et al., 2017a). Studies have evaluated the antioxidant activities of 12 compounds, such as 3,4-dihydroxy benzoic acid and Meso-Hannokinol, which were isolated from *A. tsao-ko*. It was found that showed good DPPH radical scavenging activity in a dose-dependent manner. When the concentration was 100 μg/mL, 3,4-dihydroxy benzoic acid showed the best DPPH free radical scavenging activity, and its free radical scavenging rate was more than 90%, which was close to the DPPH free radical scavenging activity of vitamin C at the same concentration (Liu et al., 2018a). Methanol extracts of *A. tsao-ko* possessed high flavonoid content (1.21 mg QE/g DW), the results of *in vitro* experiments showed that *A. tsao-ko* has a strong oxygen-free radical absorption capacity, the ability to scavenge ABTS free radical antioxidants, and the iron reduction capacity (Zhang et al., 2021).

6.6. Neuroprotection

According to the research results of Zhang et al. (2014), flavonoids in *A. tsao-ko* have the biological activity of inhibiting H_2O_2-induced apoptosis of PC-12 cells. In this study, eight

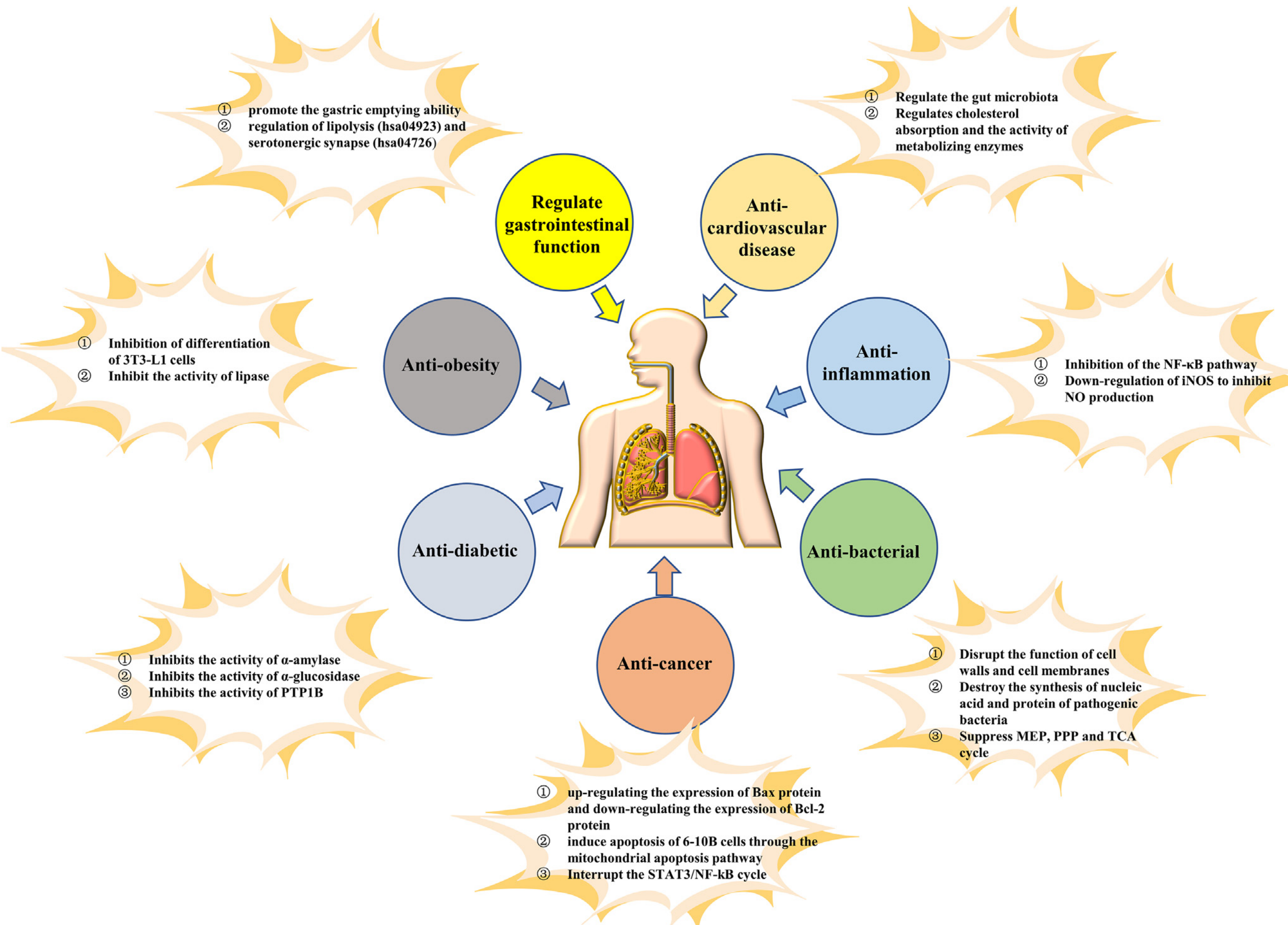


Fig. 4 Pharmacological action and mechanism of *A. tsao-ko*.

bioactive compounds were isolated from the *A. tsao-ko*, all of which had the effects of enhancing the viability of damaged PC-12 cells, of which quercetin had the most significant effect. In previous studies, it has also been shown that quercetin can effectively inhibit the biological activity of the iNOS/NO system and adrenocorticotropic hormone, thereby exerting neuroprotective effects (Zhang et al., 2011). *A. tsao-ko* has chemicals that protect against nerve damage caused by exogenous drugs, GG-A and GG-B could protect the PC-12 cells against H_2O_2 induced injury by reversing the H_2O_2 induced cells viability loss, and their protective effects were close to that of VC (50 μg/mL) (Zhang et al., 2016). After treatment with compounds GG-A and GG-B the decreasing trend of H_2O_2-induced cell viability was inhibited in a dose-dependent manner, and the researchers also found that GG-B showed higher activity in enhancing the cell viability. In addition, some studies have shown that *A. tsao-ko* has anti-epileptic biological activity. Its ethanolic extract significantly reduced the time and duration of seizures in PTZ animals (Wang et al., 2021c). Gao et al. (2018) used Tsaoko-Anemarrhenae decoction to study epileptic rats (SPF grade SD male rats) models, the anti-epileptic mechanism of Tsaoko-Anemarrhenae decoction was discussed from the perspective of miRNA regulation. The mechanism was to down-regulate the expression of miR-29 and up-regulate the expression of miR-21 to target and regulate the expression of apoptosis-related genes Bax, P53, and Bcl-2, inhibit cell apoptosis and play an anti-epileptic effect.

6.7. Regulate gastrointestinal function

In China, in addition to being used as condiments and spices, *A. tsao-ko* used as a traditional medicine for the treatment of digestive diseases and infectious diseases. The researchers obtained a lot of inspiration from the classical Chinese prescriptions, combined with the characteristics of modern pharmacology, improved the prescriptions, and obtained good clinical effects in the treatment of diseases. In traditional medicine, *A. tsao-ko* is often used in TCM to treat abdominal pain and diarrhea. According to this principle, Dai, (2003) used *A. tsao-ko* to treat 42 patients with abdominal distension after cesarean section and found that the effective rate of the treatment could reach 92.7%, which showed the effect of *A. tsao-ko* postpartum abdominal distension to promote gastrointestinal gas, and the fruit has no toxic side effects and can be widely used in postpartum women with abdominal distension. Yang, (2011) studied the effects of the volatile oil of *A. tsao-ko* on gastric emptying and intestinal propulsion in mice. The results showed that volatile oil of *A. tsao-ko* could significantly or inhibit promote the gastric emptying ability of mice. The intestinal peristalsis of the mouse indicates that AEO has a significant inhibitory effect on intestinal propulsion. At the same time, with the increase of the dose, the inhibitory effect of AEO on intestinal propulsion also increases. A study showed that the water extract of *A. tsao-ko* could promote the peristalsis of the small intestine of constipated mice, and effectively improve the symptoms of constipation in mice (Yang et al., 2020). Recently, studies have used GC–MS combined with network pharmacological analysis to construct a component-target pathway network, revealing that there are 12 compounds in *A. tsao-ko* that play a potentially critical role in the treatment of dyspepsia. And through KEGG enrichment analysis of 17 signal pathways, the results show that the signal pathway of regulation of lipolysis (hsa04923) and serotonergic synapse (hsa04726) play an important role in the treatment of dyspepsia.

In summary, the mechanism of *A. tsao-ko* in the treatment of dyspepsia may be related to a variety of compounds, target genes, and signal pathways (Shi et al., 2021). In regulating gastrointestinal function, oral decoction has low production cost, significant curative effect, and no toxic side effects have been found, so it can be clinically promoted. However, its functional mechanism is still unclear, and its physiological regulation mechanism can be explored through the results of these clinical applications and *in vivo* experimental results combined with modern pharmacological research.

6.8. Other pharmacological properties

A. tsao-ko also has anti-allergic active ingredients. Studies have shown that EAT (80%) contain the compounds helichrysetin and cardamomin, and the inhibitory rate of β-hexosaminidase released by RBL-2H3 cells at a concentration of 50 μM is 99.1% and 21.3%, indicating that *A. tsao-ko* has threshing inhibitory effect and has the potential to be used as a natural anti-allergic drug (Shim et al., 2021a). In addition, the ethanolic extract of *A. tsao-ko* can significantly prevent ovx-induced deterioration of bone mineral density and trabecular tissue microstructure, and significantly inhibit osteoclast differentiation by down-regulating the osteoclast NF-κB/Fos/NFATC1 signaling pathway (Shim et al., 2021). *A. tsao-ko* was reported that volatile oil extracted by steam distillation and then separated by separation technology had toxic effects on Triboliumcastaneum (Herbst) and Lasiodermaserricorne (Fabricius). The exposure toxicity results showed that were considered together, suggest that the AEO and the two compounds show potential to be developed as natural insecticides/-fumigants for control of stored product insects (Wang et al., 2014). Furthermore, polyphenolic and AEO can alleviate hypercholesterolemia in hamsters through the interaction of gut flora (mainly Ruminococcaceae) and bile acid metabolism at the population level. The mechanism may be to improve hypercholesterolemia by increasing the production of short-chain fatty acids, which increases the mutual communication between the intestinal flora and host cells, inhibited the activity of HMG-CoA-R (Liu et al., 2021).

7. Origin identification and variety identification

7.1. Origin identification

As we all know, the material basis of CHM is different chemical compounds, especially the secondary metabolites of plants. Different growth environments will produce different secondary metabolites, resulting in differences in quality. The geographic origin of the fruit directly affects its flavor and medicinal effects of *A. tsao-ko*. *A. tsao-ko* originates from different regions, and its component is bound to be different. Among modern regulatory techniques, chromatography and its combined techniques have been successfully used to assess the quality of botanical drugs from different geographic sources. However, the pharmacological effect of *A. tsao-ko* is the result of the multi-component synergistic effect among its chemical compounds. Therefore, the overall efficacy of *A. tsao-ko* cannot be evaluated if only the labeled compounds are considered (Huang et al., 2018). In recent years, spectroscopy technology has been widely used in the identification of CHM, with the advantages of low cost, green, non-destructive and fast analysis (Liu et al., 2020; Pei et al., 2019; Wang et al., 2021a). Studies have shown that the use of infrared spectroscopy and ultraviolet–visible spectroscopy, combined with chemometrics and data fusion strategies, can effectively identify the geographic origin of *A. tsao-ko* ((Liu et al., 2021). The application of spectral technology provides a fast and nondestructive means for the geographic traceability of *A. tsao-ko*, and provides a theoretical basis for the establishment of *A. tsao-ko* quality evaluation system.

7.2. Variety identification

In recent years, two varieties of yellow-flowered fruit (*A. tsao-ko*) and white-flowered fruit (*Amomum paratsao-ko*) have been discovered in the planting area of Yunnan Province (Qin et al., 2021). Both *A. tsao-ko* and *Amomum paratsao-ko* belong to the genus *Amomum Roxb* in the Zingiberaceae. The fruits are similar in shape and used. The traditional method of observing the macroscopic characteristics is difficult to distinguish, so during the harvest period, they are often mixed. Luo, (2014) used traits and microscopic identification to identify the two varieties. However, regardless of trait identification or microscopic identification, the characteristics are very similar and it is difficult to distinguish. Huang et al. (2014) used GC–MS to study the volatile oil compounds of the two varieties. Although the morphological characteristics of the two varieties are similar, the chemical substances and content contained in them are very different, so the two varieties must be identified. For a long time, the data fusion strategy of vibrational spectroscopy combined with chemometric methods is often used in the identification of CHMs (Li and Wang, 2018; Wang et al., 2020). Qin et al. (2021) combined GC–MS or NIR with multivariate analysis to develop a discriminatory model, the classification accuracy rate is 100%. The identification method solves the problem that it is difficult to distinguish the two species, and provides a reference for distinguishing *A. tsao-ko* from its conformis. This study provides a theoretical basis for the identification of specificity between *A. tsao-ko* and its related species.

8. Economic value

8.1. Applications and market dynamics

The main uses of *A.tsao-ko* were in the food industry, where it was used as food additives for more than 90% of the time and as Chinese patent medicine for less than 5%. As a flavoring and aroma-

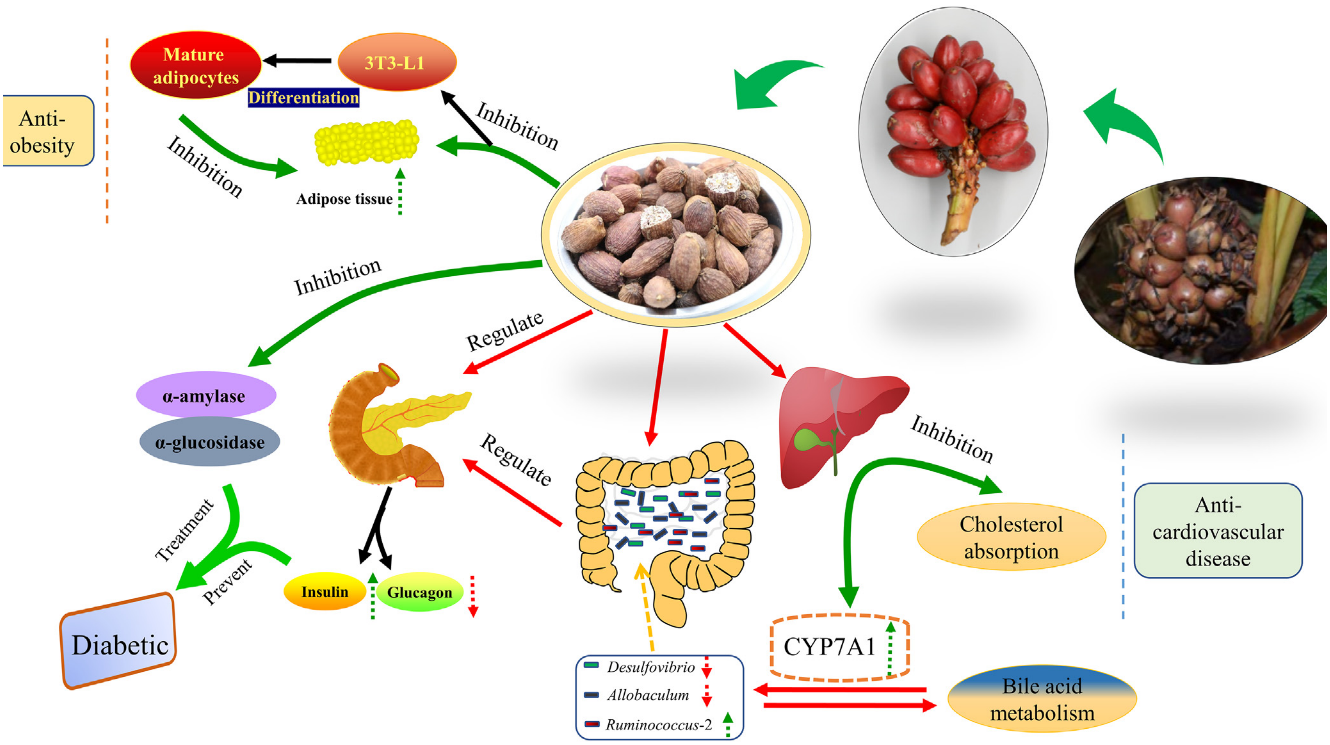


Fig. 5 Pathway of active ingredients of *A. tsao-ko* in regulating metabolic syndrome.

tizing agent, *A.tsao-ko* is commonly used in the food industry, mainly in dried fruits, powders, and flavorings (Zhang et al., 2014). There are many types of Chinese patent medicines with CHM compatibility, such as tou gu sou feng wan, yi shen wan, kai yu shu gan wan, kuan xion li ge wan, jie bai wan (Pu et al., 2015) (Fig. 6). Furthermore, although fewer products are commercially available, *A.tsao-ko* is used in the cosmetic industry. There is considerable potential for sun protection products based on AEO, since they have a good UV absorption effect, making them suitable for perfumery and skin care products.

Considering *A. tsao-ko* unique characteristics, the price is in a stable phase, according to the survey. Due to its distinctive

Fig. 6 Example of the application of *A.tsao-ko* (Image material from https://cn.bing.com/.).

aroma, *A. tsao-ko* has an important position in the flavoring market. Meanwhile, *A. tsao-ko* is a traditional CHM in Southeast Asia and is in steady demand, albeit in smaller quantities. The price of *A. tsao-ko* has remained relatively stable since 2016. In 2017, the price of *A. tsao-ko* rose suddenly as a result of a drought and a snow and ice disaster in 2016. There is a fourfold increase in price in July compared to expected. As new stock appeared in August, the price of *A. tsao-ko* gradually decreased until September 2018, when it leveled off. There was no significant fluctuation in *A. tsao-ko's* price following this period. Recently, there has been a gradual decline in the price, possibly due to the policy of vigorous *A. tsao-ko* cultivation (**Figure S1**).

8.2. The economic value of cultivating

At present, *A. tsao-ko* of China's market is in short supply and must be imported from Vietnam, Myanmar, and other countries, and imports are increasing. Its cultivation has the advantages of low investment (30,000–45,000 yuan/hm$^{2)}$, quick results (4 to 5 years for flowering and fruiting), long benefit time (up to 20 years), and high economic value. It is poverty alleviation in China's southwest border region. The pillar industry to tackle tough problems (Liu et al., 2017; Zhang et al., 2011). A survey showed that as of 2018, the total output value of *A. tsao-ko* reached 350 million, the national annual consumption of *A. tsao-ko* and dried fruit was about 12,550 tons, and the world's total output of *A. tsao-ko* and dried fruit was about 12,550 tons, showing a market situation in short supply. Nujiang prefecture regards *A. tsao-ko* as a core industry to help peasants increase their income, helping the poor to increase their income per capita by more than 2,700 yuan (Liu et al., 2021). In addition, Vietnam is also one of the main producers of the international market of *A. tsao-ko*, which is of great significance for the Vietnamese people to get rid of poverty and become rich.

In summary, the cultivation of *A. tsao-ko* is of great significance, and the development of spice and TCM cultivation can increase the income of the western provinces of China and promote economic development. Regrettably, due to the high price in recent years, the planting volume of *A. tsao-ko* has increased greatly, coupled with the lack of planting and production standards, research on variety selection, planting technology, processing methods, and insect control technology has led to product quality varies. Therefore, it is necessary to explore effective management mechanisms and production standards.

9. Conclusion

A. tsao-ko is not only a widely used spice but is also an important medicinal plant which may be considered as potential nutraceutical and pharmaceutical agents. Available literature has demonstrated that *A. tsao-ko* has medicinal value and presence of a variety of bioactive compounds that play an important physiological role in human health. In modern pharmacology, *A. tsao-ko* is used to assist in the treatment of cancer, inflammatory, cardiovascular disease, diabetes, gastrointestinal diseases, and so on. With the rapid development of extraction and isolation techniques, many novel active substances have been isolated from *A. tsao-ko*, including Diarylheptanoids, Flavanol-fatty alcohol hybrids and Flavanol-menthane conjugates, which pharmacological studies have shown to have hypoglycemic pharmacological studies have shown that they have hypoglycemic effects and can be used as potential raw materials for the development of treatments for diabetes. However, despite this multiplicity of potentially pharmacological activity that *A. tsao-ko* possess, more in-depth information is required concerning how exactly exposure to their compounds achieves a specific molecular response. In the future, further in-depth investigations on the following aspects should be emphasized to increase the popularity and application of *A. tsao-ko* in functional food, medicine, and other fields: (1) the extraction and structure–activity relationships of bioactive monomers in *A. tsao-ko*; (2) the distribution, metabolism, and toxicology of different Chemical compounds from *A. tsao-ko* in the human body; (3) Increase clinical trials to determine the specific efficacy of active ingredients in *A. tsao-ko*.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This work was funded by Yunnan Province Agricultural Basic Research Joint Special Project (Grant number: 202301B D070001-050), Special Program for the Major Science and Technology Projects of Yunnan Province (1. Grant number: 202202AE090001; 2. Grant number: 202102AE090051-1-01).

Author Contributions

Yuan-Zhong Wang conceived the review. Gang He collected literature and drafted manuscript. Shao-Bing Yang helped in manuscript revision. All authors read and approved the final manuscript for publication.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.arabjc.2023.104936.

References

Akram, M., Syed, A.S., Kim, K., Lee, J.S., Chang, S., Kim, C.Y., Bae, O., 2015. Heme oxygenase 1-mediated novel anti-inflammatory activities of *Salvia plebeia* and its active components. J. Ethnopharmacol. 174, 322–330. https://doi.org/10.1016/j.jep.2015.08.028.

álvarez-Martínez, F. J., Barrajón-Catalán, E., Herranz-López, M., and Micol, V., 2021. Antibacterial plant compounds, extracts and essential oils: An updated review on their effects and putative mechanisms of action. Phytomedicine. 90, 153626. 10.1016/j.phymed.2021.153626

Bai, Y., Li, D.H., Zhou, T.T., Qin, N.B., Li, Z.L., Yu, Z.G., Hua, H. M., 2016. Coumarins from the roots of angelica dahurica with antioxidant and antiproliferative activities. J. Funct. Foods. 20, 453–462. https://doi.org/10.1016/j.jff.2015.11.018.

Bakkali, F., Averbeck, S., Averbeck, D., Idaomar, M., 2008. Biological effects of essential oils - a review. Food Chem. Toxicol. 46 (2), 446–475. https://doi.org/10.1016/j.fct.2007.09.106.

Bianconi, V., Banach, M., Pirro, M., 2021. Why patients with familial hypercholesterolemia are at high cardiovascular risk? beyond LDL-C levels. Trends Cardiovas. Med. 31 (4), 205–215. https://doi.org/10.1016/j.tcm.2020.03.004.

Boer, H.D., Newman, M., Poulsen, A.D., Droop, A.J., Fér, T., Thu Hi n, L.T., Hlavatá, K., Lamxay, V., Richardson, J.E., Steffen, K., Leong-Akorničková, J., 2018. Convergent morphology in *Alpinieae* (Zingiberaceae): recircumscribing *Amomum* as a monophyletic genus. Taxon 67 (1), 6–36. https://doi.org/10.12705/671.2.

Chen, L.L., Deng, H.D., Cui, H.M., Fang, J., Zuo, Z.C., Deng, J.L., Li, Y.L., Wang, X., Zhao, L., 2018. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget 9 (6), 7204–7218. https://doi.org/10.18632/oncotarget.23208.

Chen, C., You, F., Wu, F.H., Luo, Y.S., Zheng, G.H., Xu, H.L., Liu, Y., 2020. Antiangiogenesis efficacy of ethanol extract from *Amomum tsaoko* in ovarian cancer through inducing ER stress to suppress p-STAT3/NF-kB/IL-6 and VEGF loop. Evid.-Based Compl. Alt. 2020, 1–11. https://doi.org/10.1155/2020/2390125.

Cui, Q., Wang, L.T., Liu, J.Z., Wang, H.M., Guo, N., Gu, C.B., Fu, Y.J., 2017. Rapid extraction of *Amomum tsao-ko* essential oil and determination of its chemical composition, antioxidant and antimicrobial activities. J. Chromatogr. B. 1061–1062, 364–371. https://doi.org/10.1016/j.jchromb.2017.08.001.

Maiara Da Costa Lima, and de Souza, E. L., 2021. A systematic quantitative analysis of the published literature on the efficacy of essential oils as sanitizers in fresh leafy vegetables. Crit. Rev. Food Sci. 61(14), 2326-2339. 10.1080/10408398.2020.1776676

Dai, F.R., 2003. Clinic analyses on treating 42 cases of postcesarean abdominal distension with Tsaoko. Chin. J. Ethnomed. Ethnopharma. 5, 281–282. https://doi.org/10.3969/j.issn.1007-8517.2003.05.013.

Dai, M., Peng, C., Peng, F., Xie, C., Wang, P., Sun, F., 2015a. Anti-Trichomonas vaginalis properties of the oil of *Amomum tsao-ko* and its major component, geraniol. Pharm. Biol. 54 (3), 445–450. https://doi.org/10.3109/13880209.2015.1044617.

Dai, M., Peng, C., Sun, F.H., 2016a. Anti-infectious efficacy of essential oil from Caoguo (Fructus Tsaoko). J. Tradit. Chin. Med. 36 (6), 799–804. https://doi.org/10.1016/s0254-6272(17)30018-3.

Dang, H., Meng, M.H.W., Zhao, H., Iqbal, J., Dai, R., Deng, Y., Lv, F., 2014. Luteolin-loaded solid lipid nanoparticles synthesis, characterization, & improvement of bioavailability, pharmacokinetics in vitro and vivo studies. J. Nanopart. Res. 16, 1–10. https://doi.org/10.1007/s11051-014-2347-9.

Ding, R. C., Long, Q. H., Wang, P., Liu, L., Huang, X., and Ming, S., 2020. The experience of using Dayuanyin in the treatment of new coronavirus pneumonia. J. Tradit. Chin. Med. 61(17), 1481-1484 + 1511.

Gan, X., 2004. Analysis of separating prescription on antiepileptic effect of Add-Subtract Tsaoko Anemarrhenae Decoction. Beijing Univ. Chin. Med. p 96

Gao, J.J., Chen, Z.G., Lin, Z.X., 2018. Investigating the mechanism of Tsaoko Anemarrhenae Decoction in the treatment of epilepsy from miRNA regulation. Fujian J. TCM. 49 (04), 36–40.

Gao, M.X., Jiang, P.W., Li, M.H., Yang, P., Dai, M., 2021. Mechanism of apoptosis induced by essential oil from *Amomum tsaoko* in nasopharyngeal carcinoma 6–10B cells. Nat. Prod. Res. 33 (6), 992–997. https://doi.org/10.16333/j.1001-6880.2021.6.013.

TGhani, T., Paul, S. K., Begum, A., Noorjahan, Sarkar, M., Hussain, T., Anar, M. G. A., Rana, M. S., and Hossain, M. S., 2020. Effect of BMI(Body Mass Index) on BMD (Bone Mineral Density) in postmenopausal women. J. Dhaka Med. Coll. 28(1), 60-66. 10.3329/jdmc.v28i1.45758

Guo, N., Zang, Y.P., Cui, Q., Gai, Q.Y., Jiao, J., Wang, W., Zu, Y. G., Fu, Y.J., 2017. The preservative potential of *Amomum tsaoko* essential oil against E. coil, its antibacterial property and mode of action. Food Control. 75, 236–245. https://doi.org/10.1016/j.foodcont.2016.12.013.

Hasan, M., Iqbal, J., Awan, U., Saeed, Y., Ranran, Y., Liang, Y., Deng, Y., 2015. Mechanistic study of silver nanoparticle's synthesis by dragon's blood resin ethanol extract and antiradiation activity. J. Nanosci. Nanotechno. 15 (2), 1320–1326. https://doi.org/10.1166/jnn.2015.9090.

He, X.F., Chen, J.J., Li, T.Z., Zhang, X.K., Guo, Y.Q., Zhang, X.M., Hu, J., Geng, C.A., 2020. Nineteen new Flavanol-Fatty alcohol hybrids with alpha-glucosidase and PTP1B dual inhibition: one unusual type of antidiabetic constituent from *Amomum tsao-ko*. J Agric. Food Chem. 68 (41), 11434–11448. https://doi.org/10.1021/acs.jafc.0c04615.

He, X.F., Chen, J.J., Huang, X.Y., Hu, J., Zhang, X.K., Guo, Y.Q., Zhang, X.M., Geng, C.A., 2021a. The antidiabetic potency of *Amomum tsao-ko* and its active flavanols, as PTP1B selective and α-glucosidase dual inhibitors. Ind. Crop. Prod. 160,. https://doi.org/10.1016/j.indcrop.2020.112908 112908.

He, X.F., Chen, J.J., Li, T.Z., Hu, J., Zhang, X.K., Guo, Y.Q., Zhang, X.M., Geng, C.A., 2021b. Tsaokols A and B, unusual flavanol-monoterpenoid hybrids as α-glucosidase inhibitors from *Amomum tsao-ko*. Chin. Chem. Lett. 32 (3), 1202–1205. https://doi.org/10.1016/j.cclet.2020.08.050.

He, X.F., Wang, H.M., Geng, C.A., Hu, J., Zhang, X.M., Guo, Y.Q., Chen, J.J., 2020a. Amomutsaokols A-K, diarylheptanoids from *Amomum tsao-ko* and their α-glucosidase inhibitory activity. Phytochemistry 177,. https://doi.org/10.1016/j.phytochem.2020.112418 112418.

He, X.F., Zhang, X.K., Geng, C.A., Hu, J., Zhang, X.M., Guo, Y.Q., Chen, J.J., 2020b. Tsaokopyranols A-M, 2,6-epoxydiarylheptanoids from *Amomum tsao-ko* and their α-glucosidase inhibitory activity. Bioorg. Chem. 96,. https://doi.org/10.1016/j.bioorg.2020.103638 103638.

Hong, S.S., Choi, C.W., Lee, J.E., Jung, Y.W., Lee, J.A., Jeong, W., Choi, Y., Cha, H., Ahn, E., Oh, J.S., 2021a. Bioassay-guided isolation and identification of anti-obesity phytochemicals from fruits of *Amomum tsao-ko*. Appl. Biol. Chem. 64 (1). https://doi.org/10.1186/s13765-020-00576-0.

Hong, S.S., Lee, J.E., Jung, Y.W., Park, J.H., Lee, J.A., Jeong, W., Ahn, E.K., Choi, C.W., Oh, J.S., 2021b. Monoterpenoids from the fruits of *Amomum tsao-ko* have inhibitory effects on nitric oxide production. Plants 10 (2), 257. https://doi.org/10.3390/plants10020257.

Hsu, C.N., Hou, C.Y., Hsu, W.H., Tain, Y.L., 2021. Cardiovascular diseases of developmental origins: preventive aspects of gut microbiota-targeted therapy. Nutrients 13 (7), 2290. https://doi.org/10.3390/nu13072290.

Hu, Y.D., Wang, X.L., Jiao, F.M., Chen, X.Z., Xie, T., Hu, J.H., 2021. Therapeutic observation of Shipiyin combined with diosmin in the treatment of lymphedema with Spleen-Yang Deficiency Syndrome after modified radical mastectomy. Chin. J. Exp. Tradit. Med. Formulae, 1–9.

Huang, Y.F., Qin, L.F., Hu, Q.M., Lai, M.X., Qu, X.C., 2014. Gas chromatogrphy-mass spectrometry analysis of essential oil from *Amomum tsao-ko* Crevost et Lemarie and *Amomum Paratsao-ko* S. Q.Tong et Y.M.Xia grow in GuangXi. Res. Pract. on Chin. Med. 28 (02), 22–24.

Huang, Y., Tang, G.Y., Zhang, T.T., Fillet, M., Crommen, J., Jiang, Z.J., 2018. Supercritical fluid chromatography in traditional Chinese medicine analysis. J. Pharmaceut. Biomed. 147, 65–80. https://doi.org/10.1016/j.jpba.2017.08.021.

Hussain, S.A., Hameed, A., Fu, J., Xiao, H., Liu, Q., Song, Y., 2018. Comparative in vitro analysis of anti-diabetic activity of Indo-Pak black cardamom (*Amomum subulatum* Roxb.) and Chinese black cardamom (*Amomum tsao-ko* Crevost et Lemaire). Prog. Nutr. 20 (3), 403–414. https://doi.org/10.23751/pn.v20i3.6196.

Kim, M.S., Ahn, E.K., Hong, S.S., Oh, J.S., 2016. 2,8-Decadiene-1,10-Diol inhibits lipopolysaccharide-induced inflammatory responses through inactivation of mitogen-activated protein kinase and nuclear factor-κB signaling pathway. Inflammation 39 (2), 583–591. https://doi.org/10.1007/s10753-015-0283-1.

Kim, J. G., Jang, H., Le, T. P. L., Ryoung, H., Lee, M. K., Hong, J. T., Lee, D., and Hwang, B. Y., 2019b. Nitric oxide inhibitory constituents from the fruits of *Amomum tsao-ko*. Nat. Prod. Res. 25 (1), 76. 10.20307/nps.2019.25.1.76.

Kim, J.G., Jang, H., Le, T.P.L., Ryoung, H., Lee, M.K., Hong, J.T., Lee, D., Hwang, B.Y., 2019a. Pyranoflavanones and pyranochalcones from the fruits of *Amomum tsao-ko*. J. Nat. Prod. 82 (7), 1886–1892. https://doi.org/10.1021/acs.jnatprod.9b00155.

Lee, K.Y., Kim, S.H., Sung, S.H., Kim, Y.C., 2008. Inhibitory constituents of lipopolysaccharide-induced nitric oxide production in BV_2 microglia isolated from *Amomum tsao-ko*. Planta. Med. 74 (8), 867–869. https://doi.org/10.1055/s-2008-1074552.

Lee, S., Lee, J.C., Subedi, L., Cho, K.H., Kim, S.Y., Park, H., Kim, K.H., 2019. Bioactive compounds from the seeds of *Amomum tsaoko* Crevost et Lemaire, a Chinese spice as inhibitors of sphingosine kinases, SPHK1/2. RSC Adv. 9 (58), 33957–33968. https://doi.org/10.1039/C9RA07988B.

Lei, Y., Fu, R., Li, X. Y., Zhu, Y. T., Zheng, Y. H., and Chen, Y. H., 2021. Study on the effect of Shipiyi on NT-proBNP and Caspase-3 in rats with heart failure. J. Guizhou Univ. Tradit. Chin. Med

Li, S.C., Ding, J.K., Yi, Y.F., 1975. Study on chemical constituents of essential oil of *Amomum tsao-ko*. Chin. Tradit. Herb. Drugs 02, 27–32.

Li, G., Lu, Q., Wang, J., Hu, Q., Liu, P., Yang, Y., Li, Y., Tang, H., and Xie, H., 2021. Correlation analysis of compounds in essential oil of *Amomum tsaoko* seed and fruit morphological characteristics, geographical conditions, Locality of Growth. Agronomy. 11(4), 744. 10.3390/agronomy11040744

Li, P.Y., Li, L., Wang, Y.Z., 2023. Traditional uses, chemical compositions and pharmacological activities of Dendrobium: a review. J. Ethnopharmacol. 116382. https://doi.org/10.1016/j.jep.2023.116382.

Li, Y., Wang, Y.Z., 2018. Differentiation and comparison of *Wolfiporia cocos* raw materials based on multi-spectral information fusion and chemometric methods. Sci. Rep.-UK 8 (1). https://doi.org/10.1038/s41598-018-31264-1.

Liu, Y. G., Chen, H., Zhao, T. J., and Nong, S. Z., 2017. Investigation on the germplasm resource of *Amomum tsao-ko* and its habitat in Wenshan Prefecture. J. West China For. Sci. 46(05), 106-112 + 126.

Liu, G.Z., Jin, M., Cai, C.T., Ma, C.N., Chen, Z.S.Z., Gao, L.L., 2019. Soil microbial community structure and physicochemical properties in *Amomum tsaoko*-based agroforestry systems in the Gaoligong Mountains, Southwest China. Sustainability-Basel 11 (2), 546. https://doi.org/10.3390/su11020546.

Liu, X.L., Qiu, H.Y., Wang, Q., Wu, L.Y., Zhang, C.H., 2011. Qualitative study on chemical constituents of *Amomum tsao-ko*. China Condiment. 36 (01), 104–106.

Liu, F., Wang, X., Pan, M., Zhang, K., Zhou, F., Tong, J., Xiang, H., 2023. Exposure to air pollution and prevalence of metabolic syndrome: a nationwide study in China from 2011 to 2015. Sci. Total Environ. 855,. https://doi.org/10.1016/j.scitotenv.2022.158596 158596.

Liu, H., Yan, Q.S., Zou, D.L., Bu, X.L., Zhang, B.J., Ma, X.C., Leng, A.J., Zhang, H.L., Li, D.W., Wang, C., 2018. Identification and bioactivity evaluation of ingredients from the fruits of *Amomum tsaoko* Crevost et Lemaire. Phytochem. Lett. 28, 111–115. https://doi.org/10.1016/j.phytol.2018.10.007.

Liu, Z.M., Yang, S.B., Wang, Y.Z., Zhang, J.Y., 2021. Multi-platform integration based on NIR and UV–Vis spectroscopies for the geographical traceability of the fruits of *Amomum tsao-ko*. Spectrochem. Spectrochim. Acta A. 258,. https://doi.org/10.1016/j.saa.2021.119872 119872.

Liu, L.J., Zhao, Y.M., Ming, J., Chen, J., Zhao, G.H., Chen, Z.Y., Wang, Y.J., Lei, L., 2021. Polyphenol extract and essential oil of *Amomum tsao-ko* equally alleviate hypercholesterolemia and modulate gut microbiota. Food Funct. 12 (23), 12008–12021. https://doi.org/10.1039/D1FO03082E.

Liu, L., Zuo, Z.T., Wang, Y.Z., Xu, F.R., 2020. A fast multi-source information fusion strategy based on FTIR spectroscopy for geographical authentication of wild *Gentiana rigescens*. Microchem. J. 159,. https://doi.org/10.1016/j.microc.2020.105360 105360.

Luo, X.X., 2014. Macroscopic and microscopic identification of *Amomum tsao-ko* and *Amomum paratsao-ko* fruits. J. Chin. Med. Mater. 37 (02), 227–229.

Ma, M.L., Wang, T.T., Lu, B.Y., 2021. Assessment of genetic diversity in *Amomum tsao-ko* Crevost & Lemaire, an important medicine food homologous crop from Southwest China using SRAP and ISSR markers. Genet. Resour. Crop Ev. 68 (6), 2655–2667. https://doi.org/10.1007/s10722-021-01204-6.

Mariotto, S., Suzuki, Y., Persichini, T., Colasanti, M., Suzuki, H., Cantoni, O., 2007. Cross-talk between NO and arachidonic acid in inflammation. Curr. Med. Chem. 14 (18), 1940–1944. https://doi.org/10.2174/092986707781368531.

Martemucci, G., Costagliola, C., Mariano, M., D'andrea, L., Napolitano, P., D'Alessandro, A.G., 2022. Free radical properties, source and targets, antioxidant consumption and health. Oxygen 2 (2), 48–78. https://doi.org/10.3390/oxygen2020006.

Martin, T.S., Kikuzaki, H., Hisamoto, M., Nakatani, N., 2000. Constituents of *Amomum tsao-ko* and their radical scavenging and antioxidant activities. J. Am. Oil. Chem. Soc. 77 (6), 667–673. https://doi.org/10.1007/s11746-000-0107-4.

Medzhitov, R., 2010. Inflammation 2010: new adventures of an old flame. Cell 140 (6), 771–776. https://doi.org/10.1016/j.cell.2010.03.006.

Moon, S.S., Cho, S.C., Lee, J.Y., 2005. Tsaokoarylone, a cytotoxic diarylheptanoid from *Amomum tsao-ko* fruits. B. Korean. Soc. 26 (3), 447–450. https://doi.org/10.1002/chin.200531184.

Muhsinah, A.B., Maqbul, M.S., Mahnashi, M.H., Jalal, M.M., Altayar, M.A., Saeedi, N.H., Alshehri, O.M., Shaikh, I.A., Khan, A.A.L., Shakeel Iqubal, S.M., Khan, K.A., Dawoud, A., Mannasaheb, B.A., Azzouz, S., Mohammed, T., 2022. Antibacterial activity of *Illicium verum* essential oil against MRSA clinical isolates and determination of its phyto-chemical components. J. King Saud Univ. – Sci. 34, (2). https://doi.org/10.1016/j.jksus.2021.101800 101800.

Ni, Z.J., Wang, X., Shen, Y., Thakur, K., Han, J.Z., Zhang, J.G., Hu, F., Wei, 2021. Recent updates on the chemistry, bioactivities, mode of action, and industrial applications of plant essential oils. Trends Food Sci. Tech. 110, 78–89. https://doi.org/10.1016/j.tifs.2021.01.070.

Nanayakkara, N., Curtis, A.J., Heritier, S., Gadowski, A.M., Pavkov, M.E., Kenealy, T., Owens, D.R., Thomas, R.L., Song, S., Wong, J., Chan, J.C.N., Luk, A.O.Y., Penno, G., Ji, L., Mohan, V., Amutha, A., Romero-Aroca, P., Gasevic, D., Magliano, D.J., Teede, H.J., Chalmers, J., Zoungas, S., 2021. Impact of age at type 2 diabetes mellitus diagnosis on mortality and vascular complications: systematic review and meta-analyses. Diabetologia 64 (2), 275–287. https://doi.org/10.1007/s00125-020-05319-w.

Osmari, B.F., Giuliani, L.M., Reolon, J.B., Rigo, G.V., Tasca, T., Cruz, L., 2020. Gellan gum-based hydrogel containing nanocapsules for vaginal indole-3-carbinol delivery in trichomoniasis treatment. Eur. J. Pharm. Sci. 151,. https://doi.org/10.1016/j.ejps.2020.105379 105379.

Park, J.Y., Ahn, E., Hwang, M.H., Park, Y.J., Cho, Y., Ko, H., Jeong, W., Yang, S.H., Seo, D., Oh, J.S., 2021. Improvement of obesity and dyslipidemic activity of *Amomum tsao-ko* in C57BL/6 mice fed a high-carbohydrate diet. Molecules 26 (6), 1638. https://doi.org/10.3390/molecules26061638.

Pei, Y.F., Zuo, Z.T., Zhang, Q.Z., Wang, Y.Z., 2019. Data fusion of fourier transform Mid-Infrared (MIR) and Near-Infrared (NIR) Spectroscopies to identify geographical origin of wild *Paris polyphylla* var. yunnanensis. Molecules 24 (14). https://doi.org/10.3390/molecules24142559.

Pradeep, S., Kim, S.W., Wu, S.Y., Nishimura, M., Chaluvally-Raghavan, P., Miyake, T., Pecot, C.V., Kim, S., Choi, H.J., Bischoff, F.Z., Mayer, J.A., Huang, L., Nick, A.M., Hall, C.S., Rodriguez-Aguayo, C., Zand, B., Dalton, H.J., Arumugam, T., Lee, H.J., Han, H.D., Cho, M.S., Rupaimoole, R., Mangala, L.S., Sehgal, V., Oh, S.C., Liu, J., Lee, J., Coleman, R.L., Ram, P., Lopez-Berestein, Fidler, I.J., Sood, A.K., 2014. Hematogenous metastasis of ovarian cancer: rethinking mode of spread. Cancer Cell. 26 (1), 77–91. https://doi.org/10.1016/j.ccr.2014.05.002.

Pu, Y.H., Yang, Y.H., Wu, D.X., Li, Q.H., Lin, Z.M., Zhao, Z.H., Yin, A.Q., 2015. Determination of amino acid and mineral elements in *Amomum tsaoko* from different provenances in Yingjiang, Yunnan. Subtrop. Plant Sci. 44 (04), 293–296.

Qin, H.W., Wang, Y.Z., Yang, M.Q., Yang, S.B., Zhang, J.Y., 2021. Medicinal textual research of Tsaoko fructus. Chin. J. Exp. Tradit. Med. Formulae 27 (06), 139–148.

Qin, H.W., Wang, Y.Z., Yang, W.Z., Yang, S.B., Zhang, J.Y., 2021. Comparison of metabolites and variety authentication of *Amomum tsao-ko* and *Amomum paratsao-ko* using GC–MS and NIR spectroscopy. Sci. Rep.-UK 11 (1). https://doi.org/10.1038/s41598-021-94741-0.

Qiu, H. Y., Liu, X. L., Chen, W. X., Wu, L. Y., and Wang, Q., 2012. Extraction and separation and GC-MS analysis of *Amomum tsao-ko* antibacterial substances. Sci. Tech. Food Ind. 33(11), 104-108 +112.

Rahman, M.R.T., Lou, Z.X., Yu, F.H., Wang, P., Wang, H.X., 2017. Anti-quorum sensing and anti-biofilm activity of *Amomum tsaoko* (*Amommum tsao-k*o Crevost et Lemaire) on foodborne pathogens. Saudi. J. Biol. Sci. 24 (2), 324–330. https://doi.org/10.1016/j.sjbs.2015.09.034.

Ran, Y., Wang, R., Lin, F., Hasan, M., Jia, Q., Tang, B., Qing, H., 2014. Radioprotective effects of Dragon's blood and its extract against gamma irradiation in mouse bone marrow cells. Phys. Med. 30 (4), 427–431. https://doi.org/10.1016/j.ejmp.2013.12.001Physica Medica 30 (2014) 427e431.

Ranavat, S., Becher, H., Newman, M.F., Gowda, V., Twyford, A.D., 2021. A draft genome of the ginger species Alpinia nigra and new Insights into the Genetic Basis of Flexistyly. Genes 12 (9), 1297. https://doi.org/10.3390/genes12091297.

Rossi, C., Chaves-López, C., Serio, A., Casaccia, M., Maggio, F., Paparella, A., 2022. Effectiveness and mechanisms of essential oils for biofilm control on food-contact surfaces: an updated review. Crit. Rev. Food Sci. Nutr. 62 (8), 2172–2191. https://doi.org/10.1080/10408398.2020.1851169.

Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Guariguata, L., Motala, A. A., Ogurtsova, K., Shaw, J. E., Bright, D., and Williams, R., 2019. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res. Clin. Pr. 157, 107843. 10.1016/j.diabres.2019.107843.

Sharma, G.N., Gupta, G., Sharma, P., 2018. A comprehensive review of free radicals, antioxidants, and their relationship with *Human Ailments*. Crit. Rev. Eukar. Gene. 28 (2), 139–154. https://doi.org/10.1615/CritRevEukaryotGeneExpr.2018022258.

Shim, K.S., Hwang, Y.H., Jang, S.A., Kim, T., Ha, H., 2021. Ethanol extract of *Amomum tsao-ko* ameliorates ovariectomy-induced trabecular loss and fat accumulation. Molecules 26 (4), 784. https://doi.org/10.3390/molecules26040784.

Shin, J.S., Ryu, S., Jang, D.S., Cho, Y.W., Chung, E.K., Lee, K.T., 2015. *Amomum tsao-ko* fruit extract suppresses lipopolysaccharide-induced inducible nitric oxide synthase by inducing heme oxygenase-1 in macrophages and in septic mice. Int. J. Exp. Pathol. 96 (6), 395–405. https://doi.org/10.1111/iep.12159.

Stracy, M., Snitser, O., Yelin, I., Amer, Y., Parizade, M., Katz, R., Kishony, R., 2022. Minimizing treatment-induced emergence of antibiotic resistance in bacterial infections. Science 375 (6583), 889–894. https://doi.org/10.1126/science.abg9868.

Sun, F.H., Fu, Y., 2015. Effect of Tsaoko-Anemarrhenae diction on learning and memory ability of picrotoxin-ignited epileptic rats in water maze. Zhejiang J. Tradit. Chin. Med. 50 (03), 171–173.

Tang, Z.L., Zhao, M.M., Han, Y.J., Gao, L.Y., Chen, J.T., Chen, W. X., Li, Y.S., 2020. Study on antibacterial activity of *Amomum tsao-ko* extracts against bacillus subtilis and listeria monocytogenes and preliminary investigation of its antibacterial mchanism. IOP Conf. Ser. Earth Env. Sci. 512 (1), 12080. https://doi.org/10.1088/1755-1315/512/1/012080.

Wang, W.J., Ba, Y.M., Ding, Z., 2017. Proved cases of SHAO Zhao-di treating chronic renal failure with Caoguo Zhimu Decoction. China J. Tradit. Chin. Med. Pharm. 32 (7), 3018–3020.

Wang, Q.Q., Huang, H.Y., Wang, Y.Z., 2020. FTIR and UV spectra for the prediction of triterpene acids in *Macrohyporia cocos*. Microchem. J. 158,. https://doi.org/10.1016/j.microc.2020.105167 105167.

Wang, J., Li, Y., Lu, Q., Hu, Q., Liu, P., Yang, Y., Li, G., Xie, H., Tang, H., 2021b. Drying temperature affects essential oil yield and composition of black cardamom (*Amomum tsao-ko*). Ind. Crop. Prod. 168,. https://doi.org/10.1016/j.indcrop.2021.113580 113580.

Wang, Q., Li, Y., Wang, S., Xiang, Z., Dong, W., Li, X., Dai, L., 2023. A review of the historical records, chemistry, pharmacology, pharmacokinetics and edibility of Angelica dahurica. Arab. J. Chem. https://doi.org/10.1016/j.arabjc.2023.104877.

Wang, K.N., Liu, Y.N., Shi, Y., Yan, M.Z., Rengarajan, T., Feng, X., 2021c. *Amomum tsaoko* fruit extract exerts anticonvulsant effects through suppression of oxidative stress and neuroinflammation in a pentylenetetrazol kindling model of epilepsy in mice. Saudi. J. Biol. Sci. 28 (8), 4247–4254. https://doi.org/10.1016/j.sjbs.2021.06.007.

Wang, C.Y., Tang, L., Jiang, T., Zhou, Q., Li, J., Wang, Y.Z., Kong, C.H., 2021a. Geographical traceability of *Eucommia ulmoides* leaves using attenuated total reflection Fourier transform infrared and ultraviolet-visible spectroscopy combined with chemometrics and data fusion. Ind. Crop. Prod. 160,. https://doi.org/10.1016/j.indcrop.2020.113090 113090.

Wang, W., Yang, C.R., Zhang, Y.J., 2009. Phenolic constituents from the fruits of *Amomum tsao-ko* (Zingiberaceae). Acta Bot. Yunnanica 31 (03), 284–288.

Wang, Y., You, C.X., Wang, C.F., Yang, K., Chen, R., Zhang, W.J., Du, S.S., Geng, Z.F., Deng, Z.W., 2014. Chemical constituents and insecticidal activities of the essential oil from *Amomum tsaoko* against two stored-product insects. J. Oleo Sci. 63 (10), 1019–1026. https://doi.org/10.5650/jos.ess14087.

Wu, M.H., Guo, P., Sze, W.T., Chen, H.B., Zhao, Z.Z., 2012. An ethnobotanical survey of medicinal spices used in Chinese hotpot. Food Res. Int. 48 (1), 226–232. https://doi.org/10.1016/j.foodres.2012.03.010.

Xie, L. B., Chen, J., Ju, H. D., Hu, L. X., Han, A. Y., and Yu, L. Q., 2021. Inhibition of α-glucosidase activity and regulation of blood glucose by methanol extracts from *Amomum tsao-ko*. Sci. Tech. Food Ind. 1-14. 10.13386/j.issn1002-0306.2021080077.

Xin, N., Hasan, M., Li, W., Li, Y., 2014. Juglans mandshurica Maxim extracts exhibit antitumor activity on HeLa cells in vitro. Mol. Med. Rep. 9 (4), 1313–1318. https://doi.org/10.3892/mmr.2014.1979.

Xu, H., Long, N., Lin, L., Li, J.L., Dai, M., Sun, F.H., Tang, W.L., Chen, Y.P., Zhang, F., 2017. *In vitro* antibacterial activity of *Amomum tsao-ko* essential oil against methiciilin-resistant staphylococcus aureus. J. Chengdu Med. Coll. 12 (03), 241–246.

Yan, Q., 2014. The anti-oxidant activity of the methanol extract of Tsao-ko. Tianjin Univ. Scie. tech. p 69

Yang, Z.Q., Hu, Y.F., Nong, P.Y., Yang, R.L., Zhou, D.L., 2017. Investigation of Amomum tsaoko planting area and climate factors analysis of ecological suitability of *Amomum tsaoko* in yunnan. Chin. J. Agr. Res. Reg. Plan. 38 (12), 178–186.

Yang, Y.W., Liu, X.L., Pu, C.X., Qian, Z.G., Guan, K.Y., 2014. The Influence of Altitude and Latitude on Breeding of *Amomum tsaoko* (Zingibiceae). J. Biosci. Med. 02 (01), 9–17. https://doi.org/10.4236/jbm.2014.21002.

Yang, W.Q., Tian, Y., Zhang, A.J., Chang, S.L., Sun, N., Gao, X.Y., Fan, Y.H., 2020. Effect of aqueous extract from *Amomum tsao-ko* on constipation symptoms induced by ameliorates loperamide in mice. Southwest China J. Agr. Sci. 33 (10), 2209–2214.

Yang, Y., Yang, Y., Yan, R.W., Zou, G.L., 2010. Cytotoxic, apoptotic and antioxidant activity of the essential oil of *Amomum tsao-ko*. Bioresour. Technol. 101 (11), 4205–4211. https://doi.org/10.1016/j.biortech.2009.12.131.

Yang, X. F., 2011. Studies on extraction technology and pharmacological effect of volatile oil in *Amomum tsao-ko*. Anhui Agr. Univ. p 60

Yu, L.Q., Shirai, N., Suzuki, H., Sugane, N., Hosono, T., Nakajima, Y., Kajiwara, M., Takatori, K., 2010. The effect of methanol extracts of *tsao-ko (Amomum tsao-k*o Crevost et Lemaire) on digestive enzyme and antioxidant activity *in vitr*o, and plasma lipids and glucose and liver lipids in mice. J. Nutr. Sci. Vitaminol. 56 (3), 171–176. https://doi.org/10.3177/jnsv.56.171.

Zhang, Z.J., Cheang, L.C.V., Wang, M.W., Lee, S.M., 2011. Quercetin exerts a neuroprotective effect through inhibition of the iNOS/NO system and pro-inflammation gene expression in PC12 cells and in zebrafish. Int. J. Mol. Med. 27 (2), 195.

Zhang, L.P., He, J., Zhang, J.J., Wang, H.T., 2002. Effect of Tsaoko-Anemarrbenae Decotion on intracerebral monoamines neurotransmitter content in Epileptic Rats. Chin. J. Int. Tradit. Western Med. S1, 80–82.

Zhang, T.T., Lu, C.L., Jiang, J.G., 2014. Bioactivity evaluation of ingredients identified from the fruits of *Amomum tsaoko* Crevost et Lemaire, a Chinese spice. Food Funct. 5 (8), 1747. https://doi.org/10.1039/C4FO00169A.

Zhang, T.T., Lu, C.L., Jiang, J.G., 2015. Antioxidant and anti-tumour evaluation of compounds identified from fruit of *Amomum tsaoko* Crevost et Lemaire. J. Funct. Foods 18, 423–431. https://doi.org/10.1016/j.jff.2015.08.005.

Zhang, T.T., Lu, C.L., Jiang, J.G., 2016. Neuroprotective and anti-Inflammatory effects of diphenylheptanes from the fruits of *Amomum tsaoko*, a Chinese spice. Plant Food. Hum. Nutr. 71 (4), 450–453. https://doi.org/10.1007/s11130-016-0570-5.

Zhang, X.F., Tang, Y.J., Guan, X.X., Lu, X., Li, J., Chen, X.L., Deng, J.L., Fan, J.M., 2021. Flavonoid constituents of *Amomum tsao-ko* Crevost et Lemaire and its antioxidant, antidiabetic effects in diabetic rats–*in vitro* and *in vivo* studies. Food Funct. https://doi.org/10.1039/D1FO02974F.

Zhang, W., Yang, S.C., Wei, X., Xie, S.Q., 2011. Developing status and strategies of *Amomum tsao-ko* plantation in Yunnan. Modern. Tradit. Chin. Med. Mater. Med.-World Sci. Tech. 13 (05), 899–903.

Zhang, Q., Yang, Y., 2015. Anti-tumor effect of the essential oil from *Amomum tsao-ko* on H22 tumor bearing mice. J. Wuhan Univ. 61 (02), 179–182.

Zhao, M.X., Cai, J., Yang, Y., Xu, J., Liu, W.Y., Akihisa, T., Zhang, J., 2023. Traditional uses, chemical composition and pharmacological activities of Alstonia R. Br. (Apocynaceae): a review. Arab. J. Chem., 104857 https://doi.org/10.1016/j.arabjc.2023.104857.

Zhao, P., Liu, X.X., Tian, J.W., 2021. Research progress in the relationship between intestinal flora metabolites and cardiovascular disease. Chin. J. Arterioscl. 29 (12), 1094–1098.

Zhou, Y., Hong, Y., Huang, H.H., 2016. Triptolide attenuates inflammatory response in membranous glomerulo-nephritis rat via downregulation of NF-κB signaling pathway. Kidney Blood Press. R 41 (6), 901–910. https://doi.org/10.1159/000452591.

Zhou, C.Q., Li, C.Z., Siva, S., Cui, H.Y., Lin, L., 2021. Chemical composition, antibacterial activity and study of the interaction mechanisms of the main compounds present in the Alpinia galanga rhizomes essential oil. Ind. Crop. Prod. 165,. https://doi.org/10.1016/j.indcrop.2021.113441 113441.

Zong, Y., Ding, M.L., Jia, K.K., Ma, S.T., Ju, W.Z., 2020. Exploring active compounds of Da-Yuan-Yin in treatment of COVID-19 based on network pharmacology and molecular docking method. Chin Tradit. Herbal Drugs 51 (04), 836–844.

Ma, J., Zhang, L.X., Ming, P.J., 2008. Studies on the chemical composition of Amomum tsao-ko introduced into cultivation in Xishuangbanna. Chin. Tradi. Patent Med. 32 (08), 1192–1194.

Caceres, A.I., Liu, B., Jabba, S.V., Achanta, S., Morris, J.B., Jordt, S., 2017. Transient receptor potential cation channel subfamily M member 8 channels mediate the anti-inflammatory effects of eucalyptol. Brit. J. Pharmacol. 174, 867–879. https://doi.org/10.1111/bph.13760.

Ito, K., Ito, M., 2013. The sedative effect of inhaled terpinolene in mice and its structure–activity relationships. J Nat Med. 67, 833–837. https://doi.org/10.1007/s11418-012-0732-1.

Melo Júnior, J.D.M.D., Damasceno, M.D.B.M., Santos, S.A.A.R., Barbosa, T.M., Araújo, J.R.C., Vieira-Neto, A.E., Wong, D.V.T., Lima-Júnior, R.C.P., Campos, A.R., 2017. Acute and neuropathic orofacial antinociceptive effect of eucalyptol. Inflammopharmacol. 25, 247–254. https://doi.org/10.1007/s10787-017-0324-5.

Ruberto, G., Baratta, M.T., 2000. Antioxidant activity of selected essential oil components in two lipid model systems. Food Chem. 69, 167–174. https://doi.org/10.1016/S0308-8146(99)00247-2.

Ma, W., Zhao, L., Zhao, W., Xie, Y., 2019. (E)-2-Hexenal, as a p otential natural antifungal compound, inhibits aspergillus flavus spore germination by disrupting mitochondrial energy metabolism. J. Agric. Food Chem. 67, 1138–1145. https://doi.org/10.1021/acs.jafc.8b06367.

Scalbert, A., Johnson, I.T., Saltmarsh, M., 2005. Polyphenols: antioxidants and beyond. Am. J. Clin. Nutr. 81, 215S–217S.

Denny, A. , & Buttriss, J., 2007. Plant foods and health: focus on plant bioactives. plant foods & health focus on plant bioactives. doi: 10.1002/9781118253649.ch1

Li, Z.J., Wan, H.Y., Gu, L.L., Han, Y., Zheng, Y.L., Zhang, M.X., Liu, W.T., 2017. Extraction and LC-MS/MS analysis of the polyphenols from Amomum tsaoko. Sci. Technol. Food Ind. 38, 294–299.

Shi, C., Gong, H., LI, R, LI, L.L, Chen, H.X., 2021. Correlation between the content total flavonoids and total polyphenols in Amomum tsaoko with different polar extracts and their antioxidant activities. Chemical Reagents 1–9. https://doi.org/10.1016/j.fbio.2023.102508.

Lee, S., Lee, J.C., Subedi, L., Cho, K.H., Kim, S.Y., Park, H., Kim, K.H., 2019. Bioactive compounds from the seeds of Amomum tsaoko Crevost et Lemaire, a Chinese spice as inhibitors of sphingosine kinases, SPHK1/2. RSC Adv. 9, 33957–33968. https://doi.org/10.1039/C9RA07988B.

Liu, H., Yan, Q.S., Zou, D.L., Bu, X.L., Zhang, B.J., Ma, X.C., Leng, A.J., Zhang, H.L., Li, D.W., Wang, C., 2018. Identification and bioactivity evaluation of ingredients from the fruits of Amomum tsaoko Crevost et Lemaire. Phytochem. Lett. 28, 111–115. https://doi.org/10.1016/j.phytol.2018.10.007.

Shi, S., Luo, Y.F., Ma, Y., Chu, Y.J., Wang, Y.D., Chen, X.H., Chu, Y., 2021. Identification of in vitro-in vivo components of Caoguo using accelerated solvent extraction combined with gas chromatography-mass spectrometry integrated with network pharmacology on indigestion. Ann. Transl. Med. 9, 1247. https://doi.org/10.21037/atm-21-3245.

Shim, K.S., Hwang, Y.H., Jang, S.A., Kim, T., Ha, H., 2021. Ethanol extract of Amomum tsao-ko ameliorates ovariectomy-induced trabecular loss and fat accumulation. Molecules. 26, 784. https://doi.org/10.3390/molecules26040784.