

## Analysis methods and food application of *Gastrodia elata* and related products: A review

Chang Liu\*, Jianfeng Zhan, Weixin Wang and Ting Hu

Hubei Key Laboratory of Economic Forest Germplasm Improvement and Resources Comprehensive Utilization, Hubei Collaborative Innovation Center for the Characteristic Resources Exploitation of Dabie Mountains, Huanggang Normal University, Huanggang 438000, China

\*Corresponding author: Chang Liu, College of Biological and Agricultural Resources, Huanggang Normal University, Huanggang 438000, China., E-mail: liuchang@hgnu.edu.cn

DOI: 10.26599/JFB.2024.95028393

Received: December 15, 2024; Revised received & accepted: December 28, 2024

Citation: Liu, C., Zhan, J., Wang, W., and Hu, T. (2024). Analysis methods and food application of *Gastrodia elata* and related products: A review. J. Food Bioact. 28: 31–40.

### Abstract

*Gastrodia elata* Blume (*G. elata*) widely reputed as an important traditional herbal medicine and food in China and other Asian countries, can manage headache, epilepsy, pediatric acute, and chronic convulsions in modern clinical practice. It has been revealed that *G. elata* contains a variety of chemical substances, which have attracted more and more attention from the food science community. Hence, a comprehensive search of published literature from the beginning to 2024 in Web of Science and CNKI, and the keyword of *G. elata* was used. This review systematically summarizes analytical methods of bioactive phytochemicals in *G. elata*. We also depicted known biological harmful constituents in this review. In addition, abundant food products made from *G. elata* have been developed and sold on market, and different processing methods of *G. elata* containing foods have significant effects on the bioactive phytochemical composition of *G. elata*. Hence, we further summarized the impacts of food processing on the development of *G. elata* related functional food products. In a nutshell, this review summarizes the bioactive phytochemicals, analysis methods, and application of *G. elata* and its associated food products, and aims to provide a valuable reference for the full utilization of resources of *G. elata*.

**Keywords:** *Gastrodia elata* Blume; Chemical substances; Gastrodin; Analysis method; Food application.

### 1. Introduction

*Gastrodia elata* Blume (*G. elata*) is a plant belonging to the orchid family, which has a wide geographical range in China and other Asian countries, especially preferring to grow in mountainous areas. Based on the traditional Chinese medicine theory, *G. elata* has been used as herbal medicine since ancient times in China because of its warm nature and suppressing excessive live-yang (Yang et al., 2024). In modern clinical practice, *G. elata* is employed for the treatment of headaches, dizziness, epilepsy, pediatric acute and chronic convulsions, etc. (Su et al., 2023). Currently, studies about the chemical components in *G. elata* and their pharmacological effects have attracted huge attention, due to their great medical value. Phytochemical research of *G. elata* has isolated or charac-

terized varieties of compounds, including phenols, polysaccharides, organic acids, and glycosides among others. Some of these molecules have been proved that possess the function of inhibiting oxidative stress (Zhang et al., 2024), anti-depression (Jiang et al., 2024), anti-neuroinflammation (Li et al., 2020; Shao et al., 2018), and antidiabetic effects (Bai et al., 2021). For example, gastrodin, a phenolic glycoside identified in 1978, is one of the main active components in *G. elata* which has been systematically investigated on its pharmacological effects (Liu et al., 2018). Gastrodin has demonstrated neuroprotective effects and good efficacy in the treatment of Parkinson's disease (Yan et al., 2019; Zhao et al., 2024), Alzheimer's disease (Luo et al., 2022), and Tourette syndrome (Wang et al., 2021) in animal models, which has been approved as herbal drugs for the treatment of neurasthenia and mi-

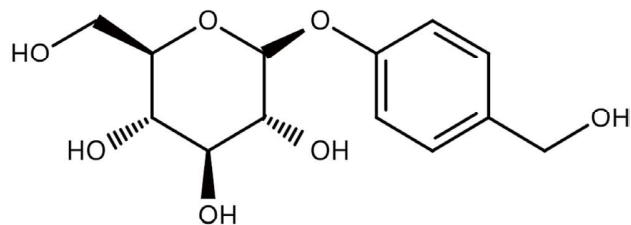


Figure 1. The chemical structure of gastrodin.

graine in China. For example, gastrodin at the concentration of 10–50 mg/kg could exert a neuroprotective effect on retinal ganglion cells in an acute glaucoma animal model via inhibiting microglia activation and microglial-mediated neuroinflammation (Wang et al., 2017). Except for medicinal applications, the tuber of *G. elata* can serve as raw food material for cooking or functional food development. In the literature review process, we noticed that barely any researcher has systematically reviewed the analysis method and acquisition route for types of chemical components in *G. elata* which is the fundamental techniques for pharmacology and food application. In this article, the developments in the analysis methods, acquisition routes, and food applications of important chemical substances in *G. elata* are summarized to provide guidelines for further research of bioactive in *G. elata* and its application in food.

## 2. Chemical constituents in *Gastrodia elata* Blume

A number of chemical substances have been identified from *G. elata* since the 1950s, including phenolic compounds, organic acids, polysaccharides, peptides, and others. Among them, some molecules have been proven to exhibit varying pharmacological effects, such as sedative-hypnotic, neuroprotection, vascular protection, and antidiabetic.

Phenolic compounds are abundant in *G. elata* and exhibit remarkable pharmacological properties. They are compounds replacing hydrogen atoms on the benzene ring with one or more hydroxyl groups, including phenols, phenolic glycosides, phenolic ethers, phenolic aldehydes, nitrogen-containing phenols, and sulfur-containing phenols. Among them, gastrodin belongs to phenolic glycoside, chemically known as 4-(hydroxymethyl) phenyl  $\beta$ -D-glucopyranoside ( $C_{13}H_{18}O_7$ ), and its chemical structure is illustrated in Figure 1. The content of gastrodin of 4-hydroxybenzyl alcohol (HBA) is considered as the chemical marker in the quality standardization of *G. elata*, which should not be less than 0.25% according to the Chinese pharmacopoeia. Parishins are a family of esters formed with different numbers of gastrodin or its derivatives and varying positions of citric acid, which have also been identified as a kind of bioactive ingredients in *G. elata*. Parishin C has multiple biological properties, such as antipsychotic (Shin et al., 2010), neuroprotective (Wang et al., 2021), and antidepressant effects (Jiang et al., 2024). Parishin J and B show significant protective effects in the treatment of myocardial hypoxia/reoxygenation injury (Wang et al., 2020). Organic acids have also been found in *G. elata*, including succinic acid, citric acid, palmitic acid, L-phenyllactic acid (Gong et al., 2024), cinnamic acid, and caffeic acid (Wu et al., 2022). In particular, citric acid can be formed by *in vivo* hydrolyzation of parishins, which have anti-oxidative (Abdel-Salam et al., 2014), neuroprotective and hepatoprotective effects (Abdel-Salam et al., 2016).

In addition to small molecules, there is a diversity of large molecules in *G. elata*. Polysaccharides, as one of the most attractive active ingredients, have been reported to have anti-cancer, anti-ox-

idant, anti-virus, immunological, neuroprotective, and hypotensive effects (Yang et al., 2024). An anti-fungal protein was found in *G. elata*, named GAFF-1 (Xu et al., 1998). Moreover, the polypeptide in *G. elata* extract was confirmed to have antimicrobial activity for gram-negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa*, the gram-positive bacterium *Staphylococcus aureus* and the fungus *Candida albicans* (Kong et al., 2019).

## 3. Analysis method

### 3.1. Gastrodin and other phenolic compounds

Gastrodin is one of the most significant phenolic constituents in *G. elata* since it has been regarded as the main active ingredient in herbal medicine and functional food. Thus, many methods have been developed for the analysis of gastrodin in *G. elata*. Moreover, various detection approaches in biological samples were proposed to support the pharmacokinetic studies on *G. elata*. Besides its medicinal application, *G. elata* has been consumed as a food for a long history in China and was added to the catalogue of “substances traditionally considered as both food and herbal medicine” in 2023, allowing it to be processed and sold as a food in the legal sense. Hence, there are few methods applied for phenolic compounds detection in food made from *G. elata*. Different methods used for quantitative analysis of phenolic compounds in varied types of samples are shown in Table 1.

#### 3.1.1. Plant material

Previous studies have found that *G. elata*, most notably the tuber part, contains a variety of phenolic compounds, including gastrodin, 4-hydroxybenzyl alcohol, 4-hydroxybenzaldehyde, and parishins. According to the Chinese Pharmacopoeia, the minimal content of gastrodin and 4-hydroxybenzyl alcohol is 0.25% for the quality control of *G. elata*. As to parishins, their contents in *G. elata* are relatively low and in the range of 0.03–0.13% (Shan et al., 2021). The phenolic compounds possess conjugated structure. Thus, as shown in Table 1, high-performance liquid chromatography with ultraviolet detection (HPLC-UV) was the most commonly applied assay for the quantitative determination of phenolic compounds in *G. elata*. The detection wavelength is usually set at either 220 or 270 nm. A reversed-phase C18 column is used with water (phase A) and methanol or acetonitrile (phase B) as mobile phases. To improve the resolution, formic acid, phosphoric acid, and acetic acid can be added to adjust the pH of mobile phase. Besides HPLC-UV, high-performance liquid chromatography with fluorescence detection (HPLC-FLD) was also used for the determination of phenolic compounds in *G. elata*. The excitation and emission wavelength are set to 275 nm and 295 nm, respectively. Compared with the HPLC-UV, HPLC-FLD is of great sensitivity. Noteworthy, few methods applied near-infrared (NIR) spectroscopy for the determination of the phenolic compounds in *G. elata*. NIR relies on the absorption of electromagnetic radiation with a wavelength range spanning from 800–2,500 nm (Pasquini, 2018). The main advantage of NIR is non-destructive analysis of samples without sample preparation. However, the intrinsic complexity of NIR spectra spells trouble for its application, which made it significant to develop a robust and reliable calibration model to analyze the spectra data.

The sample preparation of plant material is quietly simple and involves mainly liquid extraction with polar solvents. Prior to the extraction, the initial step in the sample preparation is drying the

Table 1. Summary of quantitative methods for gastrodin and other phenolic compounds

| Sample type     | Analyzes  | Sample preparation   | Instru-<br>mentation | Method validation   | Reference           |
|-----------------|---|--|----------------------|---|---------------------|
| <i>G. elata</i> | Gastrodin, 4-hydroxybenzyl alcohol, 4-hydroxybenzaldehyde   | Solvent extraction: ethanol-water (75:25, v/v), sonication   | HPLC-UV              | Linearity range: 8.5–890 mg/L (gastrodin), 10–500 mg/L (4-hydroxybenzyl alcohol), 6.4–400 mg/L (4-hydroxybenzaldehyde). LOD: 10 µg/L (gastrodin), 5 µg/L (4-hydroxybenzyl alcohol), 0.5 µg/L (4-hydroxybenzaldehyde). Recovery: 96.6–98.5%  | (Li et al., 2001)   |
| <i>G. elata</i> | Gastrodin, 4-hydroxybenzyl alcohol, vanillyl alcohol, 4-hydroxybenzaldehyde, vanillin                     | Solvent extraction: methanol or water, reflux  | HPLC-UV              | Linearity range: 13.95–1,116 mg/L (gastrodin), 12.58–1,006 mg/L (4-hydroxybenzyl alcohol), 4.23–338 mg/L (vanillyl alcohol), 0.24–18.8 mg/L (4-hydroxybenzaldehyde), 0.22–17.6 mg/L (vanillin). Recovery: 93.6–103.4%   | (Liu et al., 2002)  |
| <i>G. elata</i> | Gastrodin, vanillyl alcohol   | Solvent extraction: water, pressurized hot water extraction or microwave-assisted extraction or reflux | HPLC-UV              | Linearity range: 0–100 mg/L   | (Teo et al., 2008)  |
| <i>G. elata</i> | Gastrodin   | Solvent extraction: water, reflux  | HPLC-UV              | Linearity range: 0.25–10.00 µg. LOD: 0.13 µg  | (Lee et al., 2015)  |
| <i>G. elata</i> | Gastrodin   | Solvent extraction: ethanol-water (70:30) or water, reflux   | HPLC-UV              | Linearity range: 10–90 mg/L. LOD: 0.5 mg/L. Recovery: 94.56–105.94%   | (Chen et al., 2015) |
| <i>G. elata</i> | Gastrodin, parishin E, parishin B, parishin   | Solvent extraction: methanol-water (50:50, v/v), sonication  | UPLC-UV              | Linearity range: 8.89–44.48 mg/L (gastrodin), 6.08–60.80 mg/L (parishin E), 34.50–138.00 mg/L (parishin B), 40.66–203.30 mg/L (parishin). LOD: 0.024 mg/L (gastrodin), 0.143 mg/L (parishin E), 0.104 mg/L (parishin B), 0.359 mg/L (parishin). Recovery: 88.02–105.38%   | (Chen et al., 2016) |
| <i>G. elata</i> | Gastrodin, 4-hydroxybenzyl alcohol, parishin A, parishin B, parishin C, parishin E                        | Solvent extraction: methanol-water (50:50, v/v), sonication  | HPLC-FLD             | Linearity range: 0.05–10 mg/L. LOQ: 0.05 mg/L. Recovery: 92.20–114.98%  | (Tang et al., 2018) |
| <i>G. elata</i> | Gastrodin, 4-hydroxybenzyl alcohol, parishin E, 4-hydroxybenzaldehyde, parishin B, parishin C, parishin A | Solvent extraction: methanol-water (60:40, v/v), sonication  | HPLC-UV              | Linearity range: 1.906–6.483 mg/mL (gastrodin), 0.075–1.773 mg/mL (4-hydroxybenzyl alcohol), 2.273–7.052 mg/mL (parishin E), 0.079–2.588 mg/mL (4-hydroxybenzaldehyde), 1.450–5.190 mg/mL (parishin B), 0.286–0.356 mg/mL (parishin C), 0.181–19.301 mg/mL (parishin A). LOD: 0.042 mg/mL (gastrodin), 0.001 mg/mL (4-hydroxybenzyl alcohol), 0.037 mg/mL (parishin E), 0.001 mg/mL (4-hydroxybenzaldehyde), 0.004 mg/mL (parishin B), 0.005 mg/mL (parishin C), 0.020 mg/mL (parishin A). Recovery: 91.80–98.05% | (Li et al., 2019)   |
| <i>G. elata</i> | Gastrodin, 4-hydroxybenzyl alcohol, parishin A, parishin B, parishin C, parishin E                        | Solvent extraction: ethanol-water (41:59, v/v), sonication   | HPLC-UV              | Linearity range: 5.21–166.64 mg/L (gastrodin), 2.15–68.68 mg/L (4-hydroxybenzyl alcohol), 9.75–312.00 mg/L (parishin E), 8.42–269.28 mg/L (parishin B), 5.04–161.36 mg/L (parishin C), 23.83–762.56 mg/L (parishin A). LOD: 2.19 mg/L (gastrodin), 1.38 mg/L (4-hydroxybenzyl alcohol), 0.47 mg/L (parishin E), 3.76 mg/L (parishin B), 2.81 mg/L (parishin C), 3.92 mg/L (parishin A). Recovery: 96.99–101.72%   | (Hu et al., 2019)   |

(continued)

Table 1. (continued)

| Sample type                              | Analyzes   | Sample preparation   | Instru-<br>mentation | Method validation   | Reference            |
|--|--|--|----------------------|---|----------------------|
| <i>G. elata</i>                          | Gastrodin, 4-hydroxybenzyl alcohol, parishin A, parishin B, parishin E   | Solvent extraction: methanol-water (50:50, v/v), sonication  | HPLC-FLD             | Linearity range: 0.05–10 mg/L   | (Yu et al., 2020)    |
| <i>G. elata</i> (tuber, stem and flower) | Gastrodin, 4-hydroxybenzyl alcohol, 4-hydroxybenzaldehyde, parishin A, parishin B, parishin C  | Solvent extraction: methanol-water (50:50, v/v), sonication  | HPLC-UV              | /   | (Shan, et al., 2021) |
| <i>G. elata</i>                          | Gastrodin, 4-hydroxybenzyl alcohol, parishin E, 4-hydroxybenzaldehyde, parishin B, parishin C, parishin A, vanillyl alcohol, catechin, caffeic acid, epicatechin, quercetin, cinnamic acid | Solvent extraction: methanol-water-HCl (70:30:1, v/v), sonication  | HPLC-UV              | Linearity range: 135.6–813.8 mg/L (gastrodin), 47.5–380 mg/L (4-hydroxybenzyl alcohol), 26.5–212 mg/L (parishin E), 0.21–5.76 mg/L (4-hydroxybenzaldehyde), 92.5–740 mg/L (parishin B), 61.2–490 mg/L (parishin C), 103.8–830 mg/L (parishin A), 0.6–4.8 mg/L (vanillyl alcohol), 0.7–5.6 mg/L (catechin), 0.7–5.6 mg/L (caffeic acid), 6–48 mg/L (epicatechin), 0.5–4 mg/L (quercetin), 0.6–4.8 mg/L (cinnamic acid). LOD: 0.351 mg/L (gastrodin), 0.205 mg/L (4-hydroxybenzyl alcohol), 0.108 mg/L (parishin E), 0.023 mg/L (4-hydroxybenzaldehyde), 0.051 mg/L (parishin B), 0.308 mg/L (parishin C), 0.451 mg/L (parishin A), 0.158 mg/L (vanillyl alcohol), 0.035 mg/L (catechin), 0.021 mg/L (caffeic acid), 0.068 mg/L (epicatechin), 0.025 mg/L (quercetin), 0.105 mg/L (cinnamic acid) | (Wu, et al., 2022)   |
| <i>G. elata</i>                          | Gastrodin, 4-hydroxybenzyl alcohol   | Solvent extraction: ethanol-water (50:50, v/v), sonication   | HPLC-UV              | Recovery: 95.82–98.71%  | (Wang et al., 2023)  |
| <i>G. elata</i>                          | Gastrodin  | Solvent extraction: ethanol-water (50:50, v/v), sonication. Purification with molecularly imprinted polymers | HPLC-UV              | Recovery: 97.75–103.43%   | (Zhao et al., 2023)  |
| <i>G. elata</i>                          | Gastrodin  | Solvent extraction: water, reflux. Purification with molecularly imprinted polymers                          | HPLC-UV              | Linearity range: 0.001–100.00 mg/L; LOD: 0.03 µg/L; LOQ: 0.09 µg/L. Recovery: 90.5–97.6%  | (Ji et al., 2015)    |
| <i>G. elata</i>                          | Gastrodin  | /  | FT-NIR               | /   | (Wang et al., 2023)  |
| <i>G. elata</i>                          | Gastrodin, 4-hydroxybenzyl alcohol, parishin A, parishin B   | /  | NIR                  | Linearity range: 1.03–4.95 mg/g (gastrodin), 1.78–6.92 mg/L (4-hydroxybenzyl alcohol), 2.62–8.26 mg/L (parishin A), 0.72–4.76 mg/L (parishin B)   | (Si et al., 2023)    |
| <i>G. elata</i>                          | Gastrodin, 4-hydroxybenzyl alcohol   | /  | NIR                  | /   | (Li et al., 2024)    |
| Plasma                                   | Gastrodin, 4-hydroxybenzyl alcohol   | Protein removal: methanol  | HPLC-MS              | Linearity range: 2.00–200.00 mg/L (gastrodin), 0.83–104.00 mg/L (4-hydroxybenzyl alcohol). LOQ: 2.00 mg/L (gastrodin), 0.83 mg/L (4-hydroxybenzyl alcohol). Recovery: 91.1–108.6%   | (Zhang et al., 2008) |

(continued)

Table 1. (continued)

| Sample type                    | Analyzes  | Sample preparation   | Instru-mentation | Method validation  | Reference              |
|--------------------------------|---|--|------------------|--|------------------------|
| Plasma                         | Gastrodin, parishin B, parishin C, parishin E             | Protein removal: 1% formic acid methanol   | LC-MS/MS         | Linearity range: 1.32–4,800 µg/L (gastrodin), 18–1,800 µg/L (parishin), 1.46 µg/L (parishin B), 0.97 µg/L (parishin C), 0.067 µg/L (parishin E). LOD: 0.35 µg/L (gastrodin), 0.83 µg/L (parishin), 18–2,000 µg/L (parishin B), 6–500 µg/L (parishin C), 4–400 µg/L (parishin E). Recovery: 95.3–101% | (Liu et al., 2017)     |
| Plasma                         | Gastrodin   | Protein removal: methanol  | UFLC-MS/MS       | Linearity range: 50–20,000 µg/L. LOQ: 50 µg/L. Recovery: 94.1–95.2%  | (Guan et al., 2017)    |
| Plasma                         | Gastrodin, parishin A, parishin B, parishin C, parishin E | Protein removal: methanol-acetonitrile (50:50, v/v)  | LC-MS/MS         | Linearity range: 10.0–3,000.0 µg/L (gastrodin), 1.37–333.0 µg/L (parishin A/B/C), 1.37–3,000.0 µg/L (parishin E). LOQ: 10.0 µg/L (gastrodin), 1.37 µg/L (parishin A/B/C/E). Recovery: 85.97–120.12%  | (Dong et al., 2020)    |
| Plasma                         | Gastrodin, 4-hydroxybenzyl alcohol                        | Protein removal: methanol  | HPPLC-UV         | Linearity range: 0.1–80 mg/L (gastrodin), 0.05–40 mg/L (4-hydroxybenzyl alcohol)   | (Cheng and Deng, 2021) |
| Urine                          | Gastrodin   | Magnetic dispersion solid phase extraction: magnetic activated carbon/microporous resin ternary composite material | HPPLC-UV         | Linearity range: 0.03–10 mg/L. LOD: 5.4 mg/L. Recovery: 94.87–106.3%   | (Chen et al., 2024)    |
| liver and kidney               | Gastrodin   | Tissue homogenates with normal saline. Protein removal: methanol   | HPPLC-UV         | Linearity range: 12.5–1,600 mg/L. LOQ: 12.5 mg/L. Recovery: 100.4%   | (Yang et al., 2011)    |
| Liquor                         | Gastrodin   | Dry with nitrogen stream and redissolve with water   | HPPLC-UV         | Linearity range: 1–500 mg/L. LOD: 0.74 mg/kg. Recovery: 99.1–104.2%  | (Lv et al., 2022)      |
| <i>G. elata</i> enzyme drink   | 4-hydroxybenzyl alcohol, 4-hydroxybenzaldehyde            | Centrifugation (10,000 rpm, 5 min)   | HPPLC-UV         | /  | (Zhao et al., 2022)    |
| <i>G. elata</i> buccal tablets | Gastrodin   | Solvent extraction: methanol, sonication   | HPPLC-UV         | Linearity range: 0.191–5.73 µg. Recovery: 97.2–98.1%   | (Yang et al., 2023)    |
| <i>G. elata</i> tablets        | Gastrodin   | Solvent extraction: ethanol-water (50:50, v/v), sonication   | HPPLC-UV         | Linearity range: 0.1–0.6 µg; LOD: 2.50 ng; LOQ: 4.20 ng. Recovery: 96.39–100.40%   | (Wang et al., 2019)    |
| <i>G. elata</i> capsules       | Gastrodin, 4-hydroxybenzyl alcohol                        | Solvent extraction: methanol-water (80:20, v/v), sonication  | HPPLC-UV         | Linearity range: 0.3125–6.2500 mg/L (gastrodin), 0.3125–6.2500 mg/L (4-hydroxybenzyl alcohol). Recovery: 99.47–100.40%   | (Song et al., 2024)    |
| <i>G. elata</i> granules       | Gastrodin, parishin B, parishin E                         | Solvent extraction: methanol, sonication   | HPPLC-UV         | Linearity range: 50.00–600.00 mg/L (gastrodin), 5.00–350.00 mg/L (parishin B), 10.00–319.00 mg/L (parishin E). Recovery: 98.82–106.15%   | (Du et al., 2024)      |

HPPLC-UV: high-performance liquid chromatography with ultraviolet detection, UPLC-UV: ultra-performance liquid chromatography with fluorescence detection, FT-NIR: Fourier transform near-infrared, NIR: near-infrared, HPLC-MS: high-performance liquid chromatography with mass spectrometry, UFLC-MS/MS: ultra-fast liquid chromatography with MS/MS, LC-MS/MS: liquid chromatography with MS/MS, LOD: limit of detection, LOQ: limit of quantification.

plant and grinding it into powder, which could improve the kinetics of analytic extraction and the contact of the sample surface with the solvent (Sasidharan et al., 2011). Due to the high polarity of phenolic compounds, the plant samples were extracted with methanol, ethanol, or a mixture of alcohol solvents and water. During the solvent extraction process, varied methods were employed to obtain satisfied recovery rates of compounds, including microwave-assisted extraction, pressurized extraction, sonication-assisted extraction, and reflux extraction. Aside from solvent extraction, solid-phase extraction with molecularly imprinted polymers can be performed as an approach of purification process.

### 3.1.2. Biological sample

The quantitative analyses of analytes in biological samples are the crucial part of pharmacokinetic studies, including plasma, urine, and tissues. Different from plant sample analysis, the biological sample analysis is of a grand challenge because of low abundant analytes and complex matrix. Thus, high-performance liquid chromatography-mass spectrometry (HPLC-MS) or high-performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS) are widely used in the quantitative analysis of phenolic compounds in plasma due to their excellent sensitivity. The chromatographic separation is performed on a C18 column with water (phase A) and acetonitrile or methanol (phase B). Similarly, formic acid can be used to adjust the pH of mobile phase. As for mass detection, multiple reaction monitoring (MRM) or full-scan analysis is carried out for the quantitation of analytes. In general, the HPLC-MS/MS is of better sensitivity than HPLC-MS and HPLC-UV. Taking gastrodin as an example, lower LOQs were attained for the plasma sample (1.32–50 µg/L) as illustrated in Table 1.

In terms of biological sample treatment, one of the similarities is protein precipitation for both plasma and urine samples. Two choices of solvents were applied for protein precipitation during the analysis of gastrodin and other phenolic compounds in biological samples, which were methanol and a mixture of methanol and acetonitrile. After the protein removal, the residue solution can be directly injected into the analytical instrument. In addition, the internal standards were applied in biological samples to help account for variability in sample preparation (Tan et al., 2009), including bergenin, tyrosol, and geniposide, which are similar to the gastrodin or other phenolic compounds.

### 3.1.3. Food and medicinal products

Food and medicinal products made from *G. elata* have been developed, including liquor, enzyme-containing beverages, tablets, capsules, and granules. The most commonly detected ingredient in these products is gastrodin. HPLC-UV method is currently the primary analytical tool for detecting gastrodin in food and drug products. As for sample preparation, the liquid sample was concentrated and redissolved in appropriate solvents followed by instrument analysis. The pretreatment procedures of solid product samples are similar to the plant sample, which are solvent extraction with methanol, ethanol, or a mixture of an organic solvent with or without water.

## 3.2. Polysaccharide

The commonly used methods for the analyses of *G. elata* polysaccharides encompass total content, molecular weight, monosaccharide composition, surface morphology, chemical structure,

and so on. The total content of *G. elata* polysaccharide is usually determined by colorimetric methods, such as the phenol-sulfuric method and the anthrone-sulfuric acid method (Ji et al., 2022; Zhu et al., 2019). The molecular weight of polysaccharide varies from  $7.64 \times 10^4$  to  $8.75 \times 10^6$  Da, which can be determined using size-exclusion-chromatography (SEC) and high-performance gel permeation chromatography (HPGPC) (Yang et al., 2024). The composition of monosaccharides can be analyzed by high-performance anion exchange chromatography (HPAEC) with the anion-exchange column. A polysaccharide from *G. elata* (named GEP-1) was analyzed via HPAEC coupled with pulsed amperometric detector and was found mainly composed of glucose, galactose, and arabinose (Guan et al., 2022). Moreover, high-performance ion chromatography (HPIC) was also used to detect the monosaccharide composition of *G. elata* polysaccharide, and the results showed it was mainly composed of glucose, with small amounts of galactose and galacturonic acid (Gan et al., 2024).

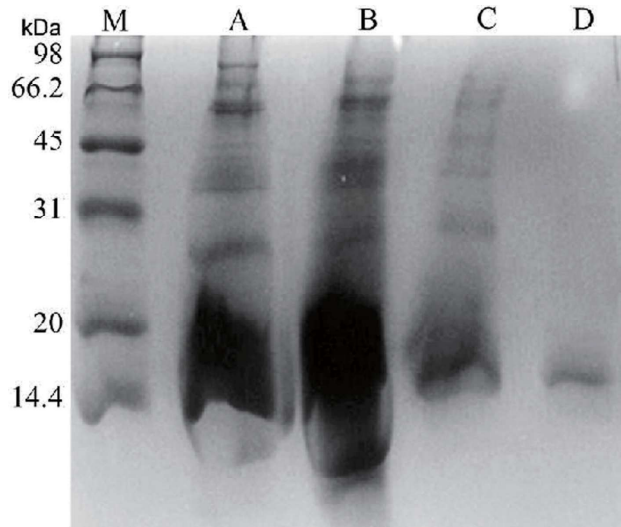
Since the bioactivity of polysaccharides is generally correlated with their structure, the surface morphology of *G. elata* polysaccharide is often examined by scanning electron microscope (SEM) to study its microstructure (Chen et al., 2024; Ji et al., 2022). The ultraviolet (UV) spectroscopy, infrared (IR) spectroscopy, and nuclear magnetic resonance (NMR) spectroscopy can provide the chemical structure information of *G. elata* polysaccharide, which are robust approaches for *G. elata* polysaccharide structure analysis (Chen, et al., 2024). In addition, the thermal characteristics of *G. elata* polysaccharide can be revealed through differential scanning calorimetry (DSC) analysis or thermogravimetric analysis (TGA) (Guan et al., 2022; Ji et al., 2022). The zeta potential and particle size of *G. elata* polysaccharide play important roles in its application in food and biomedical areas, which can be determined with phase analysis light scattering (PALS) analyzer (Ji et al., 2022).

## 3.3. Polypeptide and protein

The polypeptide and protein in *G. elata* have been proven to have antibacterial activity (Cai et al., 2019). However, compared with gastrodin and parishins, the function of polypeptide and protein in *G. elata* has not been systematically studied. Hence, it is significant to establish analysis methods of polypeptides and proteins in *G. elata* to explore the potential correlation of *G. elata* polypeptides and proteins with their bioactivities. Prior to an analysis, polypeptides are extracted from the product matrix with water solution, and enriched through an enzymolysis approach. Generally, the rhizomes of *G. elata* were extracted by saline, and papain was added to the extracted solution. Subsequently, the solution was passed through an ultrafiltration membrane to attain the polypeptide solution. The concentration of polypeptide can be detected by the bicinchoninic acid (BCA) method or Lowery's method (Cai, et al., 2019; Kong, et al., 2019). Similar to polysaccharides, the molar mass distribution of polypeptide can also be determined using HPGPC. For protein analysis, the sample preparation procedure is simpler, and the enzymolysis step is not required. The qualitative analysis can be performed by using sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and mass spectrometry (Chen et al., 2018; Zeng et al., 2018). A typical SDS-PAGE figure of protein in *G. elata* was demonstrated in Figure 2.

## 3.4. Others

Aside from bioactives, the harmful compounds in *G. elata* should also be paid attention to guarantee its edible safety. Heavy metals



**Figure 2.** SDS-PAGE analysis of antibacterial protein during successive purification steps. M, protein marker. A, crude extract of *G. elata* tubers. B, dialyzed proteins (precipitated by ammonium sulfate). C, purified proteins after chromatography on DEAE-52 (ion-exchange). D, purified protein after chromatography on Sephadex G-50 (gel-filtration) (Chen, et al., 2018).

are highly and cumulatively toxic, which possess severe adverse effects on human health. They would be absorbed from soil or water by herbal medicines. For example, *G. elata* has an absorptive tendency for Hg, Cu, and Zn (Tu et al., 2016). The analytical methods of heavy metals have been reported by various instrumental approaches, such as atomic absorption spectrometry (AAS), inductively coupled plasma-mass spectrometry (ICP-MS), and X-ray fluorescence spectrometry. The low concentration of heavy metals in samples makes it difficult to be directly detected, and the sample preparation techniques are required to extract and enrich the target analytes from samples, including solid-phase extraction (Khan et al., 2020), liquid-liquid microextraction (Sharifi et al., 2016), and solid-phase microextraction (Baghaei et al., 2023). A method using magnetic solid-phase extraction (MSPE) coupled with AAS was established for quantitative analysis of Cu, Pb, and Cd in *G. elata*. The proposed method showed good linearity in the range of 1.0–100.0 µg/L, and the recoveries of the spiked samples varied from 90.0 to 102.0% (Tu et al., 2016).

Among herbal medicine processing methods, the Sulfur Fumigation of herbs is an important post-harvest processing method

that has been used in Asian countries for a long history (Kan, Ma and Lin, 2011). Inappropriate sulfur fumigation operations can lead to excessive SO<sub>2</sub> in herbs such as *G. elata*, which places potential danger to human health (Li et al., 2024). The fluorescence analysis method is one of the most attractive techniques due to its simple operation, high sensitivity, and time-saving. A mitochondrial fluorescent probe indole-incorporated-benzoeindolium was synthesized and was successfully applied to detect SO<sub>2</sub> and its derivatives in *G. elata* with recovery rates from 96.14% to 108.3% (Zheng et al., 2022). It is noteworthy that *G. elata* is found to contain naturally occurring bisphenol F (bis(4-hydroxyphenyl) methane), which is structurally similar to bisphenol A belonging to endocrine disrupting chemicals (Huang et al., 2019). Bisphenol F can be extracted from foods/herbs and their products by aqueous methanol solution, but limited specific quantitative methods have been reported till now.

#### 4. Application in functional food

*G. elata* has been applied as a food for a long history, and there are many herbal cuisine recipes and food products using *G. elata* in China and other southeast Asia countries. With systematical research about the biological function of *G. elata*, more and more relative food products have been developed, including alcohol drinks, tea, biscuits, pastries, noodles, and beverages among others.

Food processing methods have impacts on the bioactives and flavor substances of *G. elata*, which is shown in Table 2. For example, the fermentation of *G. elata* by lactobacilli and yeast can significantly change its flavor composition and improve the concentration of pleasant flavor compounds (Tan et al., 2024). Moreover, the fermentation process can also raise the content of 4-hydroxybenzyl alcohol and 4-hydroxybenzaldehyde (Zhao, et al., 2022). Besides small molecules, the polysaccharides are also affected by fermentation, which would become fragmented and loose. Steaming and boiling can increase gastrodin content and decrease 4-hydroxybenzyl alcohol content, but lead to hydrolysis of polysaccharide and gelatinization of starch granules.

#### 5. Conclusion

This review summarized the research of chemical substances in *G. elata* in the scope of analysis method and food application, which can help readers to systemically capture the knowledge about how to analyze different kinds of compounds in *G. elata* and their ap-

**Table 2.** Summary of effects of food processing on the chemical substances in *G. elata*

| Food processing                            | Changes of chemical substances   | Reference            |
|--|--|----------------------|
| Fermentation                               | Flavor composition   | (Tan, et al., 2024)  |
| Fermentation                               | 4-hydroxybenzyl alcohol, 4-hydroxybenzaldehyde and γ-aminobutyric acid (GABA)  | (Zhao, et al., 2022) |
| Fermentation                               | Higher content of uracil, guanosine, adenosine, 5-hydroxymethylfurfural, and ergosterol. Lower content of genistein and daidzein   | (Wu et al., 2024)    |
| Solid-state co-fermentation                | surface morphology of polysaccharides  | (Chen, et al., 2024) |
| High-humidity hot air impingement steaming | Hydrolysis of polysaccharide and gelatinization of starch granules. Increased gastrodin content and decreased 4-hydroxybenzyl alcohol content                            | (Xie et al., 2021)   |
| Steam and Water Blanching                  | Hydrolysis of polysaccharides and gelatinization of starch granules. Increased gastrodin and crude polysaccharide contents and decreased 4-hydroxybenzyl alcohol content | (Xie et al., 2023)   |

plication in the food area. *G. elata* has been proven to contain a variety of chemical substances, including phenolic compounds, organic acids, polysaccharides, peptides, and others. Gastrodin and 4-hydroxybenzyl alcohol are markers for the quality control of *G. elata*. Some compounds exhibiting excellent pharmacological effects make it valuable to conduct deep research. Thus, many methods have been developed for the analysis of these compounds in plant, biological, food, and drug samples. In addition, there are a few methods for the analysis of harmful substances, which should be given more attention, such as bisphenol F.

As for its application in the food area, *G. elata* has been applied as food for a long history, and abundant relative products have been developed including liquor drinks, tea, biscuits, noodles, beverages, and so on. It is noteworthy that, different food processing methods have a varied effect on the chemical composition of *G. elata*, which can provide the guide for the development of functional food of *G. elata*.

## Funding

This research was funded by the Youth Talent Project of Education Department Scientific Research Plan of Hubei Province (GRANT number Q20232904).

## References

- Abdel-Salam, O.M.E., Youness, E.R., Mohammed, N.A., Morsy, S.M.Y., Omara, E.A., and Sleem, A.A. (2014). Citric Acid Effects on Brain and Liver Oxidative Stress in Lipopolysaccharide-Treated Mice. *J. Med. Food* 17: 588–598.
- Abdel-Salam, O.M.E., Youness, E.R., Mohammed, N.A., Yassen, N.N., Khadrawy, Y.A., El-Touky, S.E., and Sleem, A.A. (2016). Novel neuroprotective and hepatoprotective effects of citric acid in acute malathion intoxication. *Asian Pacific Journal of Tropical Medicine*. 9: 1181–1194.
- Baghaei, P.A.M., Mogaddam, M.R.A., Farajzadeh, M.A., Mohebbi, A., and Sorouraddin, S.M. (2023). Application of deep eutectic solvent functionalized cobalt ferrite nanoparticles in dispersive micro solid phase extraction of some heavy metals from aqueous samples prior to ICP-OES. *J. Food Compos. Anal.* 117: 1–11.
- Bai, Y., Mo, K., Wang, G.R., Chen, W.L., Zhang, W., Guo, Y.B., and Sun, Z.R. (2021). Intervention of Gastrodin in Type 2 Diabetes Mellitus and Its Mechanism. *Frontiers in Pharmacology*. 12: 1–14.
- Cai, X.Y., Kong, F.G., Wang, R.C., Zhai, S.Y., Guan, X., Zhang, G.R., and Wang, D. (2019). *Candida albicans vaginitis* in a murine model is reduced by polypeptide-enriched *Gastrodia elata* extracts. *Future Microbiology* 14: 839–846.
- Chen, C., Li, X.X., Li, J., Xu, Y.M., Jing, X., Wu, S.Q., Liu, X., and Zhang, X.Y. (2018). Purification and characterization of an antimicrobial protein from *Gastrodia elata* Blume tubers. *Trop. J. Pharm. Res.* 17: 1717–1723.
- Chen, L.H., Wang, Z.H., Mao, Y.Y., Chen, Y.H., and Li, J.Y. (2024). Effect of solid-state co-fermentation on the structural characteristics and bioactivities of polysaccharides in the medicinal residues of *Gastrodia Ganoderma*. *Food Bioscience*. 61: 1–11.
- Chen, S., Liu, J.Q., Xiao, H., Zhang, J., and Liu, A. (2016). Simultaneous Qualitative Assessment and Quantitative Analysis of Metabolites (Phenolics, Nucleosides and Amino Acids) from the Roots of Fresh *Gastrodia elata* Using UPLC-ESI-Triple Quadrupole Ion MS and ESI-Linear Ion Trap High-Resolution MS. *PLoS One* 11: 1–16.
- Chen, W.C., Lai, Y.S., Lu, K.H., Lin, S.H., Liao, L.Y., Ho, C.T., and Sheen, L.Y. (2015). Method development and validation for the high-performance liquid chromatography assay of gastrodin in water extracts from different sources of *Gastrodia elata* Blume. *J. Food Drug Anal.* 23: 803–810.
- Chen, X.B., Li, H.W., Sha, O., Dai, X.C., Wu, Y.F., Xu, Z.X., and Wang, Z.W. (2024). Determination of gastrodin in urine by magnetic dispersion solid phase extraction-high performance liquid chromatography. *Chemical Research and Application*. 36: 1929–1934.
- Cheng, L.J., and Deng, Y. (2021). Characterization by HPLC of hydroxybenzyl alcohol biotransformation to gastrodin *in vivo*. *Nat. Prod. Commun.* 16: 1–8.
- Dong, J.J., Ji, D., Su, L.L., Zhang, F.Y., Tong, H.J., Mao, C.Q., and Lu, T.L. (2020). A simplified LC-MS/MS approach for simultaneous quantification and pharmacokinetics of five compounds in rats following oral administration of *Gastrodia elata* extract. *J. Anal. Sci. Technol.* 11: 1–9.
- Du, J.Y., Mo, J.Y., Xie, X., Huang, X.L., Wu, X.L., and Wang, L.S. (2024). Comprehensive quality evaluation of Tianma jiannao granules. *China Pharmacy*. 35: 2482–2487.
- Gan, Q.X., Peng, M.Y., Wei, H.B., Chen, L.L., Chen, X.Y., Li, Z.H., An, G.Q., and Ma, Y.T. (2024). *Gastrodia elata* polysaccharide alleviates Parkinson's disease via inhibiting apoptotic and inflammatory signaling pathways and modulating the gut microbiota. *Food & Function* 15: 2920–2938.
- Gong, M.Q., Lai, F.F., Chen, J.Z., Li, X.H., Chen, Y.J., and He, Y. (2024). Traditional uses, phytochemistry, pharmacology, applications, and quality control of *Gastrodia elata* Blume: A comprehensive review. *J. Ethnopharmacol.* 319: 1–22.
- Guan, H., Ling, X., Xu, J., Zhu, Y.Q., Zhang, J.Y., and Liu, X.Y. (2022). Structural Characterization of Polysaccharide Derived from *Gastrodia elata* and Its Immunostimulatory Effect on RAW264.7 Cells. *Molecules* 27: 1–23.
- Guan, J., Zhang, X.R., Feng, B., Zhao, D.H., Zhao, T., Chang, S., Wang, L.M., and Zhu, H.Y. (2017). Simultaneous determination of ferulic acid and gastrodin of Tianshu Capsule in rat plasma by ultra-fast liquid chromatography with tandem mass spectrometry and its application to a comparative pharmacokinetic study in normal and migraine rats. *J. Sep. Sci.* 40: 4120–4127.
- Hu, M.H., Yan, H., Fu, Y.Y., Jiang, Y.L., Yao, W.F., Yu, S., Zhang, L., Wu, Q.A., Ding, A.W., and Shan, M.Q. (2019). Optimal Extraction Study of Gastrodin-Type Components from *Gastrodia Elata* Tubers by Response Surface Design with Integrated Phytochemical and Bioactivity Evaluation. *Molecules* 24: 1–14.
- Huang, T.Y., Danaher, L.A., Brüscheiler, B.J., Kass, G.E.N., and Merten, C. (2019). Naturally occurring bisphenol F in plants used in traditional medicine. *Archives of Toxicology*. 93: 1485–1490.
- Ji, N., Liu, P., Zhang, N., Yang, S.Y., and Zhang, M.S. (2022). Comparison on bioactivities and characteristics of polysaccharides from four varieties of *Gastrodia elata* Blume. *Frontiers in Chemistry*. 10: 1–18.
- Ji, W.H., Zhang, M.M., Wang, D.J., Wang, X., Liu, J.H., and Huang, L.Q. (2015). Superhydrophilic molecularly imprinted polymers based on a water-soluble functional monomer for the recognition of gastrodin in water media. *J. Chromatogr. A* 1425: 88–96.
- Jiang, N., Yao, C., Zhang, Y., Chen, Y., Chen, F., Luo, Y., Choudhary, M.I., Pan, R., and Liu, X. (2024). Antidepressant effects of Parishin C in chronic social defeat stress-induced depressive mice. *J. Ethnopharmacol.* 325: 1–12.
- Kan, W.L., Ma, B., and Lin, G. (2011). Sulfur Fumigation Processing of Traditional Chinese Medicinal Herbs: Beneficial or Detrimental? *Frontiers in Pharmacology*. 2: 1–7.
- Khan, W.A., Arain, M.B., and Soylyak, M. (2020). Nanomaterials-based solid phase extraction and solid phase microextraction for heavy metals food toxicity. *Food and Chemical Toxicology*. 145: 1–13.
- Kong, F., Cai, X.Y., Zhai, S.Y., Wang, R.C., Zheng, X.Y., Ma, Y., Bi, H., and Wang, D. (2019). Possible mechanisms of the antimicrobial effects of polypeptide-enriched *Gastrodia elata* Blume extracts. *Mol. Med. Rep.* 20: 4723–4730.
- Lee, J.G., Moon, S.O., Kim, S.Y., Yang, E.J., Min, J.S., An, J.H., Choi, E.A., Liu, K.H., Park, E.J., Lee, H.D., and Song, K.S. (2015). Rapid HPLC determination of gastrodin in *Gastrodiae Rhizoma*. *J. Korean Soc. Appl. Biol. Chem.* 58: 409–413.
- Li, H.X., Ding, M.Y., Lv, K., Wei, Y., and Yu, J.Y. (2001). Identification and determination of the active compounds in *Gastrodia elata* Blume by HPLC. *J. Liq. Chromatogr. Relat. Technol.* 24: 579–588.
- Li, S.S., Zhang, F.J., Li, L.X., Zhang, H., Duan, X.W., Shi, L., Cui, X.M., and Li, X.Q. (2024). Rapid determination of active ingredient contents in *Rhizoma Gastrodiae* using near-infrared spectroscopy combined with



- artificial rabbits optimization-least square support vector regression. *Food Science*. 45: 207–213.
- Li, X.F., Xiang, B., Shen, T., Xiao, C., Dai, R., He, F.Y., and Lin, Q. (2020). Anti-neuroinflammatory effect of 3,4-dihydroxybenzaldehyde in ischemic stroke. *International Immunopharmacology*. 82: 1–11.
- Li, Y.H., Zhang, Y.M., Zhang, Z.J., Hu, Y.P., Cui, X.M., and Xiong, Y. (2019). Quality evaluation of *Gastrodia elata* tubers based on HPLC fingerprint analyses and quantitative analysis of multi-components by single marker. *Molecules* 24: 1–16.
- Li, Z.B., Huang, J., Wang, L., Li, D., Chen, Y.P., Xu, Y.Q., Li, L., Xiao, H., and Luo, Z.S. (2024). Novel insight into the role of sulfur dioxide in fruits and vegetables: Chemical interactions, biological activity, metabolism, applications, and safety. *Critical Reviews in Food Science and Nutrition*. 64: 8741–8765.
- Liu, C.L., Liu, M.C., and Zhu, P.L. (2002). Determination of gastrodin, *p*-hydroxybenzyl alcohol, vanillyl alcohol, *p*-hydroxybenzaldehyde and vanillin in tall *Gastrodia* tuber by high-performance liquid chromatography. *Chromatographia*. 55: 317–320.
- Liu, J.Q., Chen, S., Cheng, J.T., Zhang, J., Wang, Y.S., and Liu, A. (2017). An optimized and sensitive pharmacokinetic quantitative method of investigating gastrodin, parishin, and parishin B, C and E in beagle dog plasma using LC-MS/MS after intragastric administration of tall *Gastrodia* capsules. *Molecules* 22: 1–11.
- Liu, Y., Gao, J.L., Peng, M., Meng, H.Y., Ma, H.B., Cai, P.P., Xu, Y., Zhao, Q., and Si, G.M. (2018). A review on central nervous system effects of gastrodin. *Frontiers in Pharmacology*. 9: 1–18.
- Luo, K.X., Wang, Y.H., Chen, W.S., Feng, X.J., Liao, Y.H., Chen, S.C., Liu, Y., Liao, C.D., Chen, M.X., and Ao, L.J. (2022). Treatment combining focused ultrasound with gastrodin alleviates memory deficit and neuropathology in an Alzheimer's disease-like experimental mouse model. *Neural Plast.* 2022: 1–13.
- Lv, P., Fu, Y.L., Tao, B., Mao, M.D., Zhao, J.Y., and He, Z.Y. (2022). Determination of gastrodin in tianma medicinal liquor by high-performance liquid chromatography. *China Port Science and Technology*. 4: 83–87.
- Pasquini, C. (2018). Near infrared spectroscopy: A mature analytical technique with new perspectives – A review. *Analytica Chimica Acta*. 1026: 8–36.
- Sasidharan, S., Chen, Y., Saravanan, D., Sundram, K.M., and Yoga Latha, L. (2011). Extraction, isolation and characterization of bioactive compounds from plants' extracts. *Afr. J. Tradit. Complement. Altern. Med.* 8: 1–10.
- Shan, T.Y., Yin, M.Z., Wu, J.X., Yu, H.W., Liu, M.L., Xu, R., Wang, J.T., Peng, H.S., Zha, L.P., and Gui, S.Y. (2021). Comparative transcriptome analysis of tubers, stems, and flowers of *Gastrodia elata* Blume reveals potential genes involved in the biosynthesis of phenolics. *Fitoterapia*. 153: 1–11.
- Shao, Q.H., Zhang, X.L., Chen, Y., Zhu, C.G., Shi, J.G., Yuan, Y.H., and Chen, N.H. (2018). Anti-neuroinflammatory effects of 20C from *Gastrodia elata* via regulating autophagy in LPS-activated BV-2 cells through MAPKs and TLR4/Akt/mTOR signaling pathways. *Mol. Immunol.* 101: 640–640.
- Sharifi, V., Abbasi, A., and Nosrati, A. (2016). Application of hollow fiber liquid phase microextraction and dispersive liquid-liquid microextraction techniques in analytical toxicology. *J. Food Drug Anal.* 24: 264–276.
- Shin, E.-J., Whang, W.K., Kim, S., Bach, J.-H., Kim, J.-M., Nguyen, X.-K.T., Nguyen, T.-T.L., Jung, B.D., Yamada, K., Nabeshima, T., and Kim, H.-C. (2010). Parishin C attenuates phencyclidine-induced schizophrenia-like psychosis in mice: Involvements of 5-HT<sub>1A</sub> Receptor. *J. Pharmacol. Sci.* 113: 404–408.
- Si, K.Y., Yan, C.R., Huang, Y.P., Kong, D.T., Yang, J.J., Wang, L.H., Liu, X.Y., and Hou, Y. (2023). Study by the rapid determination of the content of four components in *Gastrodia* based on near-infrared spectroscopy. *Yunnan Chem. Technol.* 50: 65–68.
- Song, Y.L., An, X.L., and Kong, P. (2024). HPLC determination of gastrodin and gastrodigenin in Tianma Xifeng capsules. *China Journal of Pharmaceutical Economics*. 19: 108–111.
- Su, Z.H., Yang, Y.G., Chen, S.Z., Tang, Z.S., and Xu, H.B. (2023). The processing methods, phytochemistry and pharmacology of *Gastrodia elata* Bl.: A comprehensive review. *J. Ethnopharmacol.* 314: 1–32.
- Tan, A., Hussain, S., Musuku, A., and Massé, R. (2009). Internal standard response variations during incurred sample analysis by LC-MS/MS: Case by case trouble-shooting. *J. Chromatogr. B* 877: 3201–3209.
- Tan, Y.L., Fu, Y.C., Huang, R., Liu, L.Y., Li, X., Luo, Y.D., and Gao, M.X. (2024). Analytical study on quality of Wufeng *Gastrodia elata* from Hubei province and changes of characteristic flavor substances during fermentation. *Food and Fermentation Industries* 1–10.
- Tang, C.L., Wu, B.C., Wu, J.Y., Zhang, Z., and Yu, B.C. (2018). Novel Strategies Using total gastrodin and gastrodigenin, or total gastrodigenin for quality control of *Gastrodia elata*. *Molecules* 23: 1–11.
- Teo, C.C., Tan, S.N., Yong, J.W.H., Hew, C.S., and Ong, E.S. (2008). Evaluation of the extraction efficiency of thermally labile bioactive compounds in *Gastrodia elata* Blume by pressurized hot water extraction and microwave-assisted extraction. *J. Chromatogr. A* 1182: 34–40.
- Tu, Y.J., Ju, S.Q., and Wang, P.Y. (2016). Flame atomic absorption spectrometric determination of copper, lead, and cadmium in *Gastrodia* rhizoma samples after preconcentration using magnetic solid-phase extraction. *Spectrosc. Lett.* 49: 249–256.
- Wang, C.H., Zeng, Y.J., Hou, Y.B., Zeng, C.H., Wang, M., and Wang, Y.H. (2023). Effects of *Armillaria* species on growth and quantity of active medicinal components of *G. elata* Bl. f. *elata* tubers along an altitude gradient: Evidence from empirical experiments. *Phytochem. Lett.* 54: 101–106.
- Wang, J.-W., Liu, Y.-M., Zhao, X.-F., and Zhang, H. (2017). Gastrodin protects retinal ganglion cells through inhibiting microglial-mediated neuroinflammation in an acute ocular hypertension model. *Int J Ophthalmol.* 10: 1483–1489.
- Wang, Q., Li, Z., Wang, D., Yang, S., and Feng, Y. (2020). Myocardial protection properties of parishins from the roots of *Gastrodia elata* Bl. *Biomedicine & Pharmacotherapy*. 121: 1–9.
- Wang, T., Chen, H., Xia, S., Chen, X., Sun, H., and Xu, Z. (2021). Ameliorative effect of parishin C against cerebral ischemia-induced brain tissue injury by reducing oxidative stress and inflammatory responses in rat model. *Neuropsychiatr. Dis. Treat.* 17: 1811–1823.
- Wang, X., Li, B., and Tang, K. (2019). Determination of gastrodin in Tianlitong tablets by HPLC. *Food and Drug*. 21: 199–201.
- Wang, Y., Zhao, L., and Li, A.Y. (2021). Gastrodin - A potential drug used for the treatment of Tourette Syndrome. *J. Pharmacol. Sci.* 145: 289–295.
- Wang, Z.J., Zuo, C.Z., Chen, M., Song, J., Tu, K., Lan, W.J., Li, C.Y., and Pan, L.Q. (2023). A novel variable selection method based on ordered predictors selection and successive projections algorithm for predicting gastrodin content in fresh *Gastrodia elata* using fourier transform near-infrared spectroscopy and chemometrics. *Foods*. 12: 1–14.
- Wu, Y.N., Zhang, H.W., Zhu, J.G., Zhang, Z.L., Ma, S.B., Zhao, Y.Q., Wang, Y.M., Yuan, J., Guo, X., Li, Y.J., and Zhang, S. (2024). The effect of fermentation on the chemical constituents of *Gastrodia* tuber halimasch powder (GTHP) estimated by UHPLC-Q-Orbitrap HRMS and HPLC. *Molecules* 29: 1–24.
- Wu, Z., Gao, R.P., Li, H., Liao, X., Tang, X., Wang, X.G., and Su, Z.M. (2022). How steaming and drying processes affect the active compounds and antioxidant types of *Gastrodia elata* Bl. f. *glauca* S. *chow*. *Food Research International*. 157: 1–16.
- Xie, Y.K., Li, X.Y., Chen, C., Zhang, W.P., Yu, X.L., Xiao, H.W., and Lu, F.Y. (2023). Effects of steam and water blanching on drying characteristics, water distribution, microstructure, and bioactive components of *Gastrodia Elata*. *Plants* 12: 1–17.
- Xie, Y.K., Li, X.Y., Zhang, Y., Zheng, Z.A., Huang, L.Q., Liu, D.H., Xiao, H.W., and Liu, Y.H. (2021). Effects of high-humidity hot air impingement steaming on *Gastrodia elata*: steaming degree, weight loss, texture, drying kinetics, microstructure and active components. *Food and Bioproducts Processing*. 127: 255–265.
- Xu, Q., Liu, Y., Wang, X.C., Gu, H.Y., and Chen, Z.L. (1998). Purification and characterization of a novel anti-fungal protein from *Gastrodia elata*. *Plant Physiol. Biochem.* 36: 899–905.
- Yan, J.Y., Yang, Z.S., Zhao, N.H., Li, Z.W., and Cao, X. (2019). Gastrodin protects dopaminergic neurons via insulin-like pathway in a Parkinson's disease model. *BMC Neuroscience*. 20: 1–11.
- Yang, F., Long, Z.X., Lu, W.Y., Liu, Y., and Zhu, J.J. (2023). Determination of gastrodin and ginsenosides in *Gastrodia* and *Ginseng* Buccal tablets. *Xiandai Shipin* 29: 218–222.
- Yang, L., Qin, S.H., and Zi, C.T. (2024). Research progress of *Gastrodia elata*

- Blume polysaccharides: a review of chemical structures and biological activities. *Frontiers in Chemistry*. 12: 1–9.
- Yang, L., Wang, X., Xin, X., and Wang, M.Z. (2011). The determination method research of gastrodin in liver and kidney of rats. *Lishizhen Med. Mater. Med. Res.* 22: 295–298.
- Yu, B.C., Li, Z., Wu, J.Y., Ying, J.M., Tang, Y.Q., Wu, B.C., Tang, C.L., and Xu, J.Y. (2020). Quality control of *Gastrodia elata* by high-performance liquid chromatography with fluorescence detection (HPLC-FLD) and principal component analysis (PCA) and hierarchical cluster analysis (HCA). *Analytical Letters*. 53: 746–759.
- Zeng, X., Li, Y.Y., Ling, H., Chen, J., and Guo, S.X. (2018). Revealing proteins associated with symbiotic germination of *Gastrodia elata* by proteomic analysis. *Botanical Studies*. 59: 1–8.
- Zhang, M.L., Zhang, Y.W., Peng, J.Y., Huang, Y.Y., Gong, Z.P., Lu, H.X., Han, L., and Wang, D.D. (2024). Gastrodin against oxidative stress-inflammation crosstalk via inhibiting mtDNA/TLR9 and JAK2/STAT3 signaling to ameliorate ischemic stroke injury. *International Immunopharmacology*. 141: 1–14.
- Zhang, W., Sheng, Y.X., and Zhang, J.L. (2008). Determination and pharmacokinetics of gastrodin and *p*-hydroxybenzylalcohol after oral administration of *Gastrodia elata* Bl. extract in rats by high-performance liquid chromatography-electrospray ionization mass spectrometric method. *Phytomedicine* 15: 844–850.
- Zhao, C.C., Hu, Q., Zhang, X., Yan, H., Li, J., Chen, F., and Zuo, Z.Y. (2023). Molecularly imprinted polymers with ionic liquid as the functional monomer for selective solid-phase extraction of gastrodin. *J. Dispersion Sci. Technol.*
- Zhao, M., Wang, Y., Yang, J., Xie, C.Z., Li, L.L., Zhang, C.J., and Yang, X.S. (2022). Optimization of fermentation process and quality evaluation of *Gastrodia elata* Jiaosu. *China Brewing*. 41: 177–182.
- Zhao, M.H., Zhou, Y.T., Sheng, R.L., Zhang, H.J., Xiang, J.B., Wang, J., Li, P., Ma, T.Y., Liu, P.W., Chen, Q., Wen, W., and Xu, S.J. (2024). Gastrodin relieves Parkinson's disease-related motor deficits by facilitating the MEK-dependent VMAT2 to maintain dopamine homeostasis. *Phytomedicine* 132: 1–11.
- Zheng, D., Zhang, T., Huang, J., Wang, M., Cao, Z., Huang, Y., Yang, Z., Deng, Y., and Fang, Y. (2022). Indole-incorporated-benzoeindolium as a novel mitochondrial and ratiometric fluorescent probe for real-time tracking of SO<sub>2</sub> derivatives in vivo and herb samples. *Dyes and Pigments*. 198: 1–10.
- Zhu, H.D., Liu, C., Hou, J.J., Long, H.L., Wang, B., Guo, D.A., Lei, M., and Wu, W.Y. (2019). *Gastrodia elata* Blume Polysaccharides: A Review of Their Acquisition, Analysis, Modification, and Pharmacological Activities. *Molecules* 24: 1–18.