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REVIEW

Glandular trichomes of medicinal plants: types, separation and purification, biological activities

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Abstract

Glandular trichomes (GTs) are one of the epidermal tissues of medicinal plants which function in the synthesis, storage, and secretion of secondary metabolites. The active ingredients of Chinese medicinal materials are mostly secondary metabolites of plants. Accordingly, it is of great research value to explore the quality of medicinal materials using the GTs of medicinal plants as the starting point. However, most of the current studies on GTs of medicinal plants are still at the simple morphological identification stage, and there are few studies on the compounds secreted by GTs and secondary metabolic processes. Here, we reviewed the literature, summarized the morphological types of medicinal plant GTs, separation and purification technology, analysis technology, and biological activities of secondary metabolites, and established a research approach to medicinal plant GTs. We hope to provide a reference for future research on GT inclusions and secondary metabolism.

Keywords: glandular trichomes, medicinal plants, separation, purification, detection technologies.

Introduction

Trichomes, one of the epidermal structures of medicinal plants, can be divided into two types according to whether they have a secretory function: glandular trichomes (GTs) and nonglandular trichomes (non-GTs) (Yu 2020). This article mainly elaborates on medicinal plant GTs because the tips of non-GTs lack synthesis and storage cells and do not synthesize and accumulate secondary metabolites.

GTs, as an important epidermal tissue, are responsible for pollination and protection (Champagne and Boutry 2016). Some plant GTs release volatile compounds in the air. Some of these compounds are attractants for pollinators, some are repellents for herbivores and ineffective pollinators, and some are even attractants for natural enemies of herbivores (Jacek *et al*. 2018, Giuliani *et al*. 2020). Environmental conditions and seasonal changes affect the growth and development of GTs, leading to differences in the types, density, morphology, and inclusions of GTs. These differences may be related to environmental stress and the adaptive survival of plants (Li *et al*. 1949, Soliman *et al*. 2019). There are differences in the types, density, morphology, and inclusions of GTs in different plant species; thus, GTs can be used as one of the distinguishing characteristics of medicinal plants (Zhang *et al*. 2016, Guesmi *et al*. 2019).

GTs, as a secretory tissue, have the remarkable characteristics of synthesizing, modifying, and storing a variety of medicinal active ingredients and contain a great complex of secondary metabolites, including terpenes, flavonoids, alkaloids, lignose, polysaccharides, glycosides, fatty acids, proteins, and alkaloids (Balcke *et al*. 2017, Konarska and Łotocka 2020). These secondary metabolites accumulate in GTs and have various

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Abbreviations: GTs - glandular trichomes; LMD - laser microdissection; non-GTs - nonglandular trichomes.
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pharmacological activities such as antitumor, antiviral, antiparasitic, antithrombotic, and antioxidation activities (Hemachandran *et al*. 2018, Liu *et al*. 2019). They have great medicinal and commercial value and can be used in the development of new drugs, and the production of natural insecticides and sterilizers (Munien *et al*. 2015). The artemisinin from GTs of *Artemisia annua* was used to develop a new antimalarial drug, which has saved hundreds of lives (Muangphrom *et al*. 2016). These secondary metabolites also play an important role in plants' resistance to biotic and abiotic stresses and are the "first line of defense" for plants to resist external invasion (Champagne and Boutry 2016, Liu *et al*. 2019).

In summary, GTs have a variety of research values. This review mainly summarizes the research progress of GTs, including their morphology and type, separation and purification technology, analysis technology and biological activities of secondary metabolites. We hope to lay the foundation for the in-depth study of medicinal plant GTs.

Morphological types of GTs of medicinal plants

GTs are composed of glandular heads, glandular stalks, and basal cells. They are specialized cells of the plant epidermis that can secrete volatile oil, resin, mucus, and other substances (Schuurink and Tissier 2020). They are mainly distributed in the stems, leaves, flowers, and other parts of plants and can sometimes be seen in seeds, fruits, sepals, and petioles. They are more common in medicinal plants of *Lamiaceae* (Maurya *et al*. 2019), *Solanaceae* (Bergau *et al*. 2016), *Asteraceae* (Muravnik *et al*. 2016), and *Fabaceae* (Barros *et al*. 2017).

General types of GTs: The types of GTs are usually classified according to the specific shapes of the three components of glandular head, glandular stalk, and basal cells (Lange 2015). To date, many types of GTs (*e.g.*, capitate, subsessile capitate, sessile capitate, sunken, peltate, barrel, and clavate types) have been reported (Gul *et al*. 2019, Muravnik *et al*. 2019). For example, GTs can be divided into capitate GTs (Fig. 1*A*) and peltate GTs (Fig. 1*B*) in *Lamiaceae*, *Solanaceae*, *Geraniaceae*, and *Phrymaceae* plants (Lange and Turner 2013, Liu *et al*. 2018), and the basic composition and differences between capitate GTs and peltate GTs are shown in Table 1. There are different types of GTs in plants of different species. *Thymus quinquecostatus* GTs are divided into three types: capitate (basal single cell, stalk 1 - 2 cells, and head single cell), finger-shaped (basal single cell, stalk 3 cells, and head single cell), and peltate (basal single cell, stalk single cell, and 12 secretory cells on the head) (Jia *et al*. 2013). *Salvia japonica* GTs are divided into two types: capitate (both single-celled on the head and stalk) and sunken (four cells on the head) (Jia *et al*. 2013). In *Nicotiana tabacum* plants, there are three types of long-stalked GTs, short-stalked GTs, and sessile capitate GTs, among which long-stalked GTs have a strong secretory function (Zhang *et al*. 2015, Li *et al*. 2017). The cells of the *A. annua* GTs are arranged in double rows, with a total of 5 pairs. These 10 cells include two stalk cells, two basal cells, four subapical cells, and two apical cells (Olsson *et al*. 2009). GTs can also be classified according to the type of compounds they produce: hydrophilic and lipophilic proteins, poly- or monosaccharides (Tissier 2012).

Special types of GTs: In some plant species from

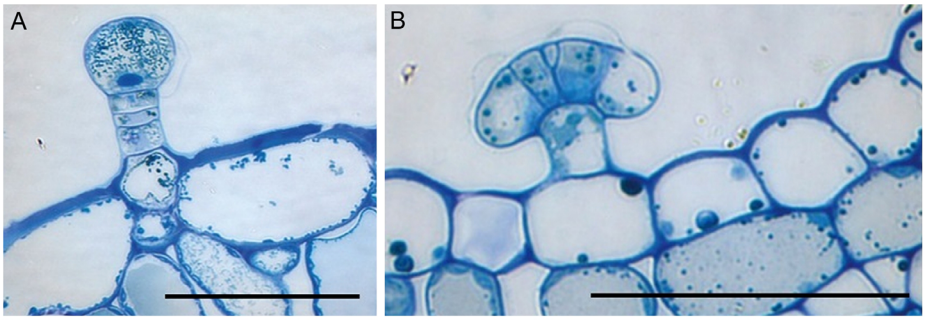

Fig. 1. Micrograph of a 1-μm-thick section stained with toluidine blue (Lange and Turner 2013). *A* - The capitate GTs of *Pelargonium grossularioides* (L.) L'Hér. ex Aiton (*bar* = 50 μm). *B* - The peltate GTs of *Diplacus aurantiacus* (Curtis) Jepson (*bar* = 50 μm).

Table 1. Basic composition and differences between capitate GTs and peltate GTs.

GT types	Basic component (Wu *et al*. 2012)	Composite (Tissier *et al*. 2017)	Accumulation mode (Champagne and Boutry 2016)	Storage capacity (Wu *et al*. 2012)
Capitate GTs	one or more head cells, one or more stalk cells and one basal cell	mainly synthesize nonvolatile or low-volatility secondary metabolites	capitate trichomes synthesize compounds that accumulate outside of the trichome head and are retained within the cuticular waxes or released into the air	limited
Peltate GTs	multiple secretory cells, one basal cell and one short-stem cell	mainly synthesize volatile secondary metabolites	peltate trichomes synthesize lipophilic compounds that are secreted and stored in a subcuticular space within an oil droplet (Champagne and Boutry 2016)	stronger

Lamiaceae, *Asteraceae*, and *Moraceae*, there is a specialized organization of GTs called glandular scales (Fig. 2*C*), which is a kind of sessile or short-stalked GTs. It is oblate and composed of 6 - 8 secretory cells arranged radially. *Mentha haplocalyx* and *Pogostemon cablin* are typical plants that contain glandular squamous tissue (Guo *et al*. 2013, Schuurink and Tissier 2020).

Separation and purification technologies of GTs

There are many epidermal tissues on the plant surface, and there are often 2 - 3 different types of GTs on the surface of medicinal plants (Jia *et al*. 2013, Jiang *et al*. 2016b). The volumes of the GTs are very small, and they are often interspersed among other epidermal tissues; thus, it is difficult to separate GTs without damaging them. In the early stage, due to the limitation of separation technology of GTs, some researchers used chemical reagents to extract the components of GTs directly and analyzed them with the commonly used method of dichloromethane extraction (Ma *et al*. 2021). They showed that rapid washing of the leaf surface with dichloromethane or acetonitrile did not seem to leach leaf components. Although this method is simple and rapid, this method cannot ensure that all components of GTs are extracted and the components of other parts are not extracted. Therefore, the accuracy of this experimental result is still questionable, and other methods must be used to isolate the GTs. The following section summarizes the traditional and modern methods of separation and purification of GTs.

Mechanical separation technology: Initially, the methods of separating the GTs were relatively primitive and relied on mechanical operations such as picking the GTs with tweezers, lightly dipping the surface of the leaf with tape, gently brushing the surface of the leaf with a toothbrush, wiping the surface of the leaf with a microscope cover glass and so on (Jiang *et al*. 2016a). However, the accuracy of these methods is low, and the requirements for experimental operators are high. It is difficult to obtain a sufficient quantity and quality of GTs in a short period of time, which cannot meet the experimental requirements.

Later, the mechanical surface grinding program appeared, a fast method to obtain plant GTs, such as the simple mechanical procedures developed by Gershenzon *et al*. (1987). This procedure was the first to use silanized grinding glass to gently grind the surface of plants in a buffer to obtain an almost colorless filtrate and then used a commercial cell disruptor to extract the GTs to obtain a cell-free preparation rich in the content of the glands. Slone and Kelsey (1985) obtained isolated GTs from mechanically homogenized leaf tissue by discontinuous or continuous Percoll density gradient centrifugation. There is also a method for separating the surface GTs of plant leaves with quartz sand vibration and friction (Hashidoko and Urashima 1995). These methods can obtain a large amount of plant GTs in a short period of time, but it is inevitable that other plant tissues and pollutants will be introduced, which will interfere with the experimental results.

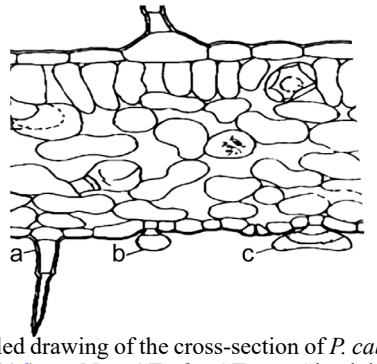

Fig. 2. Detailed drawing of the cross-section of *P. cablin* between veins (Liu 2016). *a* - Non-GTs. *b* - GTs. *c* - Glandular scale.

In addition to mechanical abrasion methods, Yerger *et al*. (1992) froze plant tissues with dry ice powder and cut plant GTs after low-temperature treatment. Jiang *et al*. (2016a) froze *Schizonepeta tenuisfolia* (Benth.) Briq. in liquid nitrogen for 2 min, used a moderately hard brush to brush the GTs, and obtained a large number of GTs in a short period of time. The freezing coating method is more efficient, but low-temperature treatment has disadvantages, which may lead to GT rupture and content flowing out.

All the abovementioned methods can realize the separation of the GTs of medicinal plants, but it is inevitable that other plant tissues and pollutants will be introduced, which will interfere with the experimental results; thus, the purification and enrichment of the GTs are essential. The purification and enrichment of GTs are based on the specificity of different plant tissues, *i.e*., the difference in shape, size, and density. Initially, plant tissues were filtered using a mesh and cheesecloth (Gershenzon *et al*. 1987); then, Percoll gradient purification (Slone and Kelsey 1985), water-selective sedimentation (Jiang *et al*. 2016a), nylon mesh filtration and collection followed by centrifugation (Hashidoko and Urashima 1995), and other purification methods emerged.

However, these purification methods can only continuously improve the purity of the GT tissues. After purification and enrichment, there will still be other nonglandular tissues, which will affect the accuracy of the experimental results. Because of the wide variety of medicinal plant trichomes, these methods cannot achieve the separation of a single type of trichome.

Dissociation of GTs by chemical methods: According to the composition of plant cell walls, some experimenters used corresponding dissociation enzymes (such as cellulose and pectinase) to dissociate the cell wall, weaken or even eliminate the connection between the GTs and the cell wall so that the GTs easily fall off (Champagne and Boutry 2016). However, these methods may result in the loss of cell structure. After purification and enrichment, there will still be other nonglandular tissues that interfere with the experiment and affect the accuracy of the experimental results.

Laser microdissection technology: Currently, an emerging cell separation technology, laser microdissection

(LMD), brings the precision of microtissue separation to a higher level. LMD can cut and separate cells at specific points, realize the separation and purification of a single type of cell population and a single cell, and maintain the integrity of cells. It has the advantages of rapidity, accuracy, automation, and flexibility and successfully solves the problem of cell heterogeneity. Samples cut by LMD can be used for the analysis of the chemical composition, transcriptomics (Xue *et al*. 2019), genomics (Yu *et al*. 2016), and proteomics (Huang *et al*. 2020); thus, this technology is widely popular in the fields of zoology and medicine (García-Berrocoso *et al*. 2018, Zhou *et al*. 2020, Kikani and Lui 2021). This technology has also been applied in the field of botany in recent years, achieving the separation of various types of plant microstructures (Sui *et al*. 2018, Verma *et al*. 2019, Zhong *et al*. 2020b).

Although the application history of LMD in the field of botany is a little short, researchers have achieved many important results based on this technology. Li *et al*. (2013) isolated a single peltate GT type of *Colquhounia coccinea* by LMD technology. Using this method, Olsson *et al*. (2009) not only cut and isolated the GTs of *A. annua* but also separated secretory cells of different types. Xiao *et al*. (2017) collected the peltate GTs of *Leonurus artemisia* by LMD and then analyzed the secondary metabolites in the peltate GTs by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). Finally, two diterpenoids were located in the peltate GTs of *Leonurus artemisia.* Through the combination of LMD and low-temperature nuclear magnetic resonance-mass spectrometry, new types of sesterterpene terpenes were discovered in *C. coccinea* and *Leucosceptrum canum* GTs (Luo *et al*. 2010, 2011, Li *et al*. 2013). Based on laser microdissection and pressure catapulting, Olofsson *et al*. (2012) successfully isolated selected GT cells of *A. annua.* Then, combined with omics technology, they confirmed that the apical and subapical cells of the GTs are biosynthesis sites of artemisinin. Currently, LMD is a commonly used separation technique in the study of medicinal plant GTs.

Detection of secondary metabolites in plant GTs

GTs are known as "biosynthesis factories" because many medicinal ingredients are synthesized in GTs. Many secondary metabolites also accumulate in the secretory cavities under the horny layers of GTs. Because of the small volume of the GTs, the number of samples obtained is usually relatively rare; thus, the sensitivity of the analytical technology is required to be high (Jiang *et al*. 2016b). In recent years, with advances in analytical technology, the study of medicinal plant GT secretions has made further developments.

Analytical technology of secondary metabolites in plant GTs: In the early stage, due to the limitation of isolation techniques, the secondary metabolites in the GTs were mostly identified by histochemical staining; specifically, temporary slides made from fresh leaves were stained with histochemical stains and observed under a microscope. For example, the GTs are pink after Sudan III staining, indicating that the GTs contain lipids (Corsi and Bottega 1999).

With the improvement of isolation techniques, the secondary metabolites of GTs are now often analyzed by gas chromatography-tandem mass spectrometry (GC-MS), liquid chromatography-tandem mass spectrometry (LC-MS), or nuclear magnetic resonance (NMR) spectroscopy. Terpenoids are the most diverse and numerous secondary metabolites in plants, and they also widely exist in plant GTs (Jiang *et al*. 2016b). In the analysis of GT secretions, gas chromatography (GC) and GC-MS are the most commonly used techniques, which are mainly used for the analysis of volatile components, including phenols and terpenes, and can also be used for derivatized polysaccharides, lignin, fatty acids, and other components. For example, Hillig (2004) used GC to analyze cannabinoids. LC-MS is commonly used to analyze nonvolatile components such as flavonoids, glycosides, and alkaloids. McDowell *et al*. (2011) used liquid chromatography tandem time-of-flight mass spectrometry (LC-TOF-MS) to detect compound types in different types of GTs in various *Solanum* species and concluded that stem GTs and leaf GTs can be distinguished according to the main components of GTs. For the analysis of a single compound, NMR is commonly used. Li *et al*. (2013) used LDM combined with low-temperature NMR-MS to isolate and identify more than 90 sesterterpene compounds from plants.

Localization and discovery of secondary metabolites in plant GTs: Several techniques have been developed to locate and discover compounds in GTs. For example, Agati *et al*. (2002) developed a new technology to detect the tissue-specific distribution of flavonoids, *i.e.*, microfluorescence spectrometry combined with multispectral fluorescence microscopy. To investigate the spatial distribution of metabolites within *Cannabis sativa* GTs, Ebersbach *et al*. (2018) exploited hyperspectral coherent anti-stokes Raman scattering microscopy imaging in combination with a nonlinear unmixing method to identify and localize Δ9-tetrahydrocannabinolic acid in the secretory cavity of GTs. Another localization and discovery technology, mass spectrometry imaging technology, exhibited the characteristics of rapidly scanning biologically specific tissue regions and locating product information in these regions. A series of experiments also directly imaged a specific secondary metabolite in plant GTs by this technology.

For example, Hölscher *et al*. (2009), based on the matrix-free ultraviolet-laser desorption/ionization-mass spectrometry imaging technique, identified highly localized UV absorption metabolites in plant tissues. In this experiment, secondary metabolites, such as hypericin and pseudohypericin in GTs of *Hypericum* species, were imaged at a single resolution. Wang *et al*. (2015b) combined LMD, low-temperature NMR spectroscopy and high-performance liquid chromatography (HPLC) to accurately cut the capitate GTs of *Paragutzlaffia henryi* and successfully located a series of diterpenoids in capitate GTs.

Study on the biological activities of secondary metabolites

Plant GTs usually do not perform photosynthesis (Laterre *et al*. 2017) but they have a strong ability to synthesize, store and secrete plant secondary metabolites and are known as the "chemical factories of cells." Extensive biological activities of these secondary metabolites have been reported including anti-parasitic, antitumor, antibacterial and antiviral, antioxidant, psychoactive, toxic and side effects, and defensive functions. These secondary metabolites are not only the active components of Chinese medicinal materials but also the material basis for the quality of medicinal plants.

Anti-parasitic activity: The famous drug artemisinin, a sesquiterpene lactone endoperoxide localized in the GTs of *A. annua* (Zhong *et al*. 2020a), has a significant therapeutic effect against malaria caused by drug-resistant *Plasmodium falciparum*. Artemisinin can bind to a wide range of targets, such as *Plasmodium*, which seriously interferes with the biochemical process of *Plasmodium*. The National University of Singapore research team has identified 124 targets of artemisinin against the most pathogenic *Plasmodium falciparum*. They found that through heme activation, artemisinin can specifically respond to *Plasmodium* infecting cells and effectively attack these pathogenic parasites (Wang *et al*. 2015a).

Antitumor activity: The components of some medicinal plant GTs have been proven to have good antitumor effects. For example, the antimalarial drug artemisinin and its derivatives have shown good curative effects in the treatment of metastatic breast cancer and colorectal cancer in clinical trials. *In vitro* and *in vivo* clinical trials and case reports have confirmed the good activity of artemisinin derivatives, which means that it is possible to develop antitumor drugs with artemisinin and its synthetic derivatives (Konstat-Korzenny *et al*. 2018). Carnosol, found in the GTs of *Rosmarinus officinalis* (Božić *et al*. 2015), has been proven to have a good antitumor effect. Gong *et al*. (2015) found that carnosol can significantly inhibit the growth of ovarian cancer SKOV3 cells in nude mice, and the apoptosis rate of cancer cells is positively correlated with the concentration of carnosol. Certain flavonoid compounds isolated from the secretion trichomes of *Xanthium strumarium* also exhibit antitumor effects (Tao *et al*. 2016).

Antibacterial and antiviral properties: Peppermint (*Mentha haplocalyx*) essential oil contained in the epidermal GTs of peppermint leaves belongs to monoterpenoids (Schuurink and Tissier 2020). Liu *et al*. (2016) confirmed that peppermint essential oil had good inhibitory activity on bronchitis bacteria.

Liu *et al*. (2020) used the mycelial growth rate method to determine the inhibitory effect of peppermint essential oil on five plant pathogens (*Botrytis cinerea*, *Sclerotinia sclerotiorum*, *Fusarium oxysporum*, *Phytophthora capsici*, *Colletotrichum vulgare*). The obtained results showed that peppermint essential oil had a good inhibitory effect on plant pathogenic fungi and exhibited great potential in the development of plant pesticides.

Desaspidin PB, detected in the exudate of the GTs of *Dryopteris* leaves, has antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, and *Bifidobacterium maize* (Chen *et al*. 2016a). Pedalitin, isolated from the GTs on the fruit surface of *Paulownia fortunei*, is an inhibitor of the hepatitis C virus (HCV) and has antiviral effects (Liu *et al*. 2019).

Antioxidant activity: Carnosic acid, synthesized in the GTs of young leaves of *Rosmarinus officinalis*, is a diterpenoid that has a catechol structure, making it a strong antioxidant (Schuurink and Tissier 2020). It has been approved as a natural preservative in food and medicine in many countries (Birtic *et al*. 2015). Flavonoids isolated from the surface GTs of *Paulownia fortunei* fruits have a strong effect on scavenging 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radicals (Liu *et al*. 2019).

Sun (2004) found that the culture solution of *Pelargonium graveolens* L'Herit callus contains a complete chemical composition of essential oils. Through research, it was concluded that GT was the chemical biosynthesis site of the essential oil of *P. graveolens*. In research on the antioxidant capacity of the essential oil of *P. graveolens* and its monomeric compounds, it is considered that the antioxidant capacity of the essential oil of *P. graveolens* is the comprehensive expression of each monomeric compound. The DPPH clearance rate of the monomer butanedione was the highest (88.14 %), followed by citronellol, geranyl acetate, citronellyl acetate, and terpineol, ranging from 25.00 to 54.81 % (Sun 2004). According to reports, the essential oil from *P. graveolens* has certain antidepressant effects, and its antidepressant effect is dose-dependent (Liu *et al*. 2021).

Artemisinin was identified as a new nuclear factor erythroid 2–related factor 2 (Nrf2) inducer. Nrf2 is regarded as a target to prevent tissue oxidative damage and various diseases related to oxidative stress, but the passive activation of Nrf2 cannot effectively protect tissues from oxidative damage. Artemisinin can be used as a targeting inducer to actively activate Nrf2-dependent antioxidant reactions, remove toxic and carcinogenic chemicals, maintain redox homeostasis, and prevent oxidative damage to organs caused by the environment (Chen *et al*. 2016b).

Psychoactive: Salvinorin A, the main bioactive component in the GTs of the *Lamiaceae* Mexican sage, is a nonnitro hallucinogen with strong psychoactive properties. It has more significant hallucinogenic effects than the common hallucinogenic lysergic acid diethylamide and mescalin (Liu *et al*. 2019).

Studies have shown that salvinorin A is a potent and selective kappa opioid receptor agonist with therapeutic potential for perceptual distortion-related diseases (such as schizophrenia, dementia, and binocular disorder), pain, drug addiction, and bipolar disorder (Siebert 2004).

Tetrahydrocannabinol (THC), the most important bioactive component in GTs of *C. sativa* (Rodziewicz *et al*.

2019, Livingston *et al*. 2020), is the main psychoactive substance in *C. sativa*, which mainly acts on the human cardiovascular system and central nervous system (Yuan *et al*. 2017). Smoking marijuana containing this product will cause blood pressure changes and make people feel relaxed and euphoric. High doses can even cause hallucinations (Grotenhermen 2003). The Agriculture Improvement Act of 2018 established a THC concentration of < 0.3 % for the cultivation of hemp as a legal crop in the US (Michlig *et al*. 2021).

The (1S,2E,4R,6R,-7E,11E)-2,7,11-cembratriene-4,6-diol (4R), isolated from the secretions of GTs in tobacco, showed neuroprotective effects in a mouse model of cerebral ischemia (Liu *et al*. 2019). Its protective effect is related to the activation of threonine-serine protein kinase (Akt) to directly protect neurons from ischemia, and it is expected to become a lead compound in the development of drugs for the treatment of ischemic stroke (Martins *et al*. 2015).

The secondary metabolites produced by GTs have defensive effects (Liu *et al*. 2019). For example, sesquiterpenoids in the GTs of the *Asteraceae* family have functions such as allergies and antifeeding (Liu *et al*. 2019). *Pelargonium graveolens* essential oil has insecticidal and repellent activities against houseflies, white moths and other insects (Saraiva *et al*. 2020).

Toxic and side effects: Peppermint oil was found to accumulate in the GTs of *Mentha haplocalyx*, and one of its constituents is menthone (Liu *et al*. 2019). Subacute toxicity studies in rats have shown that continuous administration of a certain dose of menthone could produce general toxicity and growth inhibition. The general toxicity was represented by a reduction in food consumption and body mass, and the growth inhibitory inhibition was represented by an increase in relative brain mass. At the same time, the histopathological observation of cerebellar white matter in the two highest dose groups revealed cystoid space (Madsen *et al*. 1986).

Other: Leucosceptroid B in the GTs of *Leucosceptrum canum* is a type of plant steroid that can reduce the synthesis and accumulation of fat. Transcriptome sequencing technology analysis showed that it could significantly regulate the expression of 10 genes involved in lipid metabolism in nematodes and inhibit the expression of related lipid metabolism genes (Ling *et al*. 2019). Leohein, found in the GT product of *L. artemisia*, can inhibit platelet aggregation induced by arachidonic acid in rabbits, shows potential antithrombotic activity, and has anti-inflammatory and anti-proliferative effects (Schuurink and Tissier 2020). Naringenin, detected in the GTs of the two *Scalesia* species (Liu *et al*. 2019), exhibited the effect of reducing autoimmune diseases and reducing the occurrence rate of mice with autoimmune encephalomyelitis; thus, so it is expected to become a potential drug candidate for the treatment of autoimmune diseases (Niu *et al*. 2021).

The secondary metabolites produced by GTs also have defensive effects (Liu *et al*. 2019). For example, sesquiterpenoids in the GTs of the *Asteraceae* family have functions such as allergies and antifeeding (Liu *et al*. 2019). *P. graveolens* essential oil has insecticidal and repellent activities against houseflies, white moths and other insects (Saraiva *et al*. 2020).

Conclusions and outlook

The GTs of medicinal plants play an important role in regulating the normal growth and physiological activities of plants and occupy an important position in the quality evaluation, variety selection and genuine research of Chinese medicinal materials (Liu 2016, Zhang *et al*. 2016). However, it is difficult to separate and collect GTs. Most of the studies on the GTs of medicinal plants are still in the stage of simple morphological identification. The application of LMD in the field of botany provides us with an efficient, fast and accurate method to separate plant GTs. With the innovation of the omics technology and separation technology of GTs, research on GTs in medicinal plants has gradually transitioned to the stage of studying the growth and development mechanism of GTs and the metabolism mechanism of secondary metabolites of GTs (Zhong *et al*. 2020a, Dong *et al*. 2021). *Arabidopsis thaliana* is a model plant for the study of non-GT development, but studying the development of GTs in medicinal plants also requires a model plant (Li and Wang 2015). Tomato is an excellent model plant for the study of GTs because its genome is known, it is easily transformed, and its natural population and genetic data are abundant (Li and Wang 2015). We can refer to the research model of tomato GTs to study medicinal plant GTs. Moreover, *Artemisia annua* may also become a biological model for the study of GTs; however, thus far, all genomic information on *A. annua* has not been published (Tissier 2012).

The combination of modern instrumental analysis technology and precision omics technology (Xiao *et al*. 2020) established a new approach to studying GTs. This research approach first uses LMD to quickly separate the GTs, then uses LC-MS/GC-MS to determine the composition of metabolites, and finally uses multi-omics techniques for joint analysis. Using this approach, we can not only explore the relationship between the structure of GT tissue and the secretion of its content but also qualitatively and quantitatively analyze the secondary metabolites in GT and reveal its metabolic regularity. Through this method, we can also establish a transcriptional map during the development of GT and explain the mechanism of the development of GT and its component accumulation at the level of gene expression. To reveal the growth and development mechanism of GTs, their secondary metabolites and their accumulation mechanism not only provide ideas and a basis for variety selection and quality evaluation of medicinal plants but also lay a foundation for the artificial synthesis and large-scale production of GT active ingredients.

This paper summarizes the types, separation and purification technologies, and analysis technologies of secondary metabolites of GTs in medicinal plants and the

biological activities of secondary metabolites in GTs. We hope to provide a reference for future research on GTs and the breeding of medicinal plants and the development of new drugs.

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