

A systematic summary of natural compounds in *Radix Glycyrrhizae*

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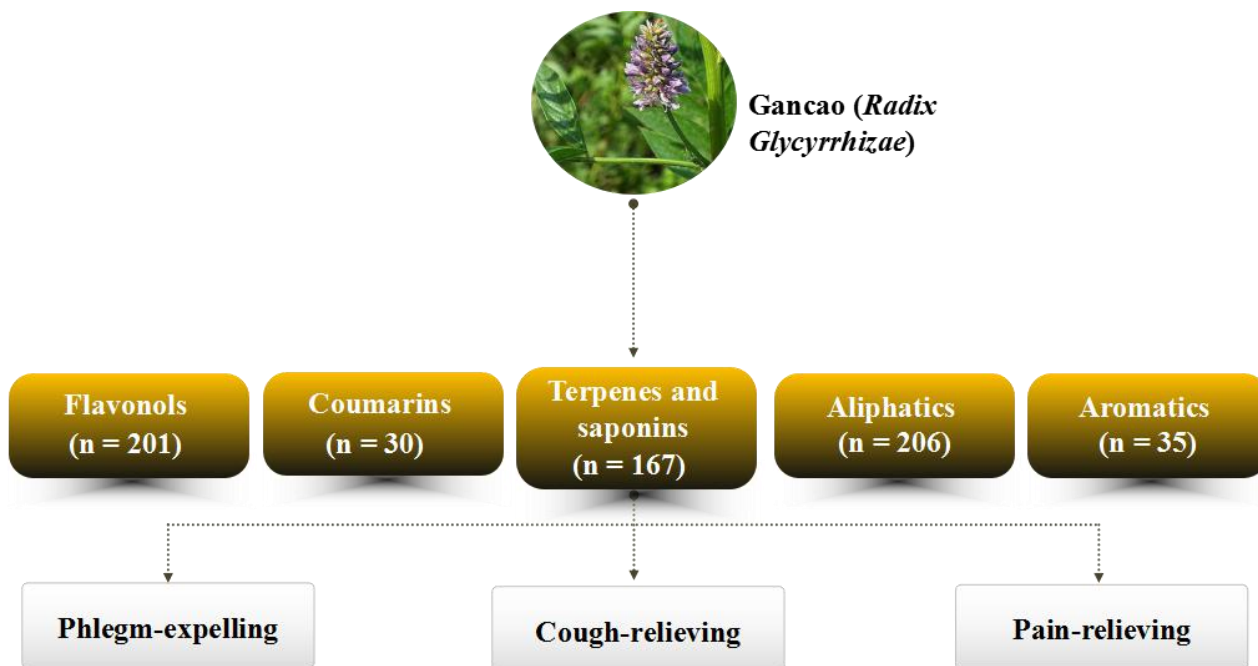
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Highlights

This study provides a basis for further study on molecular mechanisms of anti-inflammatory, phlegm-expelling, cough- and pain-relieving activities of Gancào (*Radix Glycyrrhizae*).

Editor's Summary

Gancào (*Radix Glycyrrhizae*) was first recorded in *Shennongbencaojing*, which was published in the **third century A.D.** (Han Dynasty of China).



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Abstract

Objective: To accumulate data from studies on the compounds identified from Gancao (*Radix Glycyrrhizae*, GC), and then systematically summarize and classify these compounds according to their structural characteristics. **Methods:** Five databases (CNKI, VIP, Wanfang data, CBM, and Pubmed) were used to search for studies on the chemical structure of compounds from GC. The retrieval time of the respective databases was from their inception to March 2016. According to the inclusion and exclusion criteria, the papers were carefully screened, and the data were extracted. **Results:** A total of 653 compounds from GC were collated from 252 articles, including flavonols (n = 201) belonging to 10 subgroups, terpenes and saponins (n = 167), coumarins (n = 30) belonging to 3 subgroups, aliphatics (n = 206), aromatics (n = 35), and others (n = 14). The flavones, represented by liquiritin and liquiritigenin, were the most reported compounds isolated from GC, followed by terpenes and saponins such as glycyrrhizic acid and glycyrrhetic acid. **Conclusion:** The more than 600 natural compounds in GC may be responsible for GC's anti-inflammatory, phlegm-expelling, cough- and pain-relieving activities.

Keywords: *Radix Glycyrrhizae*, Flavonol, Terpene, Saponin

摘要

目的: 本文通过汇总研究甘草成分的报道, 系统整理甘草所含成分, 并进行归类、分析和评价。

方法: 计算机检索中国知网 (CNKI)、万方 (Wanfang Data)、维普 (VIP)、中国生物医学文献数据库 (CBM) 和Pubmed五个数据库, 收集报道甘草中化学成分的相关文献, 检索时限均为从建库至2016年3月。按纳入与排除标准筛选文献、提取资料, 采用循证研究的方法进行分析。

结果: 共整理汇总了关于甘草成分研究的252篇中英文文献, 包括 653个天然成分, 其中黄酮类有10个亚类201个成分, 萜类及皂苷类167个成分, 香豆素类3个亚类30个成分, 脂肪族类化合物206个成分, 芳香族类化合物35个与其它类化合物14个成分。研究最多的成分是甘草中的黄酮类 (以甘草苷及甘草素为代表), 其次是萜类/皂苷类 (以甘草酸及甘草次酸为代表)。

结论: 这600多甘草天然成分是临床甘草制品的抗炎、祛痰止咳和止痛等作用的主要物质基础。

关键词: 甘草; 黄酮; 萜; 皂苷

Abbreviations: GC, Gancao (*Radix Glycyrrhizae*)

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Background

Gancao (*Radix glycyrrhizae*, GC), also known as honey grass, is famous for its sweet taste. GC comprises the dry roots and rhizomes of the perennial herb licorice, Guangguogancao (*Glycyrrhiza glabra* L), and Zhangguogancao (*Glycyrrhiza inflata* bat), which is mainly found in regions spanning from northern of China to inner Mongolia, Gansu. The book of *Shennongbencaojing*, from the Donghan Dynasty of China (the third century A.D.), pointed out that GC can not only strengthen bones and long muscles, but also possesses detoxification abilities. According to the *Chinese Pharmacopoeia*, the dry roots and rhizomes of GC have the ability to replenish Qi, tonify spleen, along with heat-clearing, toxicity-preventing, phlegm-dispelling, and cough-, spasm- and pain-relieving abilities, thereby harmonizing the effects of other medicines [1]. In recent years, pharmacological studies have shown that GC has anti-ulcer, anti-inflammatory, anticonvulsant, anti-tumor, anti-HIV, anti-allergic, antitussive, analgesic, and antispasmodic properties, along with the ability to lower blood cholesterol, increase bile secretion, and other pharmacological effects. In addition to its traditional use, clinically, components of GC, such as glycyrrhizic acid, glycyrrhetic acid, liquiritigenin, isoliquiritigenin, and other natural compounds, have been used to make drugs and pharmaceutical preparations commonly used in the treatment of peptic ulcers, hyperlipidemia, depression, tuberculosis, bronchial asthma, viral hepatitis, thrombotic vasculitis, contact dermatitis, allergic dermatitis, eczema, and so on. In traditional Chinese medicine, it is the specific natural ingredient that plays an important role in the pharmacological aspects and treatment effect. Recently, a variety of flavonoids, terpenoids, and saponins have been isolated from GC; some coumarins and other ingredients have also been found. Although there are many studies about the composition and structures of the components of GC, there is a lack of comprehensive and systematic classification and review, especially about its main bioactive ingredients. This article systematically collates reports about the chemical constituents of GC, and summarizes them according to the frequency of their reports.

Materials and methods

Inclusion and exclusion criteria

Inclusion criteria: Research articles on various chemical constituents of GC, such as structural identification, chemical composition analysis, and fingerprint mapping.

Exclusion criteria: Review articles on GC contained in Chinese traditional patent formulation or GC preparations, extraction methods, or pharmacological effects.

Document retrieval

CNKI, Wanfang Data, VIP, CBM, and Pubmed database were used to collect articles about the chemical constituents from GC. The retrieval period was from the

time of inception of the respective database to March 2016. For title-based searches, the English search terms were as follows: glycyrrhizae, component, ingredient, composition and constituent. In case of Pubmed, for example, the specific search strategy is shown in Table 1.

Table 1 The search strategy

Search words	
#1	Glycyrrhiza [Title]
#2	Component [Title] or Ingredient [Title] or Composition [Title] or Constituent [Title]
#3	#1 And #2

Data extraction

Excel software was used to develop the data extraction table, including the Chinese and English name, chemical name, molecular formula, molecular weight, and structure of each component. The extracted information was classified and aggregated. Information on similar chemical compositions was collated, and the number of studies reported was counted. The compositions were then classified into several categories according to the structural characteristics, and the number of components in various categories was counted.

The components of GC, whose composition was reported only once were listed in the table, whereas those whose composition was reported in more than two reports were included in the figure. According to the numbers reported in the literature, the order of the licorice components in the chart was determined.

Results

Literature search results and basic information

A total of 1756 studies were acquired, among which 1701 were retrieved from five databases, including CNKI, Wanfang Data, VIP, CBM, and Pubmed database. The remaining 55 articles were obtained from other resources. In total, 743 articles were obtained after ticking. 403 articles were obtained by reading the essays and abstracts, and 252 articles about natural components of GC were obtained by reading the full text. The article screening process and the results are shown in Figure 1.

Finally, a total of 653 natural components were collated from the 252 articles, and according to their chemical structure, they were classified into flavonoids (201 species, 200 articles), terpenoids and saponins (167 species, 153 articles), coumarins (30 species, 29 articles), aliphatic compounds (206 species, 27 articles), aromatic compounds (35 species, 14 articles), and other compounds (14 species, 17 articles). Five categories of natural components are described below.



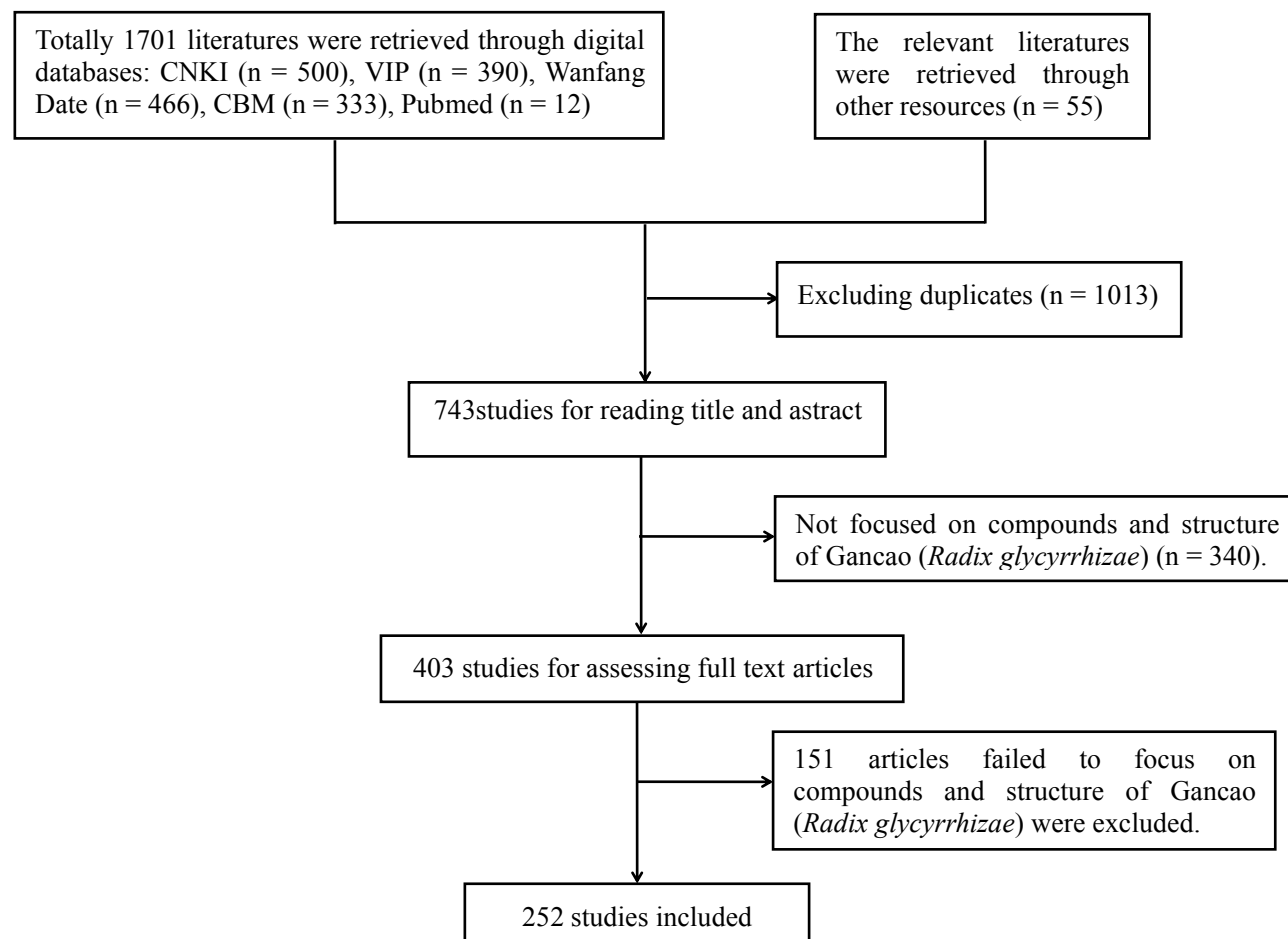


Figure 1 Flowchart of study selection

Flavonoids

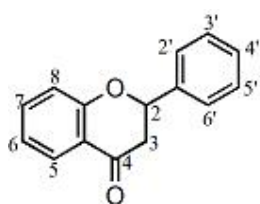
In the 252 studies on the constituents of GC, 201 flavonoids were reported in 200 articles. The basic skeleton of flavonoids is C6-C3-C6, which can be divided into nine motifs, flavanones (38 components, 133 articles), isoflavones (49 components, 60 articles), flavones (25 components, 44 articles), chalcone (24 components, 100 articles), flavonols (23 components, 23 articles), isoflavans (19 components, 31 articles), pterocarpan (6 components, 13 articles), isoflavanones (4 components, 9 articles), and isoflavones (4 components, 7 articles). The remaining was classified into other flavones (9 components, 8 articles). The details are listed as follows.

Flavanones. There were 38 types of flavanones, with their structures being reported in 133 articles, of which seven components were reported by more than two articles, including liquiritin in 94 articles, liquiritigenin in 56 articles, liquiritigenin-4'-apiosyl (1-2)-glucoside in four articles, isogrolrol in four articles, liquiritigenin-7,4'-diglucoside in three articles, glabranin in two articles, and pinocembrin in two articles. Their structures are shown in [Figure 2](#). The other 31 flavanones were reported only in one article, and are listed in [Table 2S](#).

Isoflavones. We collated 49 isoflavones, and their structures were reported by 60 articles, of which 15 components were reported by more than two articles, and their structures are shown in [Figure 3](#). There were twenty-three studies about formononetin, fourteen articles on ononin, eight articles on glabrone, seven articles on licoisoflavone A, four articles on 4',7-dimethoxyisoflavone, licoricone, isoononin, and licoisoflavone B, three articles on calycosin, prunetin, and lupiwighteone, and two articles on 5,7,4'-trihydroxy-6,8-diisoprenylisoflavone, semilicoisoflavone B, gancaonin H, and gancaonin G. The other 34 isoflavones were reported by only one study, and are listed in [Table 3S](#).

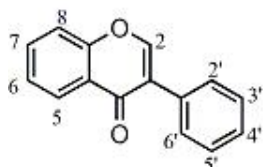
Flavones. The types of flavones and their structures were reported in 44 studies; 10 compounds were reported by more than two articles, and the structures are shown in [Figure 4](#). Among them, fourteen articles were on 4',7-Dihydroxy-flavone; eleven articles on liquiritinapioside; nine articles on licoisoflavone C; seven articles on licoisoflavone; four articles on isoviolanthin; four articles on licoisoflavone B; three articles on kanzonol E; two articles about schaftoside, violanthin, and genkwanin. The other 17 components were reported only once, and are listed in [Table 4S](#).





Liquiritin	7-OH, 4'-O-glu
Liquiritigenin	7-OH, 4'-OH
Liquiritigenin-4'-apiosyl(1-2)-glucoside	7-OH, 4'-O-glu-api
Isoglabrol	6-prenyl, 7-OH, 8-prenyl, 4'-OH
Liquiritigenin-7,4'-diglucoside	7-O-glu, 4'-O-glu
Glabranin	5-OH, 7-OH, 8-prenyl
Pinocembrin	5-OH, 7-OH

Figure 2 Chemical structures of main flavanones



Formononetin	7-OH, 4'-OCH ₃
Ononin	7-O-glu, 4'-OCH ₃
Glabrone	7-OH, 2'-OH, 3', 4'-a
Licoisoflavone A	5-OH, 7-OH, 2'-OH, 3'-prenyl, 4'-OH
4',7-Dimethoxyisoflavone	7-OCH ₃ , 4'-OCH ₃
Licoricone	7-OH, 2'-OCH ₃ , 3'-prenyl, 4'-OCH ₃ , 6'-OH
Isoononin	7-OCH ₃ , 4'-O-glu
Licoisoflavone B	5-OH, 7-OH, 2'-OH, 3', 4'-a
Calycosin	7-OH, 3'-OH, 4'-OH
Prunetin	5-OH, 7-OCH ₃ , 4'-OH
Lupiwightone	5-OH, 7-OH, 4'-OH, 8-prenyl
5,7,4'-trihydroxy-6,8-diisoprenylisoflavone	5-OH, 6-prenyl, 7-OH, 8-prenyl, 4'-OH
Semilicoisoflavone B	5-OH, 7-OH, 2'-OH, 3', 4'-a
Gancaonin H	5-OH, 6-prenyl, 7-OH, 2'-OH, 3', 4'-a
Gancaonin G	5-OH, 6-prenyl, 7-OCH ₃ , 4'-OH

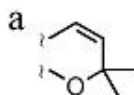
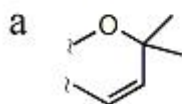
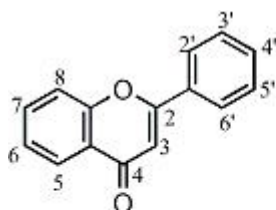
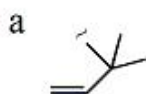
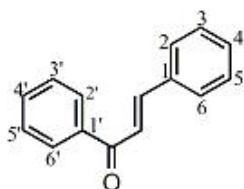


Figure 3 Chemical structures of main isoflavones



4',7-Dihydroxy-flavone	7-OH, 4'-OH
Liquiritinapioside	7-OH, 4'-O-glu-api
Licoflavone C	8-prenyl, 5-OH, 7-OH, 4'-OH
Licoflavone	6-prenyl, 7-OH, 4'-OH
Isoviolanthin	5-OH, 6-C-rha, 7-OH, 8-C-glu, 4'-OH
Licoflavone B	6-prenyl, 7-OH, 3'-prenyl, 4'-OH
KanzonolE	6-prenyl, 7-OH, 3', 4'-a
Schaftoside	5-OH, 6-C-glu, 7-OH, 8-C-arab, 4'-OH
Violanthin	5-OH, 6-C-glu, 7-OH, 8-C-glu, 4'-OH
Genkwanin	5-OH, 7-OCH ₃ , 4'-OH

Figure 4 Chemical structures of main flavones



Isoliquiritigenin	4-OH, 2'-OH, 4'-OH
Isoliquiritin	4-O-glu, 2'-OH, 4'-OH
Licochalcone A	2-OCH ₃ , 4-OH, 5-a, 4'-OH
Glypallchalcone	2-OCH ₃ , 4-OH, 4'-OCH ₃
Licuraside	4-O-glu-api, 2'-OH, 4'-OH
Isoliquiritin apioside	4-O-glu-api, 2'-OH
Licochalcone B	2-OCH ₃ , 3-OH, 4-OH, 4'-OH
Licochalcone D	2-OCH ₃ , 3-prenyl, 4-OH, 2'-OH, 4'-OH
Licochalcone C	2-OCH ₃ , 3-OH, 4-OH, 3'-prenyl, 4'-OH
Rhamno-isoliquiritin	4-O-glu-rha, 2'-OH, 4'-OH
Tetrahydroxy-methoxychalcone	2-OCH ₃ , 3-OH, 4-OH, 3'-OH, 4'-OH

Figure 5 Chemical structures of main chalcone

Chalcone. There were 24 components of chalcone, and their structures were reported in 100 papers. There were eleven kinds of ingredients reported at least twice, of which there were 56 studies on isoliquiritigenin, 35 articles on isoliquiritin, 29 articles on licochalcone A, 12 articles on glypallichalcone, 11 articles on isoliquiritin apioside, 9 articles on licuraside, 7 articles on licochalcone B, 4 articles on licumalcone D, 3 articles on licochalcone C, 3 articles on rhamno-isoliquiritin, and 2 articles on tetrahydroxy-methoxychalcone. Their structures are shown in Figure 5. The other 13 components were reported only once, and are listed in Table 5S.

Flavonols. There were 23 articles that reported 23 kinds of ingredients and the structure of flavonols, of which there were five articles on licoflavonol and isoquercitrin, 4 articles on rutin, 3 articles on glycyrrhiza-flavonol A and isolicoflavonol, and 2 articles on uralenol, neouralenol, licobenzofuran, and astragulin. The other 14 components were reported by only one study, and are listed in Table 6S. The nine aforementioned components were reported by more than two articles, and their structures are shown in Figure 6.

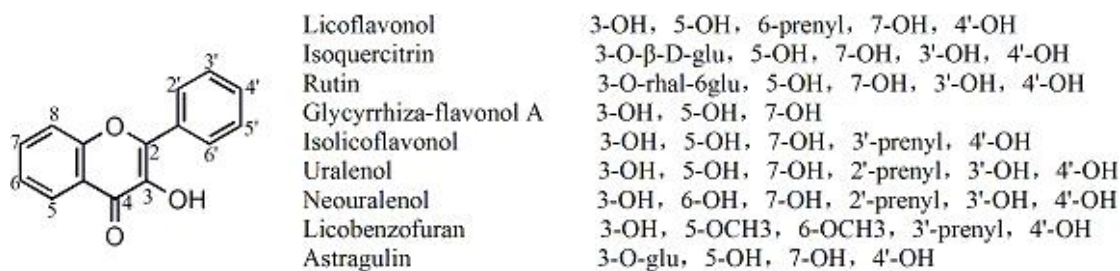


Figure 6 Chemical structures of main flavonols



Figure 7 Chemical structures of main isoflavans

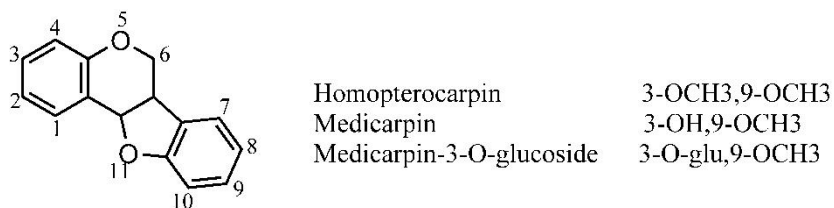


Figure 8 Chemical structures of main pterocarpanes

Isoflavans. There were 31 articles that reported 19 components of the isoflavans and their structures, of which 9 components were reported by two or more than two articles (Figure 7), including glabridin in 11 articles, licoricidin in 8 articles, phaseollinisoflavane and vestitol in 3 articles, and 4'-O-methylglabridin, hispaglabrinein A, hispaglabridin B, licorisoflavan A, and glyasperin D in 2 articles. The other 10 components were reported only once (Table 7S).

Pterocarpanes. There were 13 articles that reported six components of pterocarpanes and their structures, of which 3 components were reported by two or more articles (Figure 8), including homoptercarpin in 7 articles, medicarpin in 6 articles, medicarpin-3-O-glucoside in 3 articles. 10-methoxy medicarpin, mei dexualine, and 1-methoxyphaseollidin were reported in only one article.

Isoflavanones. The four components of isoflavanones and their structures were reported in nine studies. Among them, there were 4 articles on glisoflavanone, 3 articles on licoisoflavanone, 2 articles on 3'-(γ,γ-dimethylallyl)-kievitone, and 1 article on dihydrolicoiso. Three components were reported by two or more than two articles (Figure 9).

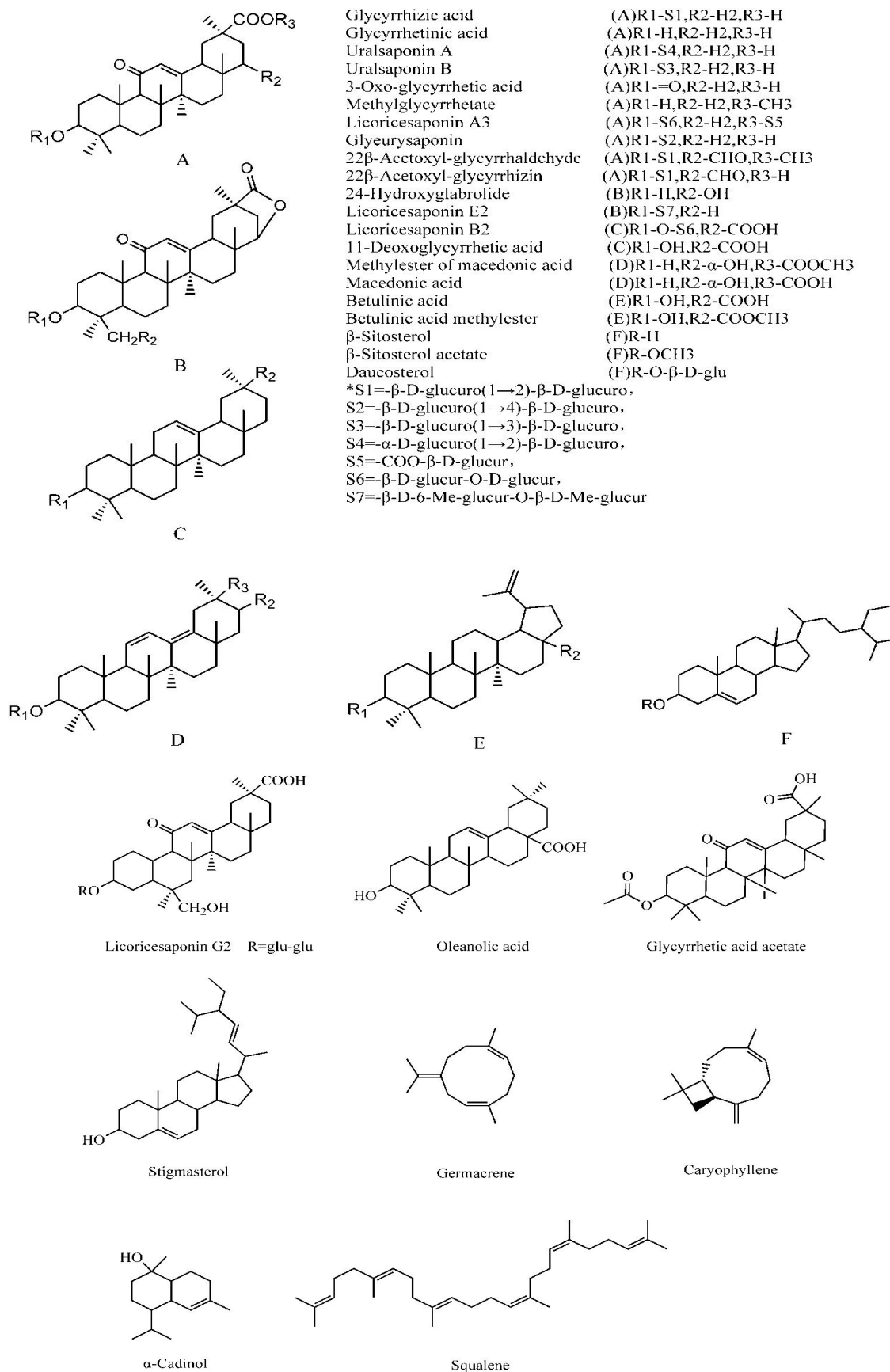


Figure 12 Chemical structures of main terpenes and saponins

reported 12 components of 3-aryl coumarins, 16 articles reported 14 components of coumestan, and 4 articles reported 4 components of other coumarins. Licorice coumarin is divided into three categories according to the structure; the first category is 3-arylcoumarin, the second category is coumestan, and the third category is other coumarins.

3-Arylcoumarins. There were 17 reports involving 12 components of 3-Arylcoumarins and their structures, of which there were 8 articles on glycy coumarin, 2 articles on glycyrin, licopyranocoumarin, and licofuranocoumarin. The other 8 components were reported only once (Table 10S). A total 4 components were reported by two or more articles (Figure 13).

Coumestans. There were 14 components of coumestans with their structures reported in 16 articles, of which 4 components were reported by two and more articles, including glycyrol in 7 articles, isoglycyrol in 5 articles; 5-O-methyl-glycyrol, and neoglycyrol in 2 articles; The other 10 compounds were reported only in one article listed in Table 11S. A total 4 components were reported by two and more articles (Figure 14).

Other coumarins. There were 4 components of other coumarins with their structures reported in 4 articles. Each component is reported by only one study. These components are: 1-methoxyphyllol, 6,7-dihydroxycoumarin, 7-methoxycoumarin, and glycyrrhizol B.

Aliphatic compounds

There were 206 components of aliphatic compounds with their structures reported in 27 articles. They mainly comprised 84 types of alkanes, 22 types of olefins, 28 types of acids, 9 types of aldehydes, 24 types of esters, 19 types of ketones, and 20 types of alcohols. A total 14 components were reported by three and more articles. Among them, there were 6 studies on heptadecane, octadecane, nonadecane, eicosane, 5 studies on linoleic acid and hexadecane, 4 studies on hexacosane, and 3 studies on hexanoic acid, hexadecanoic acid, pentadecane, 2,6,10,14-tetramethyl-hexadecane, octadecane, octane, and 1-octadecene. The chemical structures of 14 main components were shown in Figure 15. There were 40 components reported by 2 studies (Table 12S), and 152 components reported by 1 study (Table 13S).

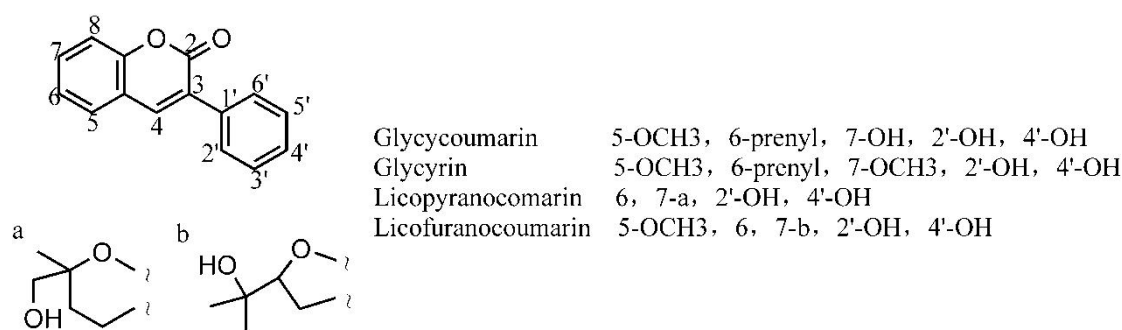


Figure 13 Chemical structures of main aliphatic compounds

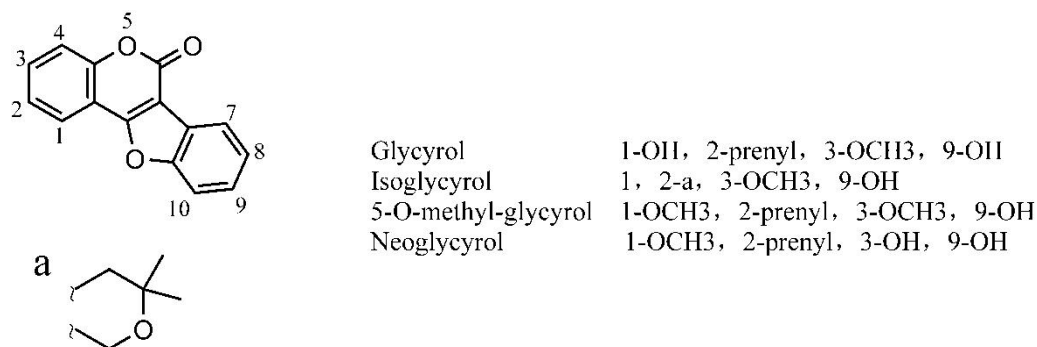


Figure 14 Chemical structures of main coumestans

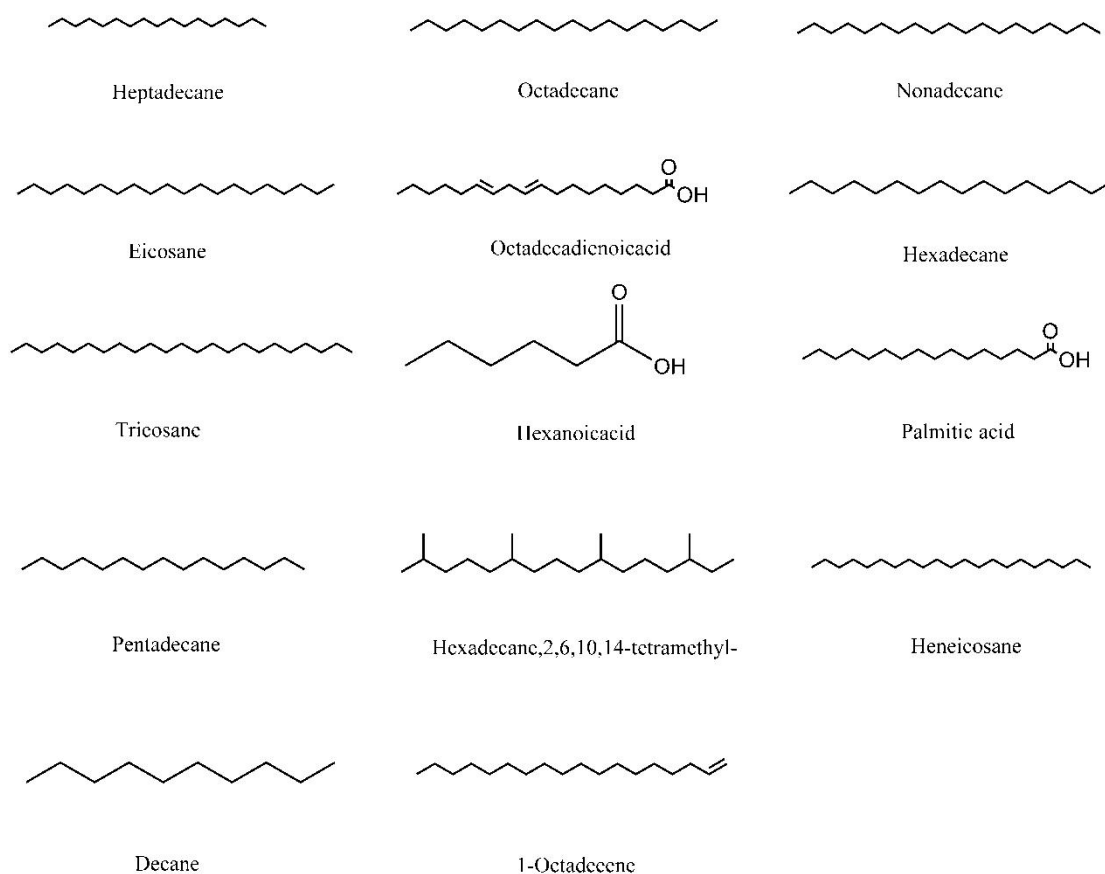


Figure 15 Chemical structures of main coumestans

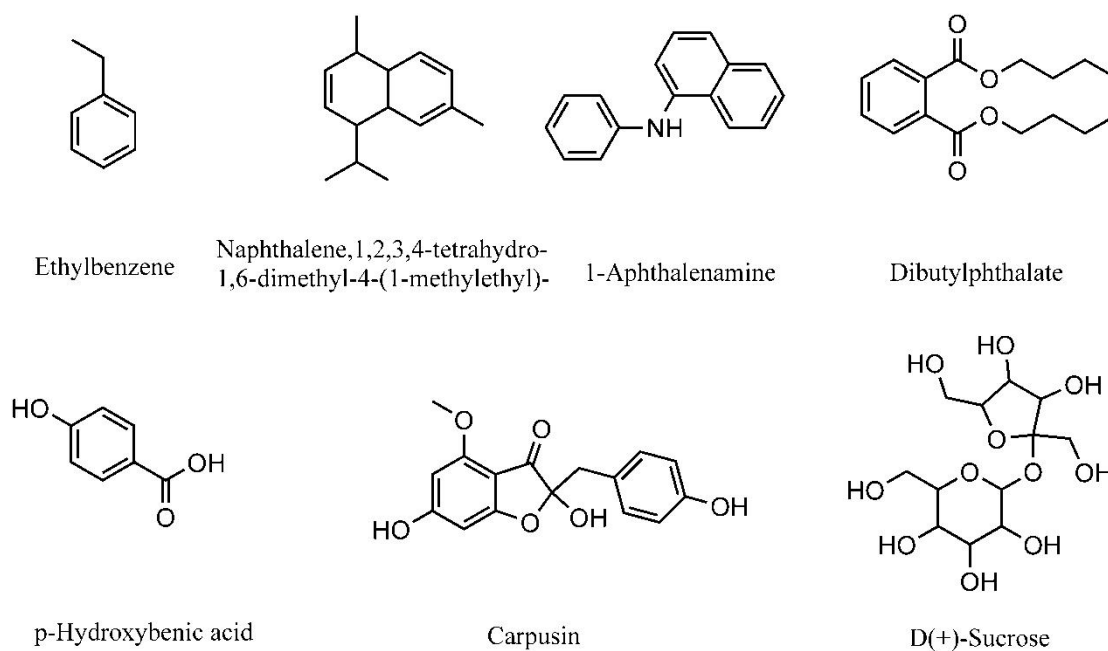


Figure 16 Chemical structures of main aromatic compounds and other compounds

Among the 206 constituents of the aliphatic compounds, there were n-alkanes containing from 5 to 8, 11 to 23, 25 to 30, 32, 34 to 36 carbons and from 1, 5 to 10, 12 to 14, 16, 18, 19, 21 carbon-carbon chains and cyclic carbons. The alcohols include: 1, 4, 6, 15, 18, 22, 27 carbon positive alcohols and with a substituent containing 2, 4, 6, 8, 16, 18 carbon chain and ring carbon alcohol. The aldehydes included 6, 7, 9, 11 to 15 carbon atoms, and a carbon chain containing 16 carbon atoms with substituents. The acids included 2, 4, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 18, 20, 22, 24, 26 carbonic acid and the presence of substituents with 2, 18, 30 carbon chains and ring-forming carbon acids. Ketones included 3, 7, 9, 11, 14, 15 carbon-containing ketones and 5, 6, 8, 10, 11, 15 carbon chains and ketones with ring-forming carbon. Esters included 2, 3, 6, 8, 14, 16, 18, 22, 24 carbon-containing acid, and methyl ester, ethyl ester, propyl ester, butyl ester combination.

Among them, there were 23 kinds of substituted compounds having carbon chains of 6 carbon, and 14 kinds of substituted compounds having carbon chains of 5 carbons and 18 carbons, respectively. There were 12 kinds of substituted compounds having 8 carbon chains. There were 11 kinds of substituted compounds in which the carbon chain contained 7 carbons. There were 10 kinds of substituted compounds having carbon chains containing 16 carbons.

Aromatic compounds and other compounds

There were 35 components of aromatic compounds with their structures reported in 14 articles. Among them, there were 3 studies on ethylbenzene, naphthalene, 1,2,3,4-tetrahydro-1,6-dimethyl-4-(1-methyl-ethyl)-, and 1-aphthalenamine, and 2 articles on dibutylphthalate and p-hydroxybenzoic acid. The other 30 compounds were reported only in one article listed in Table 14S. A total 5 components were reported by two or more articles (Figure 16).

There were 17 papers reporting the other 14 components and their structures, of which there were three articles on D (+)-sucrose and 2 articles on carpusin. The other 12 compounds were reported only in one article, and are listed in Table 14S. A total of two components were reported by two and more articles (Figure 16).

Discussion

Our study brings together more than 250 studies on the components of GC and categorizes them to sort out all the ingredients that have been isolated and reported so far. We found that flavonoids and terpenes/saponins are the most active components. Among them, the flavonoids comprise mainly isoflavones such as formononetin and ononin, flavanones such as liquiritin and liquiritigenin, flavones such as 4',7-Dihydroxy-flavone and liquiritinapioside, and chalcones such as isoliquiritigenin and isoliquiritin. The terpenes/saponins comprise tricyclic triterpenes such as glycyrrhizic acid and glycyrrhetic acid. In addition, GC also contains a small number of components of coumarins.

China Pharmacopoeia 2015 edition has the requirements for determination the content of GC, that is, determination of the content of liquiritin (dihydrogen flavonoids) and glycyrrhizic acid (tricyclic triterpenoids). We can see that the two active ingredients on the role of GC have a huge impact. Here we mainly discuss reports on flavonoids such as liquiritin, liquiritigenin, 4',7-Dihydroxy-flavone, liquiritinapioside, formononetin, ononin, glabridin, isoliquiritin, isoliquiritigenin, and licochalcone A and terpenoids/saponins such as glycyrrhizic acid, glycyrrhetic acid, β -sitosterol, and betulinic acid.

Licoflavones

Our research showed that among all constituents of GC, the flavanones are the most reported. Among the flavanones, liquiritin is the most reported, followed by liquiritigenin. Liquiritigenin is an aglycone of liquiritin, which mainly has an anti-cancer effect. Liquiritin has antidepressant [4], neuroprotective [5], myocardial cell-protective [6], and detoxification effects, along with many other therapeutic properties [7].

The most reported species of isoflavones was formononetin, followed by ononin. Formononetin is a weak phytoestrogen [8], which is a major ingredient of pratensein. It has anti-inflammatory [9], anti-cancer [10-12], and anti-tumor activities, as well as anti-osteoporosis [13] and anti-atherosclerotic [14] properties.

Among the chalcones, the composition of isoliquiritigenin was the most reported, followed by isoliquiritin. Isoliquiritigenin is an aglycone of isoliquiritin, with anti-cancer [15], anti-inflammatory [16], anti-oxidative [17], anti-HIV [18], and antispasmodic effects [19,20]. It also has a protective effect on the brain [21], liver [22], lung [23], gastrointestinal region [24]. Isoliquiritigenin is an aldose reductase inhibitor, which can significantly prevent the occurrence of diabetic complications [25]. Licochalcone A is a type of chalcone constituent specific for the genus *Glycyrrhiza glabra*, and has anti-inflammatory, anti-cancer, anti-tumor, antibacterial, antimalarial, and antiparasitic effects [26].

In addition, 4',7-dihydroxy-flavone and liquiritinapioside are the most reported flavonoids, but there are still very few reports about their pharmacological effects. Glabridin is a isoflavan-specific component of the genus *Glycyrrhiza glabra* L, which has antioxidant [27], anti-atherosclerosis, hypolipidemic, blood pressure-lowering [28], anti-inflammatory, and tyrosine-inhibiting effects, as well as whitening [29], neuroprotective and memory-enhancing properties [30]. The whitening mechanism of glabridin involves the inhibition of tyrosine activity, which prevents the binding of the substrate and tyrosinase, ultimately inhibiting the synthesis of melanin [29].

Licoflavones mainly display anti-inflammatory, anti-oxidant, anti-aging, anti-viral, anti-tumor, sedative, analgesic, enzyme-inhibiting effects. Its anti-cancer mechanism involves the inhibition of cell cycle, destruction of DNA, and induction of apoptosis [15]. Its



anti-inflammatory mechanism involves the inhibition of cyclooxygenase activity, thereby inhibiting the production of arachidonic acid [16]. Its anti-HIV mechanism involves inhibiting the production of HIV reverse transcriptase and protease [17]. Its antioxidant mechanism involves the elimination of free radicals and superoxide radicals, via the termination of a free radical chain reaction.

Glycyrrhiza terpenoids/saponins

Glycyrrhizic acid is the most reported glycyrrhiza terpenoid compound, followed by glycyrrhetic acid. Glycyrrhetic acid is the aglycone of glycyrrhizic acid; it mainly has anti-inflammatory, liver protective, anti-tumor, and anti-fibrotic effect. Its anti-inflammatory effect involves the inhibition of lipoxygenase and phospholipase A2 [6]; its hepatoprotective effect is achieved through the increased mobility of protein family 1 BOX-A binding, reduction of protein family 1 content, while increase the role of interleukin-6,10 [31, 32]. Its antitumor effect involves the inhibition of the proliferation of cancer cells by inhibiting the nucleotide reductase and decreasing the activity of DNA synthesis rate-limiting enzymes [33]. Its anti-fibrosis effect is achieved by reducing the synthesis of collagen type I and III [34]; Glycyrrhizic acid is also a steroid hormone metabolic enzyme inhibitor, which can improve endogenous and exogenous corticosteroid activity [35]. Glycyrrhizic acid is clinically used for a variety of acute and chronic hepatitis or liver injury [36], as an anti-cancer agent [37], for anti-AIDS treatment [38], and for modulating immunity [39].

Studies on the constituents of other triterpenes were lesser in number than those on glycyrrhizin and glycyrrhetic acid. More than 5 studies have been reported on β -sitosterol, betulinic acid, uralsaponin B, and daucosterol; there were very few reports about uralsaponin B. Daucosterol is the 3-O-glucoside of sitosterol; daucosterol, β -sitosterol [40], and betulinic acid [41] have anti-inflammatory, anti-oxidative, tumor-inhibitory, and immunoregulatory effects, and these three components are widely distributed in vegetables, seeds, and herbs.

Aliphatic and aromatic

In addition to flavonoids, terpenoids, saponins and coumarins, aliphatic and aromatic also form a proportion of the components of GC. In fatty acids, linoleic acid and palmitic acid have been frequently reported. Palmitic acid is the main ingredient of palm oil, which can delay the process of alcoholic liver disease and reduce serum cholesterol levels; linoleic acid is the main component of sesame oil; both linoleic acid and its methyl esters have anti-inflammatory effects. It acts by reducing the levels of IL-1 β , TNF- α , and NO at the inflammatory site. Aromatic compounds were mostly reported in only one study, and no pharmacological reports of these compounds were reported, and therefore this has not been discussed here.

Conclusion

A total of 252 reports on GC components were collected. In total, 653 components of GC were sorted and classified and their structures were drawn. They included 10 subspecies of flavonoids, terpenoids/saponins, 3 subclasses of coumarins, aliphatic compounds, aromatic compounds, and other compounds. The results showed that the most studied components were flavonoids (liquiritin and liquiritigenin as the representatives), followed by terpenoids/saponins (represented by the pentacyclic triterpene glycyrrhizic acid and glycyrrhetic acid). We speculate that these two components have anti-inflammatory, antioxidant, anti-viral, anti-tumor, and other pharmacological effects; they also possess spleen tonifying, Qi-replenishing, heat-clearing, cough- and emergency pain-relieving, and expectorant effects. Therefore, we will use these components of GC for further research to explore the molecular mechanisms underlying the effects of the components of GC.

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