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Review

Research progress of Chinese herbal medicine compounds and their bioactivities: Fruitful 2020

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ABSTRACT

Traditional Chinese medicines (TCMs) have continued to be a treasure trove. The study of chemodiversity and versatility of bioactivities has always been an important content of pharmacophylogeny. There is amazing progress in the discovery and research of natural components with novel structures and significant bioactivities in 2020. In this paper we review 271 valuable natural products, including terpenoids, steroids, flavonoids, phenylpropanoids, phenolics, nitrogen containing compounds and essential oil, etc., isolated and identified from TCMs published in journals of *Chinese Traditional and Herbal Drugs* (Zhong Cao Yao) and *Chinese Herbal Medicines* (CHMs), and focus on their structures, source organisms, and relevant bioactivities, paying special attention to structural characteristics of novel compounds and newly revealed pharmacological properties of known compounds. It is worth noting that natural products with antitumor activity still constitute the primary object of research. Among the reported compounds, two new triterpenoids, i.e., ursolic acid 3-*O*-*β*-*cis*-caffeate and mollugoside E, display remarkable cytotoxicity against PC-9 and HL-60 cell lines, respectively. Three known phenolic compounds, i.e., pyoluteorin, 4-hydroxy-3-methoxy cinnamaldehyde and 3,7-dimethoxy-5-hydroxy-1,4-phenanthrenequinone, exhibit significant cytotoxicity against multiple cell lines. Numerous studies on the free radical scavenging activity of reported compounds are currently underway. *In vitro*, three known phenolic compounds, *i.e.*, 3,4-*O*-dicaffeoylquinic acid methyl ester, 3,4,5-*O*-tricaffeoylquinic acid methyl ester and arbutin, had more considerable antioxidant activities than vitamin C. The anti-inflammatory, anti-diabetic, hypolipidemic, neuroprotective and antimicrobial activities of isolated compounds are also encouraging. The structural characteristics and bioactivities of TCM compounds highlighted here reflect the enormous progress of CHM research in 2020 and will play a positive role in the future drug discovery and development. According to pharmacophylogeny, the phylogenetic distribution of compounds with different natures and flavors can be explored, with view to better mining TCM resources.

Contents

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1. Introduction

The concept of pharmacophylogeny was proposed by Peigen Xiao in the 1980 s based on long-term studies of Chinese researchers since ancient times and especially after 1949 (Hao & Xiao, 2020). The complicated relationships and connectivity between phylogenetic relationship of medicinal plants, their chemical profiles and therapeutic utilities are consistent goals of pharmacophylogeny studies, which benefit innovative drug R&D. The study of chemodiversity and versatility of bioactivities has always been an important content of pharmacophylogeny. The last decades have witnessed a keen interest in biologically active compounds isolated from large amounts of natural resources, especially traditional medicinal plants (Hao & Xiao, 2020). Facilitated by the extensive use of the state-of-the-art techniques in the field of natural medicine and pharmacognosy, the isolation, identification and characterization of numerous compounds with novel structures and/or significant biological activities have been achieved. For the period January to December 2020, Chinese scholars reported a total of 271 highlighted compounds, including those with novel structures (**1**–**65**) and known ones with newly revealed bioactivities (**66**–**271**) in journals of *Chinese Traditional and Herbal Drugs* (Zhong Cao Yao published in Chinese) and *Chinese Herbal Medicines* (CHM published in English). The structures of all novel compounds and known compounds are presented in Fig. 1 and Fig. S1, respectively. Most components are from terrestrial plants used in traditional Chinese medicine (TCM), and a few are from microorganisms and animals; the reported structural types are diverse, e.g., terpenoids, steroids, flavonoids, phenylpropanoids, phenolic compounds, nitrogen-containing compounds, miscellaneous compounds as well as essential oil components. Except essential oil, novel compounds are found from all other types, illustrating the efficiency of mining chemodiversity from biodiversity of TCM species (Hao et al., 2015; Hao, 2018, 2021). The spotlighted pharmacological activities are antitumor (anticancer), antioxidation, anti-inflammatory, anti-diabetic and hypolipidemic, antibacterial, neuroprotection and so on. These intriguing findings in 2020 inspire researchers in various fields to explore the mystery of TCM, and also enable us to constantly feel the magic charm of Chinese herbal medicine.

2. Phytochemistry

2.1. Terpenoids

Terpenoids are second only to flavonoids and alkaloids in terms of their wide distribution in seed plant families. >55,000 terpenoid compounds of at least 206 families have been isolated (Zhang, 2018). In 2020, three novel monoterpenoids, six sesquiterpenoids, one diterpenoid and eight triterpenoids were for the first time reported. Two normal type monoterpene glycosides are *trans*-linalool-3,6-oxide-7-*O*-*β*-*D*-(6′-*O*-acetyl)-glucoside (**1**) isolated from the pericarps of *Aquilaria yunnanensis* (Thymelaeaceae) and perillic acid glucoside (**2**) obtained from the roots of *Paeonia lactiflora* (Ranunculaceae) (Sun et al., 2020a; Yan, Liu, Zhang, & Hu, 2020). An iridoid-type monoterpene jasminoide A (**3**) is a constituent of the TCM preparation Reduning Injection (Li et al., 2020a). An eremophilane-type sesquiterpene syneilesis acid (**4**) exhibited 2-methyl-2-butenoic acid and a double-bond substitutions at positions C-3 and C-6, which was detected in the whole plants of *Syneilesis aconitifolia* (Asteraceae) (Wang et al., 2020a). Three guaiane-type sesquiterpenes, (1*R*,7*R*,8*S*,10*R*)-7,8,11-trihydroxy-4-guaien-3-one (**5**), commiphorol A (**6**) and ainslifragside A (**7**), were identified from the TCM preparation Reduning Injection, the resin of *Commiphora myrrha* (Burseraceae) and whole plants of *Ainsliaea fragrans* (Asteraceae), respectively (Ding et al., 2020; Li et al., 2020a; Liu, Li, Ding, Wang, & Qiu, 2020). 2*β*,8a*α*-Dihydroxy-11-en-eremophilane (**8**) belongs to the eremophilane-type sesquiterpene group, which was isolated from the resin-containing woods of *Aquilaria sinensis* (Thymelaeceae) (Lv et al., 2020). A rare megastigmane-type norsesquiterpene glycoside actinargutaside A (**9**), isolated from the fruits of *Actinidia arguta* (Actinidiaceae), is similar to (6*S*,9*R*)-roseoside, but differs in the location of methylene at C-2 (Li et al., 2020b). 1-Keto-tilifodiolide (**10**) possessing clerodane-type diterpene skeleton was found in the aerial parts of *Salvia tiliifolia* (Lamiaceae) (Fan, Duan, Xia, & Wang, 2020).

Four different types of triterpenoids were identified from seven kinds of Chinese herbal medicines. The ursolic acid 3-*O*-*β*-*cis*-caffeate (**11**), ursolic acid 3-*O*-*β*-*trans*-caffeate (**12**), phyllanacidol B (**13**) and 20-oxo-30-nortaraxastan-3*β*-yl acetate (**14**) belong to ursane-type pentacyclic triterpenoids; ginsenoside Ro_1 (**15**) and mollugoside E (**16**) belong to oleanane-type pentacyclic triterpenoids; dihydrobetulinic acid (**17**) is a lupinane-type pentacyclic triterpenoid; majoroside Z (**18**) is a dammarane-type tetracyclic triterpenoid. Compounds **11** and **12**, as *cis*–*trans* isomers, were from the barks and stems of *Melaleuca alternifolia* (Myrtaceae). The former has a *cis*-caffeoyl moiety linked at C-3 to a hydroxyl group of ursolic acid aglycone, while the latter has a *trans*-caffeoyl moiety linked at the same carbon (Chai, Chen, Lu, Lin, & Liu, 2020). The structure of compound **13** is silimar to that of ursolic acid aglycone except for a double bond rather than a methyl group at C-20 and a cinnamoyl moiety linked at C-3 to a hydroxyl group, as well as lack of a double bond at C-12(13) (Li et al., 2020c). Both compounds **13** and **14** contained the same skeleton, except for an acetoxyl moiety instead of a cinnamoyl moiety, and the ketone group rather than a double bond (Xue et al., 2020). The sugar moieties of oleanane-type triterpene saponins **15** and **16** are present at C-3 and C-28 hydroxyl groups of the oleanic acid aglycone respectively; there are four sugar units with the mode

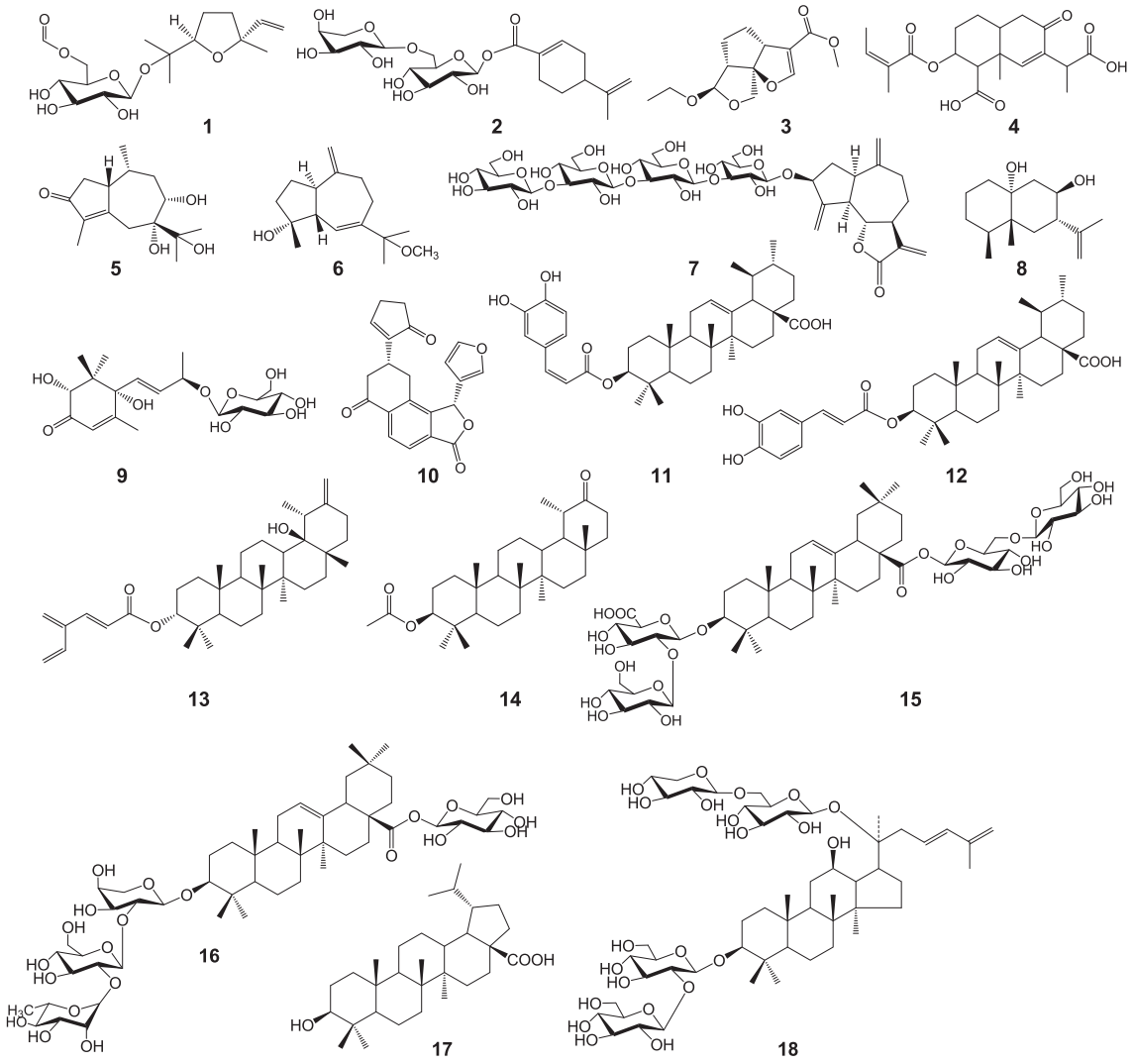

Fig. 1. Chemical structures of terpenoids.

of 1 → 2 or 1 → 6, which form a linear oligosaccharide chain (Wang et al., 2020b; Zuo, Li, Li, Wang, & Yang, 2020). Compound **17** has a methyl group instead of a double bond at C-20(29) of betulinic acid skeleton (Eignerova et al., 2017; Zhang, Xia, Xu, Chen, & Zhou, 2020). Compound **18**, as a dammarane-type triterpene saponin, has two double bonds groups attached to C-23(24) and C-25(26), along with sugar moieties such as glucose and xylose linked at C-3 and C-20 to hydroxyl groups (Zhang et al., 2020a). Compounds **13**–**18** were identified from the leaves of *Phyllanthus acidus* (Euphorbiaceae), whole plants of *Centipeda minima* (Asteraceae), roots of *Panax ginseng* (Araliaceae), aerial parts of *Mollugo pentaphylla* (Aizoaceae) and *Gendarussa vulgaris* (Acanthaceae), and the leaves of *Panax japnicas* var. *major* (Araliaceae), respectively. The structures of corresponding compounds are shown in Fig. 1.

Sesquiterpenes with diverse skeleton types are important members of the terpenoid family. Among them, the eremophilane-type and guaiane-type sesquiterpenes are mainly found in the Asteraceae. The former is widely present in genera *Ligularia*, *Senecio* and *Cacalia*. The latter was derived from genera *Youngia*, *Crepidiastrum*, *Saussurea*, *Atractylodes*, *Artemisia*, *Ambrosia*, *Carpesium*, *Ainsliaea*, and *Eupatorium*. The guaiane-type sesquiterpenes were also found in families Thymelaeaceae (*Wikstroemia* and *Stellera*), Zingiberaceae (*Curcuma*), Alismataceae (*Alisma*), Annonaceae (*Xylopia*), Umbelliferae (*Daucus* and *Torilis*), Valerianaceae (*Valeriana*), Euphorbiaceae (*Croton*), Rubiaceae (*Gardenia*), Lamiaceae (*Pogostemon*), Rutaceae and Araceae (*Acorus*) (Hou, Kulka, Zhang, Li & Guo, 2014). As isomers, oleanane-type and ursane-type pentacyclic triterpenoids are widely distributed in TCM plants (Hao, Gu & Xiao, 2017). Since 2000, >200 oleanane-type triterpenoids have been identified from 23 families, 30 genera and 52 species. Among these, numerous oleanane-type compounds were isolated principally from plants of families Fabaceae (*Medicago*), Myrsinaceae (*Maesa*) and Primulaceae (*Lysimachia*) (Li, Su, Hong, Zhu & Li, 2020). Since 2015, ursane-type triterpenoids were mainly obtained from 14 families, *i.e.*, Aquifoliaceae, Lamiaceae, Rosaceae, Actinidiaceae, Myrtaceae, Caryophyllaceae, Fagaceae, Araliaceae, Loniceraceae, Symplocaceae, Umbelliferae, Verbenaceae, Cactaceae and Rubiaceae, especially from the first three (Deng, et al., 2020). The continuous accumulation of compound data is conducive to investigating the phylogenetic signal of compound distribution and bioprospecting (Hao & Xiao, 2020).

2.2. Steroids

Steroid secondary metabolites are found in at least 153 seed plant families (Zhang, 2018). Among the novel compounds reported in 2020, six steriods (**19**–**24**) are classified into two groups on the basis of the carbon framework: C_{21} steroids and fur-

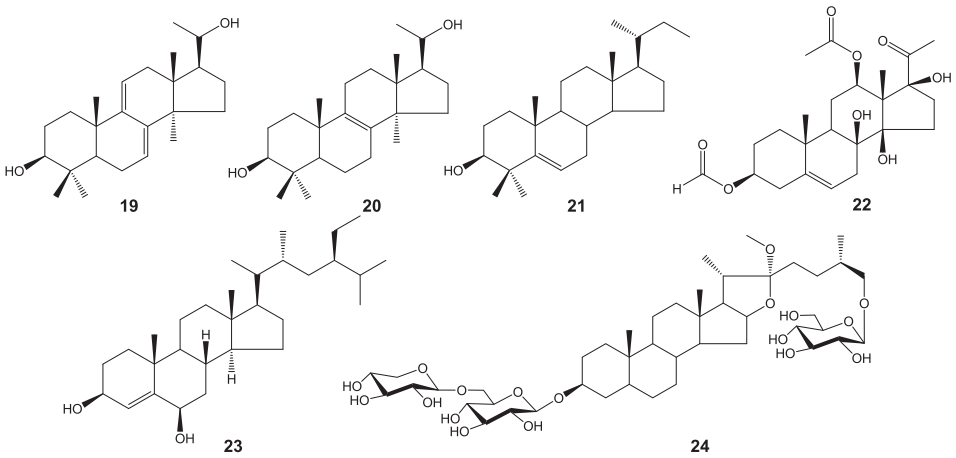

Fig. 2. Chemical structures of steroids.

ostanol steroids. Five new C_{21}-type steroids, i.e., gvterpennoid A (**19**), 4,4,14α-trimethypregn-8-en-3β,20α-diol (**20**), 24-norchol-5-en-3β-ol (**21**), 3-formyloxy-metaplexigenin (**22**), and dybinstigm A (**23**), have the common pregnane skeleton (Li et al., 2020a; Ren, Han, Li, & Xie, 2009; Sun et al., 2020a; Zhang, Xia, Xu, Chen, & Zhou, 2020). They were obtained from the aerial parts of *Gendarussa vulgaris* (Acanthaceae), roots of *Cynanchum auriculatum* (Asclepiadaceae), and leaves of *Dysoxylum binectariferum* (Meliaceae), respectively. The only furostanol steroidal glycoside 22-methoxy-trigoneoside IIb (**24**) was found in the seeds of *Trigonella foenum-graecum* (Fabaceae) (Liu, Zhang, Hou, & Tang, 2020). The structures of corresponding compounds are shown in Fig. 2.

C_{21} steroids were a group of pregnane derivatives with 21 carbon atoms. They possessed a tetracyclic pregnane carbon skeleton and differ in the number and nature of substituents and sometimes the degree of unsaturation, which generally exist in the form of glycosides. In addition to Apocynaceae, Liliaceae, Scrophulariaceae, Ranunculaceae, Dioscoreaceae, Gentianaceae, Solanaceae, and Cruciferae families, natural C_{21} steroids are most commonly found in Asclepiaceae plants (Gu & Hao, 2016), and are typical active constituents of many medicinal plants in Asclepiaceae. From 2000 to the end of 2020, 625 new C_{21} steroids are isolated from 36 species of 13 genera, *e.g. Metaplexis*, *Streptocaulon*, *Cynanchum*, *Myriopteron*, *Ceropegia*, *Gymnema*, *Asclepias*, *Stelmatocrypton*, *Stephanotis*, *Dregea*, *Periploca* and *Marsdenia*. Among them, *Cynanchum* is the main source of natural C21 steroids, and Qingyangshen (*Cynanchum otophyllum*) is the TCM with the largest number of isolated new C_{21} steroids (Zhan, Chen, Liao, Li & Lu, 2021).

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2.3. Flavonoids

Flavonoids are the most widely distributed specialized metabolites and are found in at least 245 seed plant families (Zhang, 2018). The structures of>9,000 flavonoids have been elucidated. Two new aglycones, named solacarpumon (**25**) and 5,7,2′,4′-tetra hydroxy-3,5′-dimethoxyflavone (**26**), were isolated from the fruits of *Solanum virginianum* (Solanaceae) and rhizomes of *Schoenoplectus tabernaemontani* (Cyperaceae) (Diao, Li, Xiang, Zhao, & Dai, 2020; Peng, Huang, Zhou, Chou, & Peng, 2020). Three new flavonoid glycosides, i.e., sinoflavonoid glycoside A (**27**), methoxylquercetinside (**28**) and tectoridin A (**29**), were isolated from the rhizomes of *Sinopodophyllum hexandrum* (Berberidaceae), flower buds of *Lonicera macranthoides* (Caprifoliaceae) and stems of *Wisteria sinensis* (Fabaceae), respectively (Xu, He, Jiang, Wang, & Zhu, 2020; Mei et al., 2020; Peng, Wang, Zhao, Xu, & Yang, 2020). Compound **25** has a common flavone skeleton with the methylenedioxy group between C-6 and C-7. Compounds **26** and **27** have the flavonol skeleton, and the hydroxyl at C-3 is substituted by a methoxy group. Compound **28**, as a flavonol glycoside, has a sugar chain of glucose and arabinose at C-3. Compound **29** has an isoflavone skeleton characterized by the presence of an acetyl moiety at C-6′′ of the glucose. The structures of corresponding compounds are shown in Fig. 3.

Isoflavone possesses the same basic skeleton of 3-phenylchromone as flavone, but unlike the latter, its phenyl group (B ring) was connected to C-3. Isoflavones mainly exist in Fabaceae, Caprifoliaceae, Liliaceae, Berberidaceae and Iridaceae plants, particularly in Fabaceae, such as *Glycyrrhizae Radix* et *Rhizoma*, *Astragalus membranaceus*, *Cicer arietinum*, *Glycine* max, *Psoralea corylifolia*, *Pueraria lobata*, *Trifolium pratense* and *Wisteria sinensis* (Dong, Chang, Zhang, Yang, & Du, 2018; Peng, Cui, & Feng, 2009; Peng, Wang, Zhao, Xu, & Yang, 2020; Zhu, 2011).

2.4. Phenylpropanoids

Phenylpropanoids are prominent among novel compounds of 2020. Among them, a *cis–trans* diphenylpropanoid (**30**), as a dimer of two phenylpropanine, is composed of two *p*-hydroxyl ethyl cinnamate units connected with a C-1′-O-C-1 bond, which was isolated from the leaves of *Cassia floribunda* (Fabaceae) (Zhu et al., 2020). Platycloside A (**31**), a simple phenylpropanoid glycoside, is identified from the leaves of *Platycladus orientalis* (Cupressaceae) (Wu et al., 2020a).

Coumarin and lignan, regarded as the phenylpropanoid derivatives, share the common upstream biosynthetic pathways and are

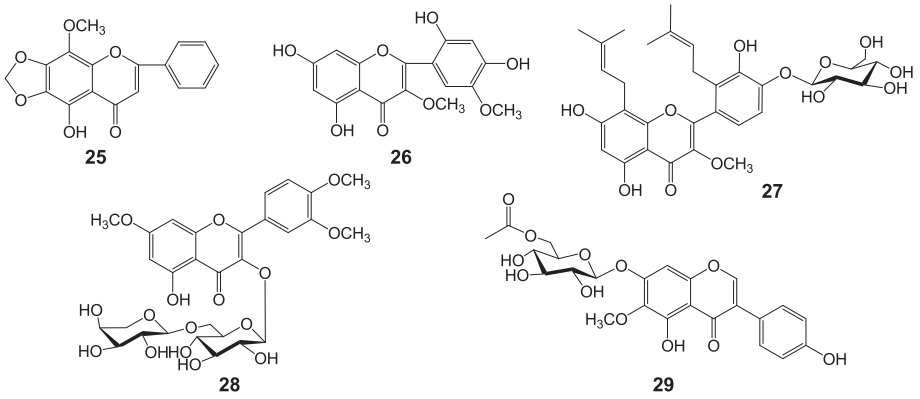

Fig. 3. Chemical structures of flavonoids.

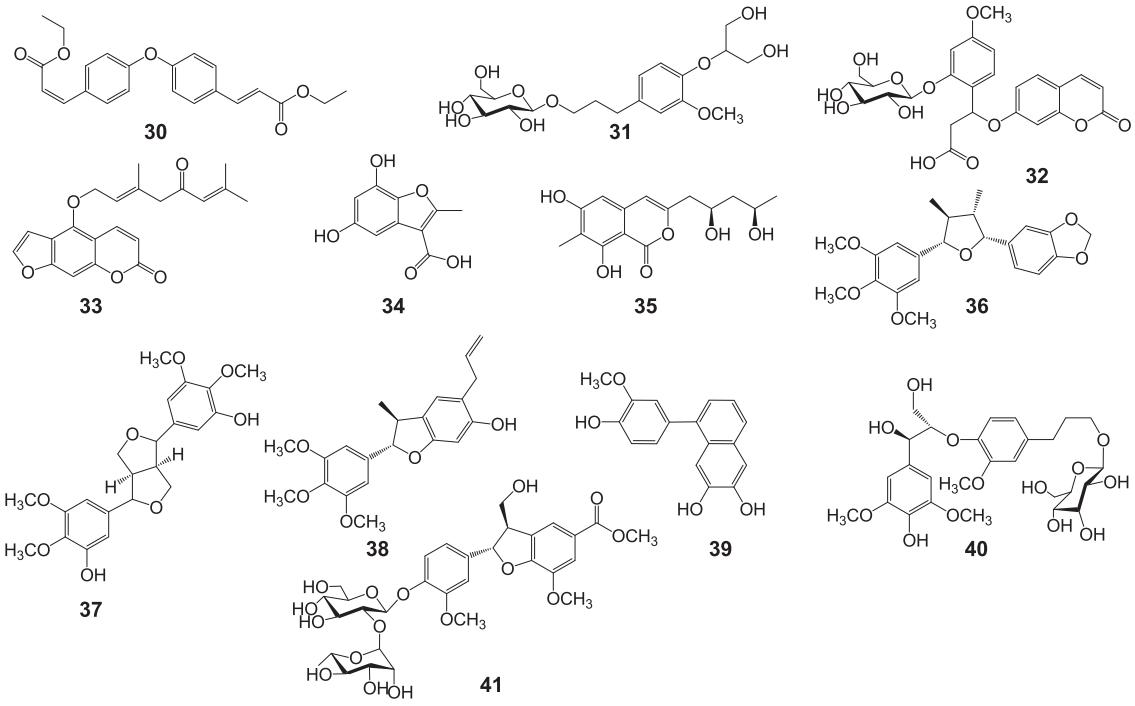

Fig. 4. Chemical structures of phenylpropanoids.

found in at least 162 seed plant families (Zhang, 2018). Four coumarin-type derivatives, i.e., gardnerol C (**32**), 5-dehydronotopterol (**33**), oxafuranone A (**34**) and glolactone A (**35**), were from the flowers of *Edgeworthia gardneri* (Thymelaeaceae), roots and rhizomes of *Notopterygium incisum* (Apiaceae), metabolites of endophytic fungus *Penicillium oxalicum* isolated from *Pseudostellaria heterophylla* (Caryophyllaceae), and metabolites of endophytic fungus *Chaetomium globosum* obtained from *Hypericum sampsonii* (Clusiaceae), respectively (Li, Yang, Zhu, & Zhong, 2020; Wu & Yang, 2020; Jia, Hu, Shao, Chai, & Liu, 2020; Huan, Xiong, Wen, He, & Zhang, 2020). Compound **33** has a special polyolefin group at C-5. The structure of compound **34** is similar to that of 5-hydroxy-7-methoxy-2-methylbenzofuran-3-carboxylic acid, except that the latter has a methoxy group instead of a hydroxyl group at C-7. Compound **35** differs structurally from the commom coumarin type and has an isocoumarin-type skeleton.

Six lignan-type derivatives reported in 2020 include artelignan (**36**), magnodatin A (**37**), 5-methoxylililflol B (**38**), 5,5′-dimethoxyl clemaphenol A (**39**), mullignanoside (**40**) and polygonneolignanoside A (**41**). Compound **36** was isolated from the aerial parts of *Artemisia annua* (Asteraceae) (Liu, Yu & Tian, 2020). In the leaves of *Magnolia denudata* (Magnoliaceae), compounds **37** and **38** were abundant (Xie et al., 2020). Compound **39**, a bistetrahydrofuran lignan, was isolated from the stems of *Trigonostemon lutescens* (Euphorbiaceae) (Zhang et al., 2020b). Two lignan glycosides **40** and **41** were from the fruits of *Morus alba* (Moraceae) and rhizomes of *Polygonatum sibiricum* (Liliaceae); the former has a neolignan skeleton and the latter has a benzofuran lignan skeleton (Chen et al., 2020a; Xu, Zhang, Xu, He, & Wang, 2020). The structures of corresponding compounds are shown in Fig. 4.

Lignans and neolignans, a large group of naturally occurring phenols, are formed by two or more phenylpropanoid units and widely spread within the plant kingdom. The families Annonaceae, Orchidaceae, Berberidaceae, Schisandraceae and Lauraceae contained a large number of classical lignans and neolignans, especially the genera *Machilus*, *Ocotea* and *Nectandra* of Lauraceae. It is worth noting that furanofuran lignans, a large class of natural bisepoxylignan, were also widespread in the plant kingdom. They

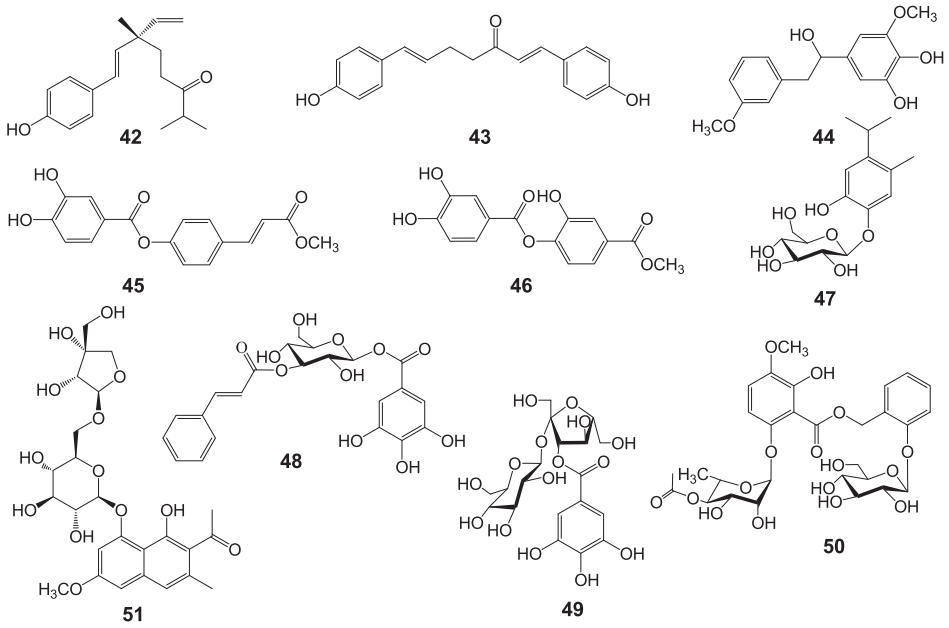

Fig. 5. Chemical structures of phenolic compounds.

have been isolated from 53 species in 41 genera of 27 families, *i.e.*, Acanthaceae, Acoraceae, Apocynaceae, Aquifoliaceae, Araliaceae, Arecaceae, Aristolochiaceae, Asteraceae, Cactaceae, Combretaceae, Cupressaceae, Cyperaceae, Dioscoreaceae, Geraniaceae, Lamiaceae, Lauraceae, Magnoliaceae, Myristicaceae, Orobanchaceae, Pedaliaceae, Piperaceae, Rhizophoraceae, Rutaceae, Saururaceae, Scrophulariaceae, Styracaceae and Thymelaeaceae. To date, lignans and their derivatives occur in over 70 families and>200 classic lignans and 100 neolignans have been identified. They usually exist in the form of dimers, and a few are trimers or tetramers. Most lignans in plants are in a free state, while some of them combine with sugar to form glycosides (Teponno, Kusari & Spiteller, 2016; Xu, Zhao, Wang & Liang, 2019; Cui, Du, Liu & Rong, 2020). These information is useful in predicting potential medicinal taxa using phylogenetic tree.

2.5. Phenolic compounds

The phenolic acid compounds are found in at least 167 seed plant families (Zhang, 2018). Natural phenolic compounds represent an enormous class of plant secondary metabolites, which consist of at least one aromatic ring with one or more hydroxyl functional groups and are commonly distributed in foods and TCM. The phenolic aglycones, i.e., 12-oxobakuchiol (**42**), curcumin P (**43**), dendhercoine A (**44**), were from the fruits of *Psoralea corylifolia* (Fabaceae), rhizomes of *Curcuma phaeocaulis* (Zingiberaceae) and whole plants of *Dendrobium hercoglossum* (Orchidaceae), respectively. The phenolic aglycones schiniphenol A (**45**) and schiniphenol B (**46**) were isolated from the peels of *Zanthoxylum schinifolium* (Rutaceae) (Lv, Xu, Zhang, & Yang, 2020; Chen, Xiong, Liu, & Peng, 2020; Cheng et al., 2020; Meng, Shang, & Yang, 2020). Compound **42** was firstly synthesized in a study of the structure–activity relationship (SAR) of immunosuppressive effects of bakuchiol and its derivatives, and later it was discovered as a naturally occurring compound. Compound **43** was an example of monooxygenated curcumin derivative with a carbonyl substitution at C-3 on the heptane chain, and compound **44** was a typical biphenyl derivative.

Five phenolic glycosides, including quinqueside A (**47**), palmatoside (**48**), 3′-*O*-galloylsucrose (**49**), disporumoside (**50**) and polygonimitin E (**51**), were found from the aerial parts of *Thymus quinquecostatus* (Labiatae), roots of *Rheum palmatum* (Polygonaceae), *n*-butanol extract of Guizhi Fuling Capsule, roots and rhizomes of *Disporum cantoniense* (Polygonateae), and the roots of *Polygonum multiflorum* (Polygonaceae), respectively (Deng et al., 2020; Xu et al., 2020; Yang et al., 2020a; You et al., 2020; Zhang et al., 2020a,c). Compound **49,** a galloyl glycoside, is one of characteristic constituents of Guizhi Fuling Capsule, and is mainly derived from *Paeoniae Radix Rubra* and *Moutan Cortex* in this TCM formula. The structures of corresponding compounds are shown in Fig. 5.

2.6. Nitrogen-containing compounds

The alkaloids are found in at least 221 seed plant families (Zhang, 2018). Kumujantine D (**52**) was a tryptamine indole alkaloid and has been isolated from the twigs and leaves of *Picrasma quassioides* (Sorrelaceae) (Zhang, Lin, Yuan, Ma, & Zhu, 2020). The structure of (3*S*,15*S*)-3β-angeloyl-15α-acetylzygadenine (**53**) was determinated to be steroidal alkaloid, which was isolated from the rhizomes of *Veratrum grandiflorum* (Liliaceae) (Shi, Liu, He, Lin, & Chen, 2020). Polygonimitin F (**54**) and polygonimitin E (**51**) were found from the roots of *Polygonum multiflorum* (Polygonaceae) (Yang et al., 2020a). The former has the amide-type alkaloid skeleton; compounds **51** and **54** differ in structural classification but had the similar activities. A polyketide derivative carrying an amino group, named asperpolykide A (**55**) was obtained from the methanol extract of endophytic fungus *Aspergillus oryzae* derived from *Paris polyphylla* var. *yunnanensis* (Liliaceae) (Hou et al., 2020). The structures of corresponding compounds are shown in Fig. 6.

The alkaloids could be the largest group of plant secondary metabolites. They are generally derived from amino acids and have one or more nitrogen atoms in their structures; they are more abundant in angiosperms. So far, the indole alkaloids with tryptophan or tryptamine as their precursors are represented by>4,000 known compounds, which are mainly derived from families Apocynaceae, Rubiaceae, Annonaceae, Loganiaceae, and Vochysiaceae,

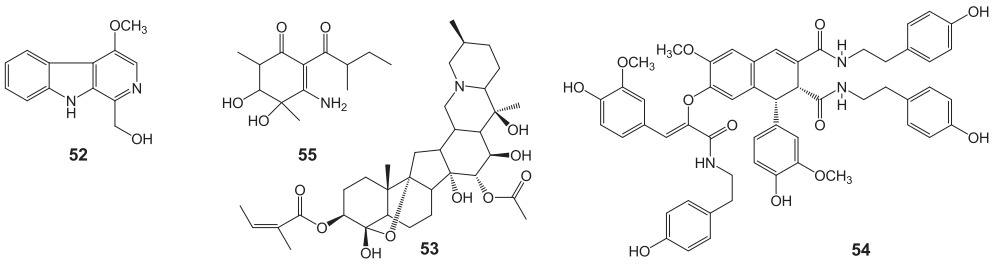

Fig. 6. Chemical structures of nitrogen-containing compounds.

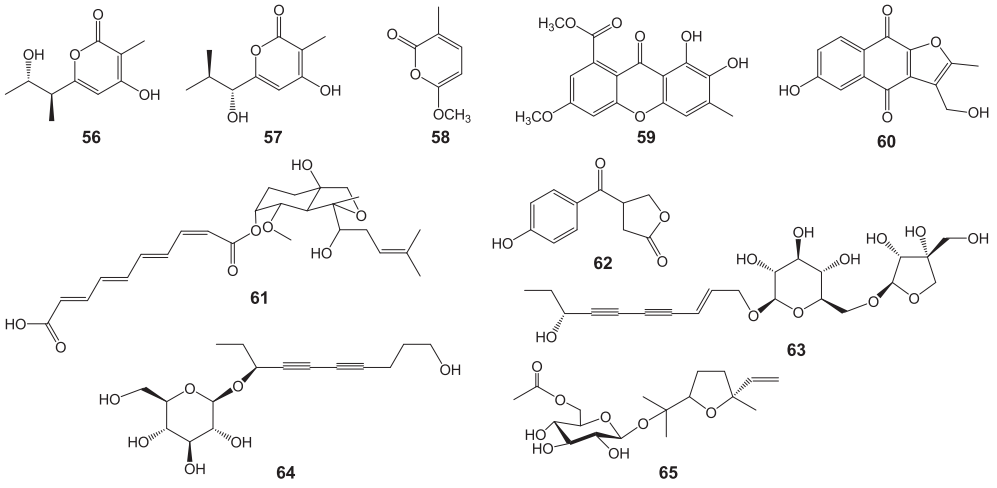

Fig. 7. Chemical structures of miscellaneous compounds.

especially from genera *Alstonia*, *Geissospermum*, *Rauvolfia*, *Psychotria*, *Aspidosperma*, *Tabernaemontana*, *Kopsia*, *Hexalobus*, *Vinca* and *Gelsemium*. The source species of Apocynaceae include *Alstonia pneumatophora*, *Alstonia rupestris*, *Alstonia scholaris*, *Aspidosperma cylindrocarpon*, *Geissospermum reticulatum*, *Rauvolfia tetraphylla*, *Rauvolfia yunnanensis*, *Kopsia arborea*, *Kopsia fruticosa*, *Kopsia hainanensis*, *Kopsia jasminiflora*, *Melodinus khasianus*, *Tabernaemontana divaricata*, *Tabernaemontana catharinensis*, *Voacanga africana* and *Vinca major*. The source species *Nauclea latifolia*, *Psychotria pilifera* and *Psychotria henryi* belong to Rubiaceae. *Hexalobus monopetalus*, *Gelsemium elegans* and *Vochysia divergens* are source species from Annonaceae, Loganiaceae and Vochysiaceae, respectively (Liu et al, 2020a; Rosales, Bordin, Gower & Moura, 2020). The phylogenetic study of taxonomic groups that are richer in bioactive alkaloids could help discovering and identifying alternative and/or complementary drugs.

2.7. Miscellaneous compounds

Two α-pyronoids were isolated from the methanol extract of endophytic fungus *Aspergillus oryzae* derived from *Paris polyphylla* var. *yunnanensis* (Liliaceae), named asper-α-pyranone A (**56**) and asper-α-pyranone B (**57**) (Yu et al., 2020). Another α-pyronoid derivative, named as stemonapyrone A (**58**), was found from the roots of *Stemona tuberosa* (Stemonaceae) (An et al., 2020). The xanthone, named 2-hydroxyisosulochrin dehydrate (**59**), was purified from the metabolites of endophytic fungus *Aspergillus wentti* Y1 isolated from *Ainsliaea macrocephala* (Asteraceae) (Yang et al., 2020b). The continued examination of aerial parts of *Thymus quinquecostatus* (Lamiaceae) gave a quinone derivative quinquequinone A (**60**) (Xu et al., 2020). A new fumagillin compound 2′-*cis*fumagiringillin (**61**) was isolated from the fermentation broth of marine fungus *Aspergillus fumigatus* MDCW-15 (Gao et al., 2020). From the twigs of *Euscaphis konishii* (Staphyleaceae), a new lactone skeleton konieuscaphide (**62**) was isolated (Chen et al., 2020b). Two polyacetylene glycosides, atractyeneyneglycoside A (**63**) and atractyeneyneglycoside B (**64**), were obtained from the rhizomes of *Atractylodes lancea* (Asteraceae) (Xu, Jiang, Feng, Yang, & Zhang, 2020). The pericarps of *Aquilaria yunnanensis* (Thymelaeaceae) yielded a new phenethyl glycoside, phenethyl-8-*O*-β-D-(6′-*O*-acetyl)-glucoside (**65**) (Sun et al., 2020a). These compounds may have unique chemotaxonomic implications. Quinones are found in at least 82 seed plant families (Zhang, 2018), whereas the phylogenetic distribution of other compounds has not been reported. The structures of corresponding compounds are shown in Fig. 7.

2.8. Essential oil

Essential oils were considered as the major bioactive and characteristic constituents of She medicine *Clematis Florida* var. *plena* flower (Ranunculaceae). Twenty compounds (**66**–**85**; Table S1), including fatty acids, alkanes, phenols, alcohols, ketones, esters and other derivatives, were detected and quantified for the first time by GC–MS analysis. They accounted for 78% of the total essential oils content. Five of them, such as palmitic acid (**74**), pytol (**76**), linoleic acid (**77**), pentadecane (**84**), n-tricosane (**82**), accounted for the highest proportion of 26.94 %, 10.58 %, 6.13 %, 4.54 % and 3.84 %, respectively. The total ion current spectrum of GC–MS of these known compounds represented firstly obvious fingerprint characteristics, which could provide a scientific basis for the component analysis and quality control of *C. Florida* var. *plena*, so as to lay a foundation for the development of She medicine resources (Shen et al., 2020).

3. Pharmacological activities

According to pharmacophylogeny, the species with closely related chemical profile are more likely to be used against the same/similar diseases. A single compound, randomly or regularly distributed on the phylogenetic tree, could display polypharmacological characteristics. The research in 2020 provides a lot of valuable information in pharmaceutical resource discovery.

3.1. Antitumor activity

In TCM, folk medicine and ethnomedicine, many plant taxa have been used in the treatment of cancer since ancient times. Phytochemical studies result in the isolation of a plethora of active compounds. The cytotoxic compounds reported in 2020 are summarized in Table 1. Most of them exhibited weak or moderate cytotoxicity. The tested cell lines included human promyelocytic leukemia cell line (HL-60), human hepatoma carcinoma cell line (SMMC-7721), human prostate cancer cell line (DU-145), human nasopharyngeal carcinoma cell line (CNE2), human cervical cancer cell line (HeLa), human gastric cancer cell line (HGC-27 and BGC-823), human hepatocellular carcinomas cell line (HepG-2), human lung adenocarcinoma cell lines (A549 and PC-9), human colon cancer cell lines (SW480, HT-29 and HCT-116), human breast cancer cell lines (MCF-7 and MDA-MB-231), human esophageal cancer cell lines (OE19 and SK-GT-4), as well as human normal liver cell line (L-02). In addition to special *in vitro* activity detection methods, the rest were measured by MTT assay.

Five sesquiterpenoids (**86**–**90**) and two chalcones (**91** and **92**), obtained from the whole plants of *Chloranthus fortunei* (Chloranthaceae), were evaluated for their cytotoxicity against HepG-2, HCT-116, HeLa and BGC-823 cell lines. **86** showed weak activity against HepG-2, HCT-116 and HeLa cell lines, **87** showed weak activity against HCT-116, HeLa and BGC-823 cell lines, while others did not exhibit cytotoxicity against above cells (IC_{50} > 100 μmol/L) (Chen et al., 2020c).

A clerodane-type diterpenoid (**10**) had no cytotoxicity against HL-60, A549, MCF-7, SW480, and SMMC-7721 cell lines (Fan,

Table 1
Activities of compounds against human tumor cell lines.

No.	Compounds	IC_{50} values (μmol/L)	Taxon
11	Ursolic acid 3-*O*-*β*-*cis*-caffeate	17.55 (PC-9); 31.46 (HT-29); 30.79 (MCF-7)	a
12	Ursolic acid 3-*O*-*β*-*trans*-caffeate	> 50 (PC-9); > 50 (HT-29); > 50 (MCF-7)	a
16	Mollugoside E	10.21 (HL-60)	b
22	3-Formyloxy-metaplexigenin	> 10 (A549); > 10 (MCF-7)	c
27	Inoflavonoid glycoside A	42.6 (HeLa)	d
39	5,5′-Dimethoxylclemaphenol A	36.42 ± 2.30 (A549); 58.48 ± 1.80 (MCF-7); 22.58 ± 3.20 (HeLa)	e
43	Curcumin P	34.06 ± 3.53 (HGC-27); > 200 (L-02)	f
86	Cycloshizukaol A	62.54 (HepG-2); 75.97 (HCT-116); 85.16 (HeLa)	g
87	Atractylenolide III	76.98 (HCT-116); 46.98 (HeLa); 67.61 (BGC-823)	g
88	4*β*-Hydroxy-8,12-epoxyeudesma-7,11-diene-1,6-dione	> 100 (HepG-2); > 100 (HCT-116); > 100 (HeLa); > 100 (BGC-823)	g
89	Curcolonol	> 100 (HepG-2); > 100 (HCT-116); > 100 (HeLa); > 100 (BGC-823)	g
90	(8α)-6,8-Dihydroxycadina-7(11),10(15)-dien-12-oic acid γ-lactone	> 100 (HepG-2); > 100 (HCT-116); > 100 (HeLa); > 100 (BGC-823)	g
91	2′-Hydroxy-4,3′,4′,6′-tetramethoxychalcone	> 100 (HepG-2); > 100 (HCT-116); > 100 (HeLa); > 100 (BGC-823)	g
92	Flavokawain A	> 100 (HepG-2); > 100 (HCT-116); > 100 (HeLa); > 100 (BGC-823)	g
95	3-*O*-[α-*L*-Rhamnopyranosyl (1 → 2)-α-*L*-rhamnopyranosyl]-28-*O*-[*β*-*D*-glucopyranosyl (1 → 6)-*β*-*D*-glucopyranosyl] oleanolic acid	38.43 (HL-60)	b
96	Raddeanoside R_8	40.28 (HL-60)	b
97	Raddeanin A	20.59 (HL-60)	b
98	Mollugogenol A	83.16 (HL-60)	b
99	Chikusetsusaponin IVa methyl ester	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
100	Chikusetsusaponin IVa butyl ester	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
101	Chikusetsusaponin IV	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
102	Chikusetsusaponin IVa	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
103	28-Desglucosylchikusetsusaponin IVa	9.94 (BGC-823); 14.17 (HCT-116); 18.23 (HeLa); 17.76 (HepG-2)	h
104	Oleanolic acid-3-*O*-*β*-*D*-(6′-methyl ester)-glucuronopyranoside	17.12 (BGC-823); 19.25 (HCT-116); 18.96 (HeLa); 12.70 (HepG-2)	h
105	(24*R*)-Majonoside R_1	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
106	(24*R*)-Pseudoginsinoside F_{11}	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
107	(20*S*)-Notoginsinoside R_2	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
108	(20*S*)-Ginsenoside Rg_2	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
109	Ginsenoside Rg_1	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
110	Ginsenoside Re	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
111	Ginsenoside Rd	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
112	Chikusetsusaponin V methyl ester	> 200 (BGC-823); > 200 (HCT-116); > 200 (HeLa); > 200 (HepG-2)	h
115	Metaplexigenin	> 10 (A549); > 10 (MCF-7)	c
116	8,2′-Diprenylquercetin-3-methylether	46.9 (HeLa)	d
117	5,7,4′-Trihydroxy-3′-(3-methylbut-2-enyl)-3-methoxy flavone	26.9 (HeLa)	d
118	8-Prenylkaempferol	16.1 (HeLa)	d
119	Sophoflavescenol	31.2 (HeLa)	d
120	Syringaresinol	42.78 ± 3.30 (A549); 54.76 ± 2.20 (MCF-7); 26.74 ± 3.60 (HeLa)	e
121	Lirioresinol B dimethyl ether	35.69 ± 2.50 (A549); 57.87 ± 1.50 (MCF-7); 29.46 ± 2.40 (HeLa)	e
122	Clemaphenol A	44.48 ± 3.60 (A549); 56.73 ± 2.90 (MCF-7); 25.68 ± 2.80 (HeLa)	e
132	1,7-Bis(4-hydroxyphenyl)-1,4,6-heptatrien-3-one	5.80 ± 1.92 (HGC-27); 16.59 ± 1.70 (MDA-MB-231); 10.44 ± 0.35 (L-02)	f
133	1,7-Bis(4-hydroxyphenyl)-4*E*,6*E*-heptadien-3-one	16.54 ± 3.79 (HGC-27); 28.47 ± 1.66 (L-02)	f
134	Veratramine	13.70 ± 0.99 (HepG2)	i
143	Pyoluteorin	5.8 (OE19)	j
144	4-Hydroxy-3-methoxy cinnamaldehyde	2.03 ± 0.25 (HL-60); 6.92 ± 0.07 (SMMC-7721); 2.42 ± 0.22 (MCF-7); 3.70 ± 0.05 (SW480)	k
145	3,7-Dimethoxy-5-hydroxy-1,4-phenanthrenequinone	2.21 ± 0.19 (HL-60); 8.72 ± 0.12 (A549); 7.66 ± 0.32 (SMMC-7721); 0.91 ± 0.01 (MCF-7); 3.25 ± 0.11 (SW480)	k

Duan, Xia, & Wang, 2020). Wangzaozin A, an ent-kaurane diterpene (**93**) from *Rabdosia racemosa* (Hemsl.) Hara, upregulated the phosphorylation of microtubule-associated protein 4 (MAP4) and keratin 8 (K8) *via* activation of extracellular-signal regulating kinase (ERK), which significantly increased the dynamics of microtubules and keratin fibers, disturbed the dynamic balance of cytoskeleton, induced cytoskeleton reorganization and inhibited the migration of A549 cells in a dose and time-dependent manner. Compound **93** could be an antitumor precursor with potential value (Yang, Ma, Zhao, Li, & Ding).

Compounds **11** and **12** are ursane-type triterpene aglycons; **11** exhibited moderate anti-proliferative effects against PC-9, HT-29 and MCF-7 cell lines in CCK-8 method detection, but **12** presented no inhibitory activity against these cell lines (IC_{50} > 50 μmol/L) (Chai, Chen, Lu, Lin, & Liu, 2020). An oleanane-type triterpene aglycon, named maslinic acid (**94**), showed significant inhibition of the growth and induced the autophagy of CNE2 nasopharyngeal carcinoma cells in a dose and time–dependent manner in CCK-8 detection. It might inhibit signal transduction pathways of PI3K/Akt/mTOR to promote autophagy in CNE2 cells (Zhou, Hu, Hu, Lin, & He, 2020). The aerial parts of *M. pentaphylla* have four oleanane-type triterpene glycosides (**16**, **95**–**97**), as well as one lupinane-type triterpene aglycone (**98**). They displayed remarkable cytotoxicity against HL-60 and certain inhibitory effects on DU-145 and Hela cell lines (Wang et al., 2020b). Extraction of beaded rhizomes of *Panax japonicus* var. *major* (Araliaceae) yielded seven oleanane-type (**99**–**105**), four protopanaxtriol-type (**106**–**109**), one protopanaxdiol-type (**110**) and two ocotillol-type (**111** and **112**) triterpene glycosides. BGC-823, HCT-116, HeLa and HepG-2 cells were exposed to these saponins in different concentrations (2.5, 5.0, 7.5, 10, 12.5, 15, 17.5, 20 μmol/L) for 48 h. Compounds **103** and **104** produced more significant cytotoxicity in a dose dependent manner in BGC-823, HCT-116, HeLa, and HepG-2 cells, yet no activities were detected for others (Wang et al., 2020bc). Ginsenoside CK (**113**), a dammarane-type tetracyclic triterpene saponin from the roots of *Panax ginseng* (Araliaceae), had significant inhibitory activity against the proliferation of SW480 cells in CCK-8 assay. The CK induced apoptosis in SW480 cells was dependent on the promotion of mitochondrial superoxide elevation, the significant increase in intracellular reactive oxygen species (ROS) levels and the significant decrease in mitochondrial membrane potential (MMP) level, which induced cytochrome *C* release, up-regulated Bax expression, down-regulated Bcl-2 expression, and initiated the subsequent events leading to apoptosis (Meng, Qiu, Wang, & Liu, 2020). Astragaloside IV (**114**), an ocotillol-type tetracyclic triterpene saponin isolated from the roots of *Astragalus membranaceus* (Fabaceae), reversed the multidrug resistance of MDA-MB-231 cells to adriamycin. The combination of **114** and doxorubicin along with liposome co-delivery system could effectively reverse or sensitize the multidrug resistance in triple-negative breast cancer and promote apoptosis (Yue et al., 2020).

Two C_{21} steroids (**2** and **115**) from the roots of *Cynanchum auriculatum* had a very low cytotoxicity on A549 and MCF-7 cell lines with SRB method (IC_{50} > 10 μmol/L) (Li et al., 2020f). Five prenylated flavonoids (**27**, **116**–**119**) from the rhizomes of *Sinopodophyllum hexandrum* showed marginal cytotoxicity against HeLa cells (Xu, He, Jiang, Wang, & Zhu, 2020).

Four bistetrahydrofuran lignans (**39**, **120**–**122**), isolated from the stems of *T. lutescens*, showed weak cytotoxity against A549 cell lines, marginal cytotoxity against MCF-7, as well as moderate cytotoxity against HeLa (Zhang et al., 2020b). The stems and leaves of *Dioscorea opposita* (Dioscoreaceae) had three bistetrahydrofuran lignans, *i.e.*, syringaresinol (**120**), (+)-8-hydroxypinoresinol (**123**) and paulownin (**124**), two benzofuran lignans, *i.e.*, (-)-dihydrodehydrodiconiferyl alcohol (**125**) and (7*R*,8*S*)- dihydrodehydrodiconiferyl alcohol-4-*O*-*β*-*D*-glucopyranoside (**126**), three nitrogen-containing compounds, *viz.* 1*H*-indazole (**127**), 3-(2-oxo propyl)-3-hydroxy-indolin-2-one (**128**) and hematinic acid (**129**), along with other compounds (2*E*,6*S*)-6-hydroxy-2,6-dimethyl-2,7-octadieic acid (**130**) and (9*Z*,11*E*)-13-methoxy-9,11-octadecadienoic acid methyl ester (**131**). The proportion of inhibiting the proliferation of MCF-7 and HepG2 cells treated with **120**, **123**–**131** at 25 μmol/L for 24 h varied from (1.70 ± 2.94) to (76.00 ± 1.00)% (Ren et al., 2020).

The cytotoxicity assay of three monooxygenated curcumin derivatives (**43**, **132**, **133**) isolated from the rhizomes of *C. phaeocaulis* was measured using human cancer and normal cells. All of them inhibited the proliferation of HGC-27 cell lines, while **132** reduced the proliferation of MDA-MB-231 cells. Moreover, **132** and **133** displayed marked cytotoxicity against normal L-02 liver cells, yet no cytotoxicity against MCF-7 cells was detected in **43** (Chen, Xiong, Liu, & Peng, 2020).

A simple piperdine (**134**) from the rhizomes of *V. grandiflorum* induced early apoptosis of HepG2 and showed moderate cytotoxic activity (Shi, Liu, He, Lin, & Chen, 2020). A bisbenzylisoquinoline alkaloid cyclanoline (**135**) was isolated from the roots of *Stephania tetrandra* (Menispermaceae). It significantly inhibited the growth of bladder cancer cells in rats, as compared to positive control cisplatin. It might promote the expression of KLF4 to inhibit Wnt/β-catenin signal transduction and the epithelial cell-mesenchymal transition of bladder cancer cells, and regulate the expression of p21 and Cyclin D1, which induced the inhibition of migration and invasion of bladder cancer cells, and delayed the pathological process of BBN-induced bladder cancer in rats (Li, Li, Zhu, & Chen, 2020).

The endophytic fungus *Aspergillus wentti* Y1 isolated from *Ainsliaea macrocephala* (Asteraceae) had five xanthone compounds, including 2-hydroxyisosulochrin dehydrate (**59**), yicathin A (**136**), isosulochrin dehydrate (**137**), 1,6-dihydroxy-3-methyl-8-carbomethoxyxanthone (**138**) and yicathin C (**139**), three anthraquinone derivatives, *i.e.*, physcion (**140**), 8-hydroxy-1,3-dimethoxy-6-methylanthraquione (**141**) and wentiquinone B (**142**), along with one pyrrolidine alkaloid pyoluteorin (**143**). In CCK-8 method, **59** and **136**–**142** showed weak antiproliferative activity against OE19 and SK-GT-4 cell lines with the inhibition rate of<40% at a concentration of 10 μmol/L, while **143** had potent cytotoxic activity against OE19 (Yang et al., 2020b).

The phenolic compound **144** and quinone **145** were isolated from roots of *Dendrobium wardianum* (Orchidaceae). In MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)–2*H*-tetrazolium) method and with cisplatin and paclitaxel as positive controls, the former was able to inhibit the growth of HL-60, SMMC-7721, MCF-7 and SW480 cells (Table 1), and the latter had promising cytotoxicity against HL-60, A549, SMMC-7721, MCF-7 and SW480 cells (Li, Ren, Hu, & Zhou, 2020).

3.2. Antioxidant activity

The determination of antioxidant activity is still meaningful, although it is ubiquitous in all plants. Food and drug ingredients with excellent antioxidant properties are still needed in the market. Compared to *L*-ascorbic acid [IC_{50} of (30.56 ± 1.11) and (26.45 ± 0.83) μmol/L], compounds **146**–**150** isolated from the leaves of *P. orientalis* showed moderate DPPH and $ABTS^{\cdot+}$ radical-scavenging activities, yet **31, 151** and **152** exhibited no activities (He et al., 2011; Wu et al., 2020a; Yang, Huang, Feng, Jiang, & Zhang, 2014).

A bioassay-guided fraction of the Damask rose (*Rosa damascena*) (Rosaceae) flower residue (DRFR) had 10 compounds, i.e., quercetin (**153**), kaempferol (**154**), astragalin (**155**), gallic acid (**156**), protocatechuic acid (**157**), methyl gallate (**158**), p-hydroxybenzoic acid (**159**), pyrogallic acid (**160**), p-hydroxyphenethyl alcohol (**161**)

and 2-phenylethyl 3,4,5-trihydroxybenzoate (**162**). DRFR demonstrated powerful scavenging activities against DPPH and $ABTS^{\cdot+}$ radicals in a dose-dependent manner, which was close to the positive control Vitamin C (Vc). It is a potential resource of natural antioxidants (Liu et al., 2020a).

In FRAP method, compounds **163**–**174** from the flowers of *Stellera chamaejasme* (Thymelaeaceae) showed significant DPPH and $ABTS^{\cdot+}$ radicals scavenging activities with IC_{50} values ranging from 0.003 to 0.05 and 0.002 to 0.6 mg/mL, respectively, which were better than Vc [IC_{50} (0.06 ± 0.001) and (0.017 ± 0.0002) mg/mL, respectively]. After detailed comparison of the activities of these analogs, a SAR analysis revealed that sugar chains at C-3 or C-8 position of flavonoids could reduce their antioxidant activities (Zhou et al., 2020). Compounds **175**–**184**, isolated from the whole plants of *Azolla imbricata* (Azollaceae), exhibited considerable *in vitro* radical scavenging activities on DPPH as compared to Vc [IC_{50} (54.22 ± 3.08) μmol/L]. Compounds **175** and **178**–**184** displayed stronger antioxidant activities than Vc, and **176** and **177** showed the lower activities than Vc (Qian et al., 2020; Ganzon, Chen, & Wang, 2018).

The methanol extract of leaves of *Lysiphyllum strychnifolium* (Fabaceae) had a phenolic acid (**156**) and two dihydrochalcone glucosides (**185** and **186**). They were tested for free radical scavenging activities using DPPH in comparison to quercetin and water-soluble vitamin E Trolox [IC_{50} (8.52 ± 0.25), (12.25 ± 0.39) mmol/L respectively]. The results displayed the high potentials in **156** and **186**, whereas **185** showed moderate antioxidative properties (Kongkiatpaiboon et al., 2020). Compounds **187**–**191** were from the peels of *Z. schinifolium*, 5.0, 1.0, 0.5, 0.1, 0.01 and 0.001 mmol/L of them displayed significant $ABTS^{+}$ radical scavenging activity as compared to Vc (IC_{50} 6.4 μmol/L) (Meng, Shang, & Yang, 2020). Compounds with free radical scavenging activity in 2020 are listed in Table 2.

3.3. Anti-inflammatory activity

Nitric oxide (NO), a pro-inflammatory mediator, plays a vital role in the inflammatory process. Inhibitors of NO release may be considered as therapeutic agents for various inflammation-related diseases. TNF-α is a cytokine involved in promoting and triggering the inflammatory process. Compound **5** showed *in vitro* anti-inflammatory effects and inhibited the TNF-α production in LPS-induced RAW 264.7 mouse macrophage cells with IC_{50} 72.24 μmol/L (Li et al., 2020a). Compound **17** inhibited the production of NO in LPS-induced RAW 264.7 macrophages with IC_{50} of (30.91 ± 0.50) μmol/L (Eignerova et al., 2017; Zhang, Xia, Xu, Chen, & Zhou, 2020). Coumarin compounds **33** and **192**–**196**, *i.e.*, 5-dehydronotopterol, anhydronotopoloxide, 7′-*O*-methylnotoptol, bergamottin, notopterol and notoptol, from the roots and rhizomes of *N. incisum* (Apiaceae), displayed moderate inhibitory effects on NO production in activated RAW 264.7 cells with IC_{50} of (32.75 ± 4.55), (35.12 ± 5.14), (20.01 ± 0.97), (8.50 ± 0.73), (16.80 ± 3.74) and (25.19 ± 2.44) μmol/L, respectively (Wu & Yang, 2020). Four tetrahydrofuran-type lignans of *M. denudate* leaves, 5-methoxyliliflol B (**38**), veraguensin (**197**), liliflol A (**198**) and liliflol B (**199**), inhibited the LPS-induced NO release in RAW 264.7 macrophages in Griess method with rates of (48.7 ± 0.3)%, (14.3 ± 1.5)%, (21.7 ± 1.3)% and (64.6 ± 1.3)%, respectively, at 50 μmol/L

Table 2
Free radical scavenging activities of isolated compounds.

No.	Compounds	IC_{50} values (μmol/L)	Taxon
31	Platycloside A	>100 (DPPH); >100 ($ABTS^{\cdot+}$)	l
146	Myricetrin	29.98 ± 0.19 (DPPH); 16.02 ± 0.21 ($ABTS^{\cdot+}$)	l
147	5,8,3′,4′-Tetrahydroxy-flavone-7-*O*-*β*-*D*-xylopyranoside	21.50 ± 0.25 (DPPH); 13.78 ± 0.21 ($ABTS^{\cdot+}$)	l
148	Isomassonianoside B	66.19 ± 0.99 (DPPH); 32.25 ± 0.23 ($ABTS^{\cdot+}$)	l
149	(-)-Isopramine 9′-*O*-*β*-*D*-glucopyranoside	29.13 ± 0.87 (DPPH); 26.37 ± 0.26 ($ABTS^{\cdot+}$)	l
150	(7*R*,8*S*,7′*S*,8′*R*)-4,9,4′,7′-Tetrahydroxy-3,3′-dimethoxy-7,9′-epoxylignan 4-*O*-*β*-*D*-glucopyranoside	64.38 ± 0.78 (DPPH); 20.05 ± 0.23 ($ABTS^{\cdot+}$)	l
151	Sugiol	>100 (DPPH); >100 ($ABTS^{\cdot+}$)	l
152	Totarol	>100 (DPPH); >100 ($ABTS^{\cdot+}$)	l
156[I]	Gallic acid	5.99 ± 0.29 (DPPH)	o
163[II]	Artemisetin	0.0062 ± 0.0001 ($ABTS^{\cdot+}$)	m
164[II]	Quercetin	0.0135 ± 0.0001 (DPPH); 0.0019 ± 0.0000 ($ABTS^{\cdot+}$)	m
165[II]	Isoscutellarein-8-*O*-*β*-*D*-glucuronopyranoside	0.0519 ± 0.0104 ($ABTS^{\cdot+}$)	m
166[II]	Quercetin-3-*O*-*β*-*D*-glucopyranoside	0.0124 ± 0.0017 (DPPH); 0.0030 ± 0.0001 ($ABTS^{\cdot+}$)	m
167[II]	Astragalin	0.0139 ± 0.0000 (DPPH); 0.0070 ± 0.0000 ($ABTS^{\cdot+}$)	m
168[II]	Hypolaetin-8-*O*-*β*-*D*-glucuronopyranoside	0.0116 ± 0.0002 (DPPH); 0.0500 ± 0.0018 ($ABTS^{\cdot+}$)	m
169[II]	Kaempferol 3-*O*-*β*-*D*-glucopyranosyl-(1 → 2)-*O*-*α*-*L*-xylopyranoside	0.2443 ± 0.0327 ($ABTS^{\cdot+}$)	m
170[II]	Uralenol	0.0038 ± 0.0001 (DPPH); 0.0068 ± 0.0002 ($ABTS^{\cdot+}$)	m
171[II]	(+)-Pinoresinol	0.0146 ± 0.0012 (DPPH); 0.0046 ± 0.0000 ($ABTS^{\cdot+}$)	m
172[II]	*Rel*-(3*R*,3′*S*,4*R*,4′*S*)-3,3′,4,4′-tetrahydro-6,6′-dimethoxy [3,3′-bi-2*H*-benzopyran]-4,4′-diol	0.0511 ± 0.0154 (DPPH); 0.0028 ± 0.0001 ($ABTS^{\cdot+}$)	m
173[II]	Matairesinol	0.0447 ± 0.0043 (DPPH); 0.0024 ± 0.0000 ($ABTS^{\cdot+}$)	m
174[II]	Cycloastragenol	0.5977 ± 0.0178 ($ABTS^{\cdot+}$)	m
175	Quercetin-3-*O*-*β*-*D*-glucoside	22.80 ± 0.95 (DPPH)	n
176	Kaempferol-3-*O*-(6′′-*O*-caffeoyl)-*β*-*D*-glucoside	77.34 ± 7.20 (DPPH)	n
177	(−)-*N*-[3′,4′-Dihydroxy-(*E*)-cinnamoyl]-*L*-tyrosine	78.73 ± 4.69 (DPPH)	n
178	(−)-*N*-[3′,4′-Dihydroxy-(*E*)-cinnamoyl]-3-hydroxy-*L*-tyrosine	21.47 ± 0.46 (DPPH)	n
179	(−)-*N*-[3′,4′-Dihydroxy-(*E*)-cinnamoyl]-*L*-tyrosine methyl ester	34.72 ± 2.91 (DPPH)	n
180	Chlorogenic acid methyl ester	20.67 ± 1.04 (DPPH)	n
181	4-*O*-Caffeoylquinic acid	47.53 ± 3.42 (DPPH)	n
182	3,4-*O*-Dicaffeoylquinic acid methyl ester	9.09 ± 0.83 (DPPH)	n
183	3,4,5-*O*-Tricaffeoylquinic acid methyl ester	7.90 ± 0.32 (DPPH)	n
184	Caffeic acid	48.21 ± 1.08 (DPPH)	n
185[I]	Trilobatin	51.59 ± 1.67 (DPPH)	o
186[I]	Yanangdaengin	5.03 ± 0.37 (DPPH)	o
187	3,4-Dihydroxyphenylethanol	19.90 ($ABTS^{\cdot+}$)	p
188	1,2-Dihydroxyphenyl-alcohol-1-*O*-*β*-*D*-glucopyranoside	10.0 ($ABTS^{\cdot+}$)	p
189	2-Methoxyphenyl-alcohol-1-*O*-*β*-*D*-glucopyranoside	15.0 ($ABTS^{\cdot+}$)	p
190	Arbutin	4.5 ($ABTS^{\cdot+}$)	p
191	Orcinol glucoside	19.0 ($ABTS^{\cdot+}$)	p

(Xie et al., 2020). 12-Oxobakuchiol (**42**), 12,13-dihydro-12,13-epoxybakuchiol (**200**), 13-methoxyisobakuchiol (**201**), 12,13-dihydro-12,13-dihydroxybakuchiol (**202**), $\triangle^{1,3}$-bakuchiol (**203**) and (12′*S*)-bisbakuchiol C (**204**) isolated from the fruits of *P. Fructus* demonstrated the potential anti-inflammatory activities on NO production in LPS-activated RAW 264.7 cells as compared to the positive control *L*-N^6-(1-iminoethyl)-lysine [*L*-NIL, (10.29 ± 1.10) μmol/L]. The inhibition of **201**–**203** was similar with that of *L*-NIL, and the inhibition of **42**, **200** and **204** was more significant than that of *L*-NIL (Lv, Xu, Zhang, & Yang, 2020). Five glycosides were isolated from the rhizomes of *A. lancea*, viz., atractyeneyneglycoside A (**63**), atractyeneyneglycoside B (**64**), (2*E*,8*R*)-decene-4,6-diyne-1,8-diol-8-*O*-*β*-*D*-glucopyranoside (**205**), (2*E*,8*S*)-decene-4,6-diyne-1,8-diol-8-*O*-*β*-*D*-glucopyranoside (**206**), and phenylmethanol 7-*O*-α-*L*-rhamnopyranosyl-(1 → 6)-*β*-*D*-glucopyranoside (**207**). They exhibited weak inhibition on LPS-induced NO production in microglia BV2 cells with the value of 22.01%, 14.09%, 11.27%, 13.57% and 31.18%, respectively (Xu, Jiang, Feng, Yang, & Zhang, 2020). Four triterpenoids, *viz*. arnidiol (**208**), 3*β*,16*β*-dihydroxylup-20(29)-ene (**209**), 16*β*-hydroxylupa-20(29)-en-3-one (**210**) and garcinielliptione Q (**211**), were isolated from the roots of *C. minima*. They inhibited the LPS-induced NO production in RAW264.7 cells with IC_{50} of (11.9 ± 0.3), (19.8 ± 1.6), (22.3 ± 0.3) and (24.5 ± 0.2) μmol/L respectively (Xue et al., 2020; Lin et al., 2012). The association between compound and bioactivity can also be investigated within the context of phylogenetic distribution, so as to protect and develop new medicinal source plants.

3.4. Anti-diabetic and hypolipidemic activities

α-Glucosidase and protein tyrosine phosphatase-1B (PTP1B) are important therapy targets for the treatment of type 2 diabetes. All hypolipidemic compounds of 2020 are presented in Table 3. Compounds **31** and **146**–**150** were identified from the leaves of *P. orientalis*; only **146** and **147** exhibited potent inhibition against α-glucosidase as compared to positive control acarbose, yet **31** and **148**–**150** exhibited no inhibitory activity (Wu et al., 2020a).

Twelve dammarane-type triterpenoids were isolated from *Gynostemma pentaphyllum* (Cucurbitaceae); seven (**212**–**218**) were from the acid hydrolyzate of total saponins and five (**219**–**223**) were from total saponins. Their IC_{50} values range from (2.10 ± 0.83) to (56.12 ± 0.26) μmol/L for α-glucosidase as compared to acarbose [IC_{50} (9.49 ± 0.26) μmol/L], and from (1.07 ± 0.05) to (62.19 ± 0.55) μmol/L for PTP1B compared to the positive control Na_3VO_4 [IC_{50} (26.20 ± 0.47) μmol/L]. These compounds showed remarkable inhibition against α-glucosidase and PTP1B except **215**, and **221** had the strongest inhibitory effect (Yin & Hu, 2005; Bai et al., 2010; Shi, Cao, Li, & Zhao, 2010; Shi, Tan, Yan, Jiang, & Hou, 2018; Wang et al., 2020a).

To discover the hypoglycemic components from acid hydrolyzates of *Panax quinquefolius* (Araliaceae) total saponins, eight active triterpenoids (**212 and 224**–**230**) were screened by *in vitro* inhibitory activities. They exhibited certain inhibitory effects on α-glycosidase as compared with acarbose [IC_{50} (9.49 ± 0.18) μmol/L] except **230**. They also possessed stronger inhibitory effects than the positive control Na_3VO_4 [IC_{50} (26.20 ± 1.78) μmol/L] against PTP1B. Compound **227**, a triterpenoid, was found firstly in the acid hydrolysates of total saponins from *P. quinquefolius*. It exhibited significantly inhibitory activity against α-glucosidase, with IC_{50} about 43 times lower than positive control. Compound **227** also displayed the strongest inhibition in PTP1B inhibition test, which was followed by **226**; both of them demonstrated competitive inhibitory pattern in a Lineweaver-Burk plot (Han et al., 2020).

The *db/db* diabetic mice were used to screen the hypoglycemic active fraction from the roots of *Phlomis tuberosa* (Lamiaceae) *in vivo*. The bioactivity-guided isolation yielded the active compounds ellagic acid (**231**), quinic acid (**232**) and 1-*O*-caffeoylquinic acid (**233**), which were demonstrated to be the competitive inhibitor of dipeptidyl peptidase-4 (DPP-4) *in vitro*; their IC_{50} values were comparable to IC_{50} (50.0 ± 1.3) μmol/L of dipeptidin A (Tian, Wang, & Yang, 2020).

As one of the most active constituents in *Ophiopogon japonicus* (Liliaceae), steroidal glycoside ophiopogonin D (OP-D, **234**) could regulate blood lipids and hepatic steatosis by improving intestinal microflora imbalance induced by high fat diet (HFD) in $ApoE^{-/-}$ mice. OP-D could alleviate the intestinal epithelial cell damage caused by bacterial LPS and reduce the metabolic syndrome caused by HFD. OP-D might interact with the intestinal microflora (Chen et al., 2020d).

3.5. Antimicrobial activity

The antibacterial activities towards methicillin-resistant *Staphylococcus aureus* (MRSA) and minimum inhibitory concentrations (MICs) were evaluated for two sesquiterpenoids (**8** and **235**) from the resin-containing woods of *A. sinensis* using the 96-well plates microdilution method. They belong to eremophilane-type and agarospirane-type sesquiterpene, respectively. SAR analysis revealed that sesquiterpene skeleton types were crucial for the antibacterial activity (Näf, Velluz, Brauchli, & Thommen, 1995; Lv, Lei, Liu, Gao, Zhao, & Liu, 2020).

Two fumagillin compounds (**61** and **236**) were secondary metabolites isolated from the fermentation broth of marine fugus *Aspergillus fumigatus* MDCW-15. In paper diffusion and doubling dilution methods, they showed antifungal activity against *Candida albicans* with an equal MIC value (Gao et al., 2020).

Ten compounds (**237**–**246**) of endophytic fungus *Aspergillus ochraceus* SX-C7 from *Selaginella stauntoniana* (Selaginellaceae) demonstrated selective antibacterial effects against four strains: *Candida albicans*, *Bacillus subtilis*, *Escherichia coli* and *Staphylococcus aureus*. All compounds exhibited either moderate or low antimicrobial activities against these strains. Of note, only **244** displayed significant inhibition against *Bacillus subtilis*. Its inhibitory effect was similar to that of positive control kanamycin (Luo et al., 2020).

ent-Labda-8(17),13*E*-dien-15-ol (**247**) was isolated from stems and leaves of *Aphanamixis sinensis* (Meliaceae). Its antibacterial activities against *S. aureus* ATCC 25923, *E. coli* CICC 10003, *Salmonella* UK-18956 were compared to that of kanamycin. In filter paper disk agar diffusion method, **247** exhibited weaker antibacterial activities against *S. aureus* ATCC 25,923 at 5 μg/mL than kanamycin (MIC 1.5 μg/mL), yet no activities against *E. coli* and *Salmonella* were detected (Chen et al., 2020e).

Five major active metabolites of chlorogenic acid, *i.e*., gallic acid (**156**), *p*-hydroxycinnamic acid (**184**), benzoic acid (**248**), 4-hydroxybenzoic acid (**249**) and dihydrocaffeic acid (**250**), were determined by broth microdilution method against methicillin-sensitive *S. aureus* (MSSA), MRSA, non ESBLs-producting *E. coli* (E-), extended-spectrum β-lactamase *E. coli* (E +), *Klebsiella pneumoniae* (E-/E +), *Acinetobacter baumannii* and *Pseudomonas aeruginosa* strains. These metabolites had strong antibacterial activities with MIC values ranging from 4 to 66 times higher than that of chlorogenic acid. The antibacterial activities of **156** and **250** against MSSA and MRSA were increased by 33–66 times. The antibacterial activity of chlorogenic acid could be attributed to some of its metabolites (Fan et al., 2020). All antimicrobial compounds are shown in Table S2.

Table 3
Hypolipidemic activities of isolated compounds.

No.	Compounds	IC_{50} values (μmol/L)	Taxon
146	Myricetrin	97.35 ± 0.18 (α-glucosidase)	l
147	5,8,3′,4′-Tetrahydroxy-flavone-7-*O*-*β*-*D*-xylopyranoside	56.27 ± 0.13 (α-glucosidase)	l
212	20(*S*)-Panaxadiol	10.73 ± 0.21 (α-glucosidase); 10.77 ± 0.08 (PTP1B)	q
212	20(*S*)-Panaxadiol	22.72 ± 0.79 (α-glucosidase); 27.23 ± 2.36 (PTP1B)	r
213	Gypensapogenin A	20.84 ± 0.28 (α-glucosidase); 37.46 ± 1.08 (PTP1B)	q
214	Gypensapogenin F	21.66 ± 0.47 (α-glucosidase); 49.12 ± 0.36 (PTP1B)	q
215	20(*R*)-Protopanaxadiol	56.12 ± 0.26 (α-glucosidase); 62.19 ± 0.55 (PTP1B)	q
216	Gypsapogenin A	2.50 ± 0.41 (α-glucosidase); 8.84 ± 0.12 (PTP1B)	q
217	(20*S*,24*S*)-3*β*,20,21*β*,23*β*,25-Pentahydroxy-21,24-epoxydammarane	29.86 ± 0.24 (α-glucosidase); 15.02 ± 0.09 (PTP1B)	q
218	(23*S*)-3*β*-Hydroxydama-20,24-diene-21-carboxylic acid 21,23-lactone	24.37 ± 0.19 (α-glucosidase); 20.65 ± 0.16 (PTP1B)[I]	q
219	(20*R*,23*R*)-3*β*,20-Dihydroxydammar-24-en-21-oic acid 21,23-lactone 3-*O*-[α-*L*-rhamnopyranosyl (1 → 2)] [*β*-*D*-xylopyranosyl ((1 → 3)]-6-*O*-acetyl-β-*D*-glucopyranoside	27.41 ± 0.97 (α-glucosidase); 6.92 ± 0.18 (PTP1B)	q
220	(20*R*,23*R*)-19-oxo-3*β*,20-Dihydroxydammar-24-en-21-oci acid 21,23-lactone3-*O*-[α-*L*-rhamnopyranosyl-(1 → 2)] [*β*-*D*-xylopyranosyl (1 → 3)]-α-*L*-arabinopyranoside	2.10 ± 0.83 (α-glucosidase); 1.07 ± 0.05 (PTP1B)	q
221	(20*S*,23*S*)-3*β*,20-Dihydroxydammar-24-en-21-oic acid 21,23-lactone 3-*O*-[α-*L*-rhamnopyranosyl (1 → 2)][*β*-*D*-xylopyranosyl (1 → 3)]-6-*O*-acetyl-*β*-*D*-glucopyranoside	31.74 ± 0.89 (α-glucosidase); 33.88 ± 0.21 (PTP1B)	q
222	(20*S*,23*S*)-3*β*,20-Dihydroxydammar-24-en-21-oic acid and 21,23-lactone 3-*O*-[α-*L*-rhamnopyranosyl (1 → 2)] [*β*-*D*-xylopyranosyl-(1 → 3)]-*β*-*D*-glucopyranoside	3.50 ± 0.12 (α-glucosidase); 8.91 ± 0.45 (PTP1B)	q
223	(20*S*)-3*β*,20,21-Trihydroxydammar-23,25-diene 3-*O*-{[α-*L*-rhamnopyranosyl (1 → 2)] [*β*-*D*-xylopyranosyl (1 → 3)]-*β*-*D*-glucopyranosyl}-21-*O*-*β*-*D*-glucopyranoside	6.95 ± 0.31 (α-glucosidase); 18.23 ± 0.35 (PTP1B)	q
224	(20*S*,24*R*)-Dammarane-20,24-epoxy-3*β*,6α,12*β*,25-tetraol	>100 (α-glucosidase); 23.63 ± 5.09 (PTP1B)	
225	20(*R*)-Dammarane-3*β*,12*β*,20,25-tetraol	15.42 ± 0.87 (α-glucosidase); 10.39 ± 0.21 (PTP1B)	r
226	20(*S*)-Dammarane-3*β*,6α,12*β*,20,25-pentol	6.26 ± 1.59 (α-glucosidase); 6.21 ± 0.21 (PTP1B)	r
227	20(*R*)-Dammarane-3*β*,12*β*,20,25-tetrahydroxy-3*β*-*O*-*β*-*D*- glucopyranoside	0.22 ± 0.21 (α-glucosidase); 5.91 ± 0.38 (PTP1B)	r
228	*β*-Sitosterol	69.41 ± 0.03 (α-glucosidase); > 100 (PTP1B)	r
229	Oleanolic acid	1.04 ± 0.34 (α-glucosidase); 18.99 ± 1.46 (PTP1B)	r
230	20(*S*)-Protopanaxadiol	12.49 ± 1.22 (α-glucosidase); 13.38 ± 0.88 (PTP1B)	r
231	Ellagic acid	72.3 ± 1.1 (DPP-4)	s
232	Quinic acid	89.2 ± 1.1 (DPP-4)	s
233	1-*O*-Caffeoyl-quinic acid	103.4 ± 1.8 (DPP-4)	s

Note: [I] IC_{50} value (mmol/L); [II] IC_{50} value (mg/mL).
Taxon: a *Melaleuca alternifolia* (Myrtaceae); b *Mollugo pentaphylla* (Aizoaceae); c *Cynanchum auriculatum* (Asclepiadaceae); d *Sinopodophyllum hexandrum* (Berberidaceae); e *Trigonostemon lutescens* (Euphorbiaceae); f *Curcuma phaeocaulis* (Zingiberaceae); g *Chloranthus fortunei* (Chloranthaceae); h *Panax japonicus* C. A. Mey. var. *major* (Nurkill) C. Y. Wu & K. M. Feng (Araliaceae); i *Veratrum grandiflorum* (Liliaceae); j endophytic fungus *Aspergillus wentti* Y1 isolated from *Ainsliaea macrocephala* (Compositae); k *Dendrobium wardianum* Warner (Orchidaceae); l *Platycladus orientalis* (Cupressaceae); m *Stellera chamaejasme* L. (Thymelaeaceae); n *Azolla imbricata* (Roxb.) Nakai (Azollaceae); o *Lysiphyllum strychnifolium* (Craib) A. Schmitz (Leguminosae); p *Zanthoxylum schinifolium* (Rutaceae); q *Gynostemma pentaphyllum* (Thunb.) Makion (Cucurbitaceae); r *Panax quinquefolius* (Araliaceae); s *Phlomis tuberosa* L. (Labiatae); t *Aquilaria sinensis* (Thymelaeceae); u marine fugus *Aspergillus fumigatus* MDCW-15; v endophytic fungus *Aspergillus ochraceus* SX-C7 from *Selaginella stauntoniana* (Selaginellaceae); w *Aphanamixis sinensis* (Meliaceae).

3.6. Neuroprotective activity

Ginsenoside Rg_1 (**109**), a main active component of *P. ginseng*, presented positive effects on the central nervous system. The Morris water maze, kit and ELISA, along with HE staining and Western blot methods, were used to evaluate the cognitive function, the oxidative damage and inflammation-related indicators, as well as the neuronal apoptosis and apoptosis-related proteins in the hippocampus of APP/PSI mice, respectively. Compound **109** could significantly improve oxidative stress, reduce inflammatory response, inhibit neuronal apoptosis and strengthen cognitive function in APP/PSI mice (Liu, Zhang, He, & Liu, 2020).

Kukoamine A (KuA, **251**), a phenylpropionamide derivative from *Cortex Lycii* (Solanaceae), protected the Parkinson's disease (PD) model against rotenone-induced PC12 cells damage *in vitro* as compared with the rotenone-treated group. The potential protective mechanisms of KuA could be related with inhibition of ROS production, protection of MMP, regulation of protein expressions involved in the mitochondrial apoptosis pathway and suppression of α-synuclein protein expression (Liu et al., 2020bb).

Mangiferin (MGN, **252**), a C-glucosyl xanthone predominantly obtained in the fruits, bark and leaves of *Mangifera indica* (Anacardiaceae), could have a beneficial role in lead (Pb)-induced neurological toxicity and oxidative stress via Nrf2 pathway. MGN targeting activation of Nrf2 was a feasible way to reduce the adverse health effects associated with Pb exposure. The neuroprotection of MGN could be achieved by activating downstream genes of Nrf2, such as antioxidant enzymes, phase II detoxification enzymes and GSH-related enzymes. MGN may be an effective alternative medicine for human oxidative stress and neurotoxicity induced by Pb (Li et al., 2020a).

Acetylcholinesterase (AChE) inhibitors are being considered as promising therapeutic agents to combat against Alzheimer's disease. Compounds **237**–**246** of *Selaginella stauntoniana* endophytic fungus *A. ochraceus* SX-C7 were screened for AChE inhibitory activity. With tacrine as the positive control, **237** showed the potent inhibitory activity against AchE with an inhibitory rate of 62.3%, while **238**, **239** and **241** exhibited certain inhibition with 20%–60% inhibitory rates, and **240**, **242**–**246** displayed weak inhibition with inhibitory rates lower than 20% (Luo et al., 2020).

3.7. Other activities

To date, there is still a lot of bioactivity space that has not been explored in plant, animal and microbial kingdoms, and studies of 2020 provide many new examples. Five galloyl glycosides, *i.e.*, 3′-*O*-galloylsucrose (**49**), 4′-*O*-galloylsucrose (**253**), 6′-*O*-galloylsucrose (**254**), 1′-*O*-galloylsucrose (**255**) and 1,2,3,4,6-pentagalloylglucrose (**256**), from *n*-butanol extract of Guizhi Fuling Capsule were reported to inhibit the calcium influx in primary mouse uterine smooth muscle cells (Zhang et al., 2020a,c). Compounds **51** and **54** were from the roots of *P. multiflorum*. At 10 μmol/L, the former showed hepatoprotective effects, as compared with the positive control bicyclol, on *N*-acetyl-*p*-aminophenol (APAP)-induced HepG2 cells with survival rate of 41.27% ($P < 0.05$), and the latter alleviated the *N*-APAP-induced HepG2 cells injury by dramatically increasing the survival rate from 33.22% to 42.26% ($P < 0.05$). In addition, they had potential α-glucosidase inhibitory activity with inhibition rate of 13.8% and 12.3% ($P < 0.05$) at 10 mmol/L respectively, comparable to the positive control acarbose (Yang et al., 2020a).

Celastrol (**257**), a derivative of ursane-type pentacyclic triterpene from *Tripterygium wilfordii* (Euonymae), showed the toxicity on human biliary epithelial cells by affecting cell viability, cell migration, cell cycle arrest and promoting apoptosis. **257** could be useful for the treatment of liver damage caused by hepatoxicity of natural medicines (Li, Li, Wu, & Li, 2020). Polyphyllin I (**258**), a steroidal saponon derivative of *Paris polyphylla* (Liliaceae), could alleviate osteoblasts injuries induced by TCP wear particles via inhibition of autophagy, but the mechanism has not been directly elucidated (Dong et al., 2020). Cinobufagin (**259**), a cardiac glycoside from the skins of *Bufo gargarizans* and *Bufo melanostictus* (Bufonidae), potently suppressed the cancer-induced bone pain (CIBP). It inhibited the mitogen-activated protein kinase (MAPK) signaling pathway in the spinal cord of rat model, and reduced the production of spinal cytokines IL-1β, TNF-α and MCP-1, thereby decreased the central sensitization and alleviated the CIBP (Jiao, Liu, Chen, Zhang, & Hu, 2020).

The iridoids isovaltrate (**260**) and isovaltrate acetoxyhydrin (**261**) from *Valeriana jatamansi* (Valerianaceae) exhibited anti-influenza A virus activities with IC_{50} values of 85.45 and 19.26 μmol/L respectively in the virus infection model A/WSN/33/2009 (H1N1), as compared to positive control oseltamivir (Liu, Wu, Liu, Li, & Li, 2020). Sanggenon C (**262**) isolated from the root bark of *Morus alba* (Moraceae) significantly improved the bleomycin-induced pulmonary fibrosis and respiratory function in mice. The mechanism might be related to inhibiting the overexpression of TGF-β1 and reducing the expression of inflammatory transcription factor NF-kB and phosphorylation (Liu et al., 2020c).

Flavonoids represent an enormous class of pharmacologically active constituents in anti-vitiligo CHMs. *In vitro* experiments on zebrafish embryos showed that kaempferide (**263**) and isorhamnetin (**264**) could promote melanin production by up-regulating the MC1R/MITF signaling pathway (Yu, Tang, Chen, Wang, & Zhang, 2020). Five phthalides, viz. *Z*-3-butylidenephthalide (**265**), *Z,Z*′-3,3′a,7, 7′a-diligustilide (**266**), 3*Z*,3*Z*′-6,8′,7,3′-diligustilide (**267**), *Z*-tokinolide A (**268**), (3′*Z*)-(3*S*,8*R*,3a′*S*,6′*R*)-4,5-dehydro-3,3′a,8,6′-diligustilide (**269**), were isolated from stems and leaves of *Ligusticum chuanxiong* (Umbelliferae). They significantly reduced the tension of thoracic aortic ring of rats precontracted by potassium chloride (KCl). After treatment with the highest concentration (12 μmol/L) of **266**–**268**, their diastolic rates were 60%, 52% and 70%, and their EC_{50} values were 9.46, 11.86 and 8.73 μmol/L, respectively (Naito et al., 1992; Lu et al., 2008; Zou et al., 2018; Wei, Xu, & Yang, 2017; Tang et al., 2020).

Hirudin (**270**) was isolated from the dried whole body of *Poecilobdella manillensis* (Hirudidae). It reduced uric acid and inhibited renal tubular reabsorption via promoting the expression of organic anion transporter 1 (OAT1) in renal tissue and downregulating the expression of urate transporter 1 (URAT1) and glucose transporter 9 (GLUT9) in the hyperuricemia rat model established by potassium oxazinate (Wu et al., 2020b). A functional natural food pigment lycopene (**271**) could improve blood glucose, blood lipid level and pancreatic inflammation in obese mice induced by HFD, and it might regulate the TLR4/MyD88/NF-kB signaling pathway. However, the ability of **271** in reducing the inflammatory response and restoring the function of pancreatic islets by inhibiting the abnormal activation of macrophages and regulating the polarization of M1 and M2 macrophages remains to be further explored (Tian et al., 2020).

4. Conclusion and prospects

In 2020, Chinese scholars have achieved a lot of gratifying results in the field of natural product chemistry. In this review, we summarize the constituents reported in journals of *Chinese Traditional and Herbal Drugs* (Zhong Cao Yao) and *Chinese Herbal Medicines* in 2020, including 65 compounds with novel chemical structures (23 with bioactivity results), together with 206 known components with outstanding biological activities. Metabolites from both plants, animals and microorganisms are worthy of attention. The review aims to disseminate the latest R&D progress of these natural medicines to researchers in the fields of traditional and herbal medicines around the world. Modern pharmacological investigations of these constituents indicate their immense potential in the treatment of various diseases such as tumor/cancer, ROS related ones, inflammation, diabetes and hyperlipidemia, infection, neural disorder, *etc.* However, as compared with *in vitro* studies, there were much less *in vivo* experiments, and no *ex vivo* results were reported. Equally importantly, the pharmacokinetic and ADME/T (absorption, distribution, metabolism, elimination/excretion, and toxicity) properties must be investigated systematically to objectively evaluate the drug-likeness of both new and old compounds (Hao et al., 2018), which contribute to finding excellent lead compounds for the development of innovative drugs in the future. Although compounds summarized here show diverse bioactivities, their mechanisms of action have not been elaborated. The network pharmacology prediction (Hao & Xiao, 2014) and the SAR studies of the compounds must be strengthened. One area that has long been overlooked is to evaluate the potential clinical utility of characterized compounds from the perspectives of TCM properties/attributes, *e.g.*, four natures and five flavors, ascending and descending, and channel tropism, *etc*. How do the compounds alter during CHM processing? Such studies will benefit the rational processing and combination of single compounds, as well as deeper understanding of incompatibility, *e.g.*, 18 incompatible medicaments and 19 medicaments of mutual antagonism. TCM theories should be used to guide the research of TCM compounds. According to pharmacophylogeny, the phylogenetic distribution of compounds with different natures and flavors can also be explored (Li, 2018), with view to better mining TCM resources. Therefore,

a lot of work remains to be accomplished to exploit the full potential of Chinese unique natural medicine resources.

Editor Note

Dacheng Hao is Editorial Board Members of Chinese Herbal Medicines. He was blinded from reviewing or making decisions on the manuscript. The article was subject to the journal's standard procedures, with peer review handled independently of this Editorial Board Member and their research groups.

Declaration of Competing Interest

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

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Appendix A. Supplementary data

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References

An, Q., Zhou, J. B., Jiang, Y. M., Liang, G. Y., Hu, Z. X., & Hao, X. J. (2020). Chemical constituents of *Stemona tuberosa*. *Chinese Traditional and Herbal Drugs, 51*(13), 3378–3382.

Bai, M. S., Gao, J. M., Fan, C., Yang, S. X., Zhang, G., & Zheng, C. D. (2010). Bioactive dammarane-type triterpenoids derived from the acid hydrolysate of *Gynostemma pentaphyllum* saponins. *Food Chemistry, 119*, 306–310.

Chai, L., Chen, M. S., Lu, W. J., Lin, X., & Liu, B. M. (2020). Chemical constituents of *Melaleuca alternifolia* and its antitumor activities. *Chinese Traditional and Herbal Drugs, 51*(3), 581–587.

Chen, Y., Zhang, Y. X., Jiang, W. H., Luo, S. F., Rao, W. T., Huang, K., & Zhou, F. H. (2020d). Effect of ophiopogonin D on serum lipids and intestinal flora in ApoE$^{-/-}$ mice with high-fat diet. *Chinese Traditional and Herbal Drugs, 51*(13), 3501–3508.

Chen, F. Y., Zou, Y., Chen, J., Huang, W. M., Bian, Y. T., & Luo, Y. M. (2020c). Studies on chemical constituents of *Chloranthus fortunei*. *Chinese Traditional and Herbal Drugs, 51*(6), 1485–1490.

Chen, H., Zhu, Y., Kong, J. B., Sun, Y. J., Gao, L., Bian, H., & Feng, W. S. (2020a). A new benzofuran lignan from rhizomes of *Polygonatum sibiricum*. *Chinese Traditional and Herbal Drugs, 51*(1), 21–25.

Chen, J. F., Xiong, L., Li, F., & Peng, C. (2020). Study on curcumins from *Curcuma phaeocaulis*. *Chinese Traditional and Herbal Drugs, 51*(1), 16–20.

Chen, J. X., Zhang, L. Y., Ni, L., Wu, M. T., Zhang, L. J., Xiao, X. M., & Zou, S. Q. (2020b). A new lactone from *Euscaphis konishii*. *Chinese Traditional and Herbal Drugs, 51*(18), 4605–4609.

Chen, Y. W., Qin, T. L., Wu, S. L., Zhang, F., Lu, G. Y., Dong, F. W., & He, H. P. (2020e). Chemical constitutents from stems and leaves of *Aphanamixis sinensis* and their antibacterial activities. *Chinese Traditional and Herbal Drugs, 51*(18), 4614–4619.

Cheng, L., Chen, Z. Y., Shang, Z. M., Zhang, M. S., Li, X. F., Zhang, J. Y., & Xiao, S. J. (2020). Chemical constituents of *Dendrobium hercoglossum*. *Chinese Traditional and Herbal Drugs, 51*(12), 3126–3130.

Cui, Q. H., Du, R. K., Liu, M. M., & Rong, L. J. (2020). Lignans and their derivatives from plants as antivirals. *Molecules, 25*(1), 183.

Deng, R. X., Huang, Y. Y., Zhang, Y. X., Lu, S. P., Meng, W. J., Zhang, Y., & Liu, P. (2020). Chemical constituents of tannin from roots of *Rheum palmatum*. *Chinese Traditional and Herbal Drugs, 51*(4), 908–911.

Diao, K. P., Li, W., Xiang, K. L., Zhao, L., & Dai, S. J. (2020). A new flavonoid isolated from fruits of *Solanum virginianum*. *Chinese Traditional and Herbal Drugs, 51*(15), 3845–3849.

Ding, N., Li, S. Y., Li, C. H., Chen, L. H., Zhu, Y. J., Wang, J. Y., ... Wang, X. Z. (2020). A new guaiane sesquiterpenes glycoside from *Ainsliaea fragrans*. *Chinese Traditional and Herbal Drugs, 51*(22), 5669–5674.

Dong, F. S., Shou, J. H., Chen, Y. F., Zhang, H. T., Lou, Y. W., Yang, Z. J., & Zhang, Y. (2020). Polyphyllin I alleviates osteoblasts injuries induced by TCP wear particles *in vitro* via inhibition of autophagy. *Chinese Traditional and Herbal Drugs, 51*(9), 2501–2508.

Dong, L., Chang, B., Zhang, Q., Yang, F., & Du, W. (2018). Chemical constituents of flavonoids from roots of *Glycyrrhiza glabra*. *Chinese Traditional and Herbal Drugs, 49*(20), 4780–4784.

Eignerova, B., Tichy, M., Krasulova, J., Kvasnica, M., Rarova, L., Christova, R., ... Sarek, J. (2017). Synthesis and antiproliferative properties of new hydrophilic esters of triterpenic acids. *European Journal of Medicinal Chemistry, 140*, 403–420.

Fan, M., Duan, B. Z., Xia, C. L., & Wang, S. (2020). A new *neo*-clerodane diterpenoid from *Salvia tiliifolia*. *Chinese Traditional and Herbal Drugs, 51*(18), 4610–4613.

Fan, R., Yi, G. J., Lu, L., Zeng, M., Zhou, Y. Y., & Cheng, Q. (2020). Antimicrobial aactivities of chlorogenic acid and 13 main metabolites *in vitro*. *Chinese Traditional and Herbal Drugs, 51*(18), 4610–4613.

Ganzon, J. G., Chen, L. G., & Wang, C. C. (2018). 4-*O*-Caffeoylquinic acid as an antioxidant marker for mulberry leaves rich in phenolic compounds. *Journal of Food and Drug Analysis, 26*(3), 985–993.

Gao, Y. K., Qiu, Z. Y., Song, Y. Q., Wang, K., Lu, Y. Y., Tang, S. Y., ... Wang, C. (2020). A new fumagillin compound from marine-derived *Aspergillus fumigatus* MDCW-15. *Chinese Traditional and Herbal Drugs, 51*(24), 6137–6141.

Gu, X. J., & Hao, D. C. (2016). Recent advances in phytochemistry and pharmacology of C21 steroid constituents from *Cynanchum* plants. *Chinese Journal of Natural Medicines, 14*(5), 321–334.

Han, S. W., Shi, S. M., Zou, Y. X., Wang, Z. C., Wang, Y. Q., Shi, L., & Yan, T. C. (2020). Chemical constituents from acid hydrolyzates of *Panax quinquefolius* total saponins and their inhibition activity to α-glycosidase and protein tyrosine phosphatase 1B. *Chinese Herbal Medicines, 12*, 195–199.

Hao, D. C. (2021). *Taxaceae and Cephalotaxaceae: Biodiversity, chemodiversity and pharmacotherapy*. London: Elsevier/Academic Press.

Hao, D. C. (2018). *Ranunculales medicinal plants: Biodiversity, chemodiversity and pharmacotherapy*. London: Elsevier/Academic Press.

Hao, D. C., Ge, G. B., Wang, P., & Yang, L. (2018). Impact of drug metabolism/pharmacokinetics and their relevance upon Taxus-based drug development. *Current Drug Metabolism, 19*(11), 930–959.

Hao, D. C., & Xiao, P. G. (2014). Network pharmacology: A Rosetta Stone for traditional Chinese medicine. *Drug Development Research, 75*(5), 299–312.

Hao, D. C., & Xiao, P. G. (2020). Pharmaceutical resource discovery from traditional medicinal plants: Pharmacophylogeny and pharmacophylogenomics. *Chinese Herbal Medicines, 12*(2), 104–117.

Hao, D. C., Xiao, P. G., Ma, H. Y., Peng, Y., & He, C. N. (2015). Mining chemodiversity from biodiversity: Pharmacophylogeny of medicinal plants of Ranunculaceae. *Chinese Journal of Natural Medicines, 13*(7), 507–520.

He, W. J., Fu, Z. H., Han, H. J., Yan, H., Zeng, Z. G., Jia, C. J., ... Tan, N. H. (2011). Benzoic acid allopyranosides and lignan glycosides from the twigs of *Keteleeria evelyniana*. *Zeitschrift Fur Naturforschung Section A, 66b*, 733–739.

Hao, D. C., Gu, X. J., & Xiao, P. G. (2017). Anemone medicinal plants: Ethnopharmacology, phytochemistry and biology. *Acta Pharmaceutica Sinica B, 7*(2), 146–158.

Hou, Y. T., Yu, H. M., Chen, Y. J., Zhu, L. J., Chen, J. Y., Zheng, C. P., ... Ye, Y. Q. (2020). A new polyketide from endophytic fungus *Aspergillus oryzae* derived from *Paris polyphylla* var. *yunnanensis*. *Chinese Traditional and Herbal Drugs, 51*(17), 4393–4396.

Huan, L. J., Xiong, Y. X., Wen, S., He, H. E., & Zhang, J. W. (2020). Secondary metabolites of endophyte *Chaetomium globosum* isolated from *Hypericum sampsonii*. *Chinese Traditional and Herbal Drugs, 51*(3), 576–580.

Hou, C. J., Kulka, M., Zhang, J. Z., Li, Y. M., & Guo, F. J. (2014). Occurrence and biological activities of eremophilane-type sesquiterpenes. *Mini-Reviews in Medicinal Chemistry, 14*(8), 664–677.

Jia, L. C., Hu, X. F., Shao, L., Chai, H. Q., & Liu, X. X. (2020). A new benzofuran from *Penicillium oxalicum*, an endophytic fungus isolated from *Pseudostellaria heterophylla*. *Chinese Traditional and Herbal Drugs, 51*(22), 5681–5686.

Jiao, L. B., Liu, D., Chen, T., Zhang, J. H., & Hu, W. (2020). Analgesic mechanism of cinobufagin in rats with bone cancer pain. *Chinese Traditional and Herbal Drugs, 51*(14), 3734–3741.

Kongkiatpaiboon, S., Duangdee, N., Tayana, N., Schinnerl, J., Bacher, M., & Chewchinda, S. (2020). Yanangdaengin, a dihydrochalcone glucoside galloyl ester as active antioxidative agent from leaves of *Lysiphyllum strychnifolium* (syn. *Bauhinia strychnifolia*). *Chinese Herbal Medicines, 12*, 452–455.

Li, H. B., Yang, B., Ge, W., Cao, Z. Y., Cao, L., Yu, Y., & Xiao, W. (2020a). Two new terpenoids from Reduning Injection. *Chinese Herbal Medicines, 12*, 183–187.

Li, S. F., Liu, H., Zhang, X. L., Li, D. Y., & Li, Z. L. (2020b). A new norsesquiterpene glycoside from fruits of *Actinidia arguta*. *Chinese Traditional and Herbal Drugs, 51*(2), 299–306.

Li, Y. J., Li, S., Wu, J. Z., & Li, X. J. Y. (2020). Toxicity and mechanisms of celastrol on human biliary epithelial cells. *Chinese Traditional and Herbal Drugs, 51*(14), 3700–3707.

Li, J. R., Li, L. J., Zhu, J. L., & Chen, H. Y. (2020). Effect and mechanism of cyclanoline on nitrosamine-induced bladder cancer in rats. *Chinese Traditional and Herbal Drugs, 51*(20), 5201–5206.

Li, J., Li, Z. L., Jia, R. F., Liu, H. X., Qian, S. H., & Yang, W. N. (2020c). A new triterpenes isolated from leaves of *Phyllanthus acidus*. *Chinese Traditional and Herbal Drugs, 51*(3), 571–575.

Li, J. J., Ren, F. C., Hu, J. M., & Zhou, J. (2020). Chemical constituents and cytotoxic activities of *Dendrobium wardianum*. *Chinese Traditional and Herbal Drugs, 51*(7), 1819–1824.

Li, J. Y. (2018). *Analysis of the association between Chinese medicinal herbs, family genera and component molecular skeleton based on association network and phylogenetic tree*. Shandong University of Traditional Chinese Medicine. Master thesis.

Li, M., Yang, J., Zhu, J. X., & Zhong, G. Y. (2020). A new coumarin from flowers of *Edgeworthia gardneri*. *Chinese Traditional and Herbal Drugs, 51*(16), 4109–4112.
Lin, K. W., Huang, A. M., Yang, S. C., Weng, J. R., Hour, T. C., Pu, Y. S., & Lin, C. N. (2012). Cytotoxic and antioxidant constituents from *Garcinia subelliptica*. *Food Chemistry, 135*, 851–859.
Liu, Yang, Cui, Ying, Lu, Liyan, Gong, Yufeng, Han, Wen, & Piao, Guishun (2020a). Natural indole-containing alkaloids and their antibacterial activities. *Archiv der Pharmazie, 353*(10), e2000120.
Liu, W. W., Song, Q., Zu, X. Y., Jiang, X. W., Yang, Y., Gao, H., & Zhao, Q. C. (2020b). Neuroprotective effects of kukoamine A against rotenone-induced neurotoxicity in PC12 cells. *Chinese Traditional and Herbal Drugs, 51*(24), 6302–6309.
Liu, G. K., Li, S. Y., Ding, L. Q., Wang, L. N., & Qiu, F. (2020). Studies of sesquiterpenes from *Myrrha*. *Chinese Traditional and Herbal Drugs, 51*(13), 3372–3377.
Liu, H., Wu, J. H., Liu, D., Li, R. T., & Li, H. M. (2020). Iridoids from *Valeriana jatamansi* and their related anti-influenza virus activity. *Chinese Traditional and Herbal Drugs, 51*(11), 2886–2894.
Liu, P. P., Yu, H. M., & Tian, Y. Q. (2020). A new lignan from *Artemisiae Annuae Herba*. *Chinese Traditional and Herbal Drugs, 51*(6), 1481–1484.
Liu, L., Zhang, K., He, M., & Liu, W. (2020). Neuroprotective effect ginsenoside Rg_1 in transgenic mice brain with Alzheimer's disease. *Chinese Traditional and Herbal Drugs, 51*(5), 1264–1272.
Liu, F. Y., Zhang, D. L., Hou, W. B., & Tang, S. A. (2020). Study on chemical constituents from seeds of *Trigonella foenum-graecum*. *Chinese Traditional and Herbal Drugs, 51*(1), 31–35.
Luo, P., Shao, G., Zhang, S. Q., Zhu, L., Ding, Z. T., & Cai, L. (2020). Secondary metabolites of endophytic fungus *Aspergillus ochraceus* SX-C7 from *Selaginella stauntoniana*. *Chinese Traditional and Herbal Drugs, 51*(15), 3856–3862.
Lv, K. Y., Lei, Z. D., Liu, Y. R., Gao, X. X., Zhao, Y. M., & Liu, D. L. (2020). Study on sesquiterpenes from *Aquilaria sinensis*. *Chinese Traditional and Herbal Drugs, 51*(9), 2390–2394.
Liu, Y., Luo, Z. L., Yan, F. L., Pan, C., Lv, B. Q., Tang, A. M., & Yang, C. F. (2020c). Effect of sanggenon C on pulmonary fibrosis induced by bleomycin in mice and potential mechanisms implicated. *Chinese Traditional and Herbal Drugs, 51*(16), 4244–4250.
Lu, X. H., Zhang, J. J., Zhang, X. X., Liang, H., & Zhao, Y. Y. (2008). Study on biligustilides from *Angelica sinensis*. *China Journal of Chinese Materia Medica, 33*(19), 2196–2201.
Lv, Q., Xu, Q. X., Zhang, Y. T., & Yang, X. W. (2020). Inhibition of bakuchiol and its derivatives in *Psoraleae Fructus* on nitric oxide production in lipopolysaccharide-activated RAW 264.7 cell lines. *Chinese Traditional and Herbal Drugs, 51*(2), 307–314.
Mei, Y. D., Li, H. B., Wang, Z. Z., Yu, Y., Yao, X. S., & Xiao, W. (2020). Glycosides from flower buds of *Lonicera macranthoides*. *Chinese Traditional and Herbal Drugs, 51*(2), 287–292.
Meng, X., Qiu, Z. D., Wang, L., & Liu, D. (2020). Mechanism of ginsenoside CK inhibiting proliferation of human colon cancer SW480 cells. *Chinese Traditional and Herbal Drugs, 51*(6), 1567–1574.
Meng, X. H., Shang, X. Y., & Yang, J. L. (2020). Phenolic chemical constituents of *Zanthoxylum schinifolium* pericarps and their anti-oxidative effects. *Chinese Traditional and Herbal Drugs, 51*(8), 2095–2101.
Naito, T., Niitsu, K., Ikeya, Y., Okada, M., & Mitsuhashi, H. (1992). A phthalide and 2-farnesyl-6-methyl benzoquinone from *Ligusticum chuangxiong*. *Phyrochemistry, 31*(5), 1787–1789.
Näf, R., Velluz, A., Brauchli, R., & Thommen, W. (1995). Agarwood oil (*Aquilaria agallocha* Roxb.). Its composition and eight new valencane-, eremophilane- and vetispirane-derivatives. *Flavour and Fragrance Journal, 10*, 147–152.
Peng, G., Huang, J., Zhou, Y. J., Chou, A., & Peng, D. (2020). Chemical constituents of *Schoenoplectus tabernaemontani*. *Chinese Traditional and Herbal Drugs, 51*(19), 4902–4906.
Peng, J. H., Cui, T., & Feng, Q. (2009). Research progress in pharmacology of *Pueraria lobata* (willd) Ohwi and its main isoflavones. *Chinese Traditional and Herbal Drugs, 40*(S1), 66–69.
Peng, Y. R., Wang, Z. X., Zhao, J. P., Xu, Q. M., & Yang, S. L. (2020). Study on isoflavones isolated from stems of *Wisteria sinensis*. *Chinese Traditional and Herbal Drugs, 51*(15), 3850–3855.
Qian, W. Q., Wu, W. L., Zhang, X. H., Kang, Y., Wang, Y. Q., Deng, Y. R., ... Huang, J. M. (2020). Chemical constituents from whole herbs of *Azolla imbricata*. *Chinese Traditional and Herbal Drugs, 51*(17), 4397–4404.
Ren, Y. J., Cao, Y. G., Zhang, B. B., He, C., Guo, M. H., Qi, M., ... Feng, W. S. (2020). Chemical constituents and antitumor activity from stems and leaves of *Dioscorea opposita*. *Chinese Traditional and Herbal Drugs, 51*(4), 918–924.
Ren, X. J., Han, M. Y., Li, Y., & Xie, Z. X. (2009). Synthesis of 3β-hydroxy-24-norchol-5-en-23- oic acid. *Acta Chimica Sinica, 67*(14), 1700–1704.
Rosales, P. F., Bordin, G. S., Gower, A. E., & Moura, S. (2020). Indole alkaloids: 2012 until now, highlighting the new chemical structures and biological activities. *Fitoterapia, 143*, 104558.
Shen, T. M., Huang, C. Q., Wu, J. J., Yang, C. Z., Chen, Y., & Liu, Z. Y. (2020). GC-MS analysis of volatile oil from traditional She medicine *Clematis Florida* var. *plena* flower. *Chinese Traditional and Herbal Drugs, 51*(24), 6362–6366.
Shi, L., Cao, J. Q., Li, W., & Zhao, Y. Q. (2010). Three new triterpene saponins from *Gynostemma pentaphyllum*. *Helvetica Chimica Acta, 93*, 1785–1794.
Shi, J. M., Liu, X. H., He, C. L., Lin, L. W., & Chen, D. L. (2020). A new alkaloid from *Veratrum grandiflorum*. *Chinese Traditional and Herbal Drugs, 51*(13), 3365–3371.
Sun, H., Zhang, Y. C., Huo, H. X., Xia, H., Wang, C. C., Liu, D. F., & Li, J. (2020a). Chemical constituents from pericarps of *Aquilaria yunnanensis*. *Chinese Traditional and Herbal Drugs, 51*(1), 9–15.
Shi, L., Tan, D. H., Yan, T. C., Jiang, D. H., & Hou, M. X. (2018). Cytotoxic triterpenes from the acid hydrolyzate of *Gynostemma pentaphyllum* saponins. *Journal of Asian Natural Products Research, 20*(2), 182–187.
Tang, F., Tan, Y. Z., Ao, H., Yan, H. L., Luo, W., Yang, Q., ... Peng, C. (2020). Discovery of phthalides with vasodilating activity in stems and leaves of *Ligusticum chuanxiong*. *Chinese Traditional and Herbal Drugs, 51*(5), 1190–1195.
Teponno, R. B., Kusari, S., & Spiteller, M. (2016). Recent advances in research on lignans and neolignans. *Natural Product Reports, 33*(9), 1044–1092.
Tian, T., Wang, Z. T., & Yang, Y. B. (2020). Chemical constituents and hypoglycemic activity of *Phlomis tuberosa*. *Chinese Traditional and Herbal Drugs, 51*(12), 3131–3138.
Wang, F. Q., Sun, L. Q., Wang, J. L., Zhao, M., Li, J., Shi, Z. C., & Zhang, S. J. (2020a). Chemical constituents from *Syneilesis aconitifolia*. *Chinese Traditional and Herbal Drugs, 51*(11), 2878–2885.
Wang, J. X., Yang, M., Deng, G. W., Zhang, X. L., He, B., Liu, Y. R., & Song, Z. J. (2020b). Chemical compositions and anticancer activity of *Mollugo pentaphylla*. *Chinese Traditional and Herbal Drugs, 51*(4), 902–907.
Wei, W., Xu, W., & Yang, X. W. (2017). Two new phthalide dimers from the rhizomes of *Ligusticum chuanxiong*. *Journal of Asian Natural Products Research, 19*(7), 704–711.
Wu, L. P., Yu, Y. R., Liu, M. Y., Jiang, H. Y., Zhong, S. Y., Li, L. R., & Huang, J. (2020a). A new phenylpropanoid glycoside from leaves of *Platycladus orientalis*. *Chinese Traditional and Herbal Drugs, 51*(3), 563–570.
Wu, L. X., Liang, H., Zhao, Y. X., He, H. M., Liang, X. M., Zhou, W. H., & Liu, X. H. (2020b). Effect of hirudin on expressions of urate transporters OAT1, URAT1 and GLUT9 in hyperuricemia rats. *Chinese Traditional and Herbal Drugs, 51*(22), 5776–5780.
Wu, X. Y., & Yang, X. W. (2020). Coumarins from *Notopterygium incisum* and their inhibitory effect against lipopolysaccharide-induced nitric oxide production in RAW 264.7 macrophage cells. *Chinese Traditional and Herbal Drugs, 51*(13), 3383–3391.
Xie, Z. Q., Ding, L. F., Nie, W., Lei, T., Wu, S. F., Song, D. L., & Wu, X. D. (2020). A new tetrahydrofuran-type lignan from leaves of *Magnolia denudata*. *Chinese Traditional and Herbal Drugs, 51*(22), 5675–5680.
Xu, Y. L., He, J. L., Jiang, S. P., Wang, Y. J., & Zhu, W. P. (2020). A new prenylated flavonoid glycoside from *Sinopodophyllum hexandrum*. *Chinese Traditional and Herbal Drugs, 51*(17), 4388–4392.
Xu, K., Jiang, J. S., Feng, Z. M., Yang, Y. N., & Zhang, P. C. (2020). Two new polyacetylene glycosides from rhizomes of *Atractylodes lancea*. *Chinese Traditional and Herbal Drugs, 51*(20), 5105–5113.
Xu, X., Wang, X. P., Shen, M., Sui, H., Wang, L., Fan, S. S., ... Zhe, G. M. (2020). A new quinone and a new phenolic glycoside from *Thymus quinquecostatus*. *Chinese Traditional and Herbal Drugs, 51*(5), 1171–1174.
Xu, X., Zhang, Y. Q., Xu, J. W., He, X. J., & Wang, Y. H. (2020). Chemical constituents of alcohol extract of *Mori Fructus*. *Chinese Traditional and Herbal Drugs, 51*(6), 1476–1480.
Xu, W. H., Zhao, P., Wang, M., & Liang, Q. (2019). Naturally occurring furofuran lignans: Structural diversity and biological activities. *Natural Product Research, 33*(9), 1357–1373.
Xue, P. H., Li, J. Y., Liu, D., Kang, N., Deng, Y. R., Zhao, F., & Qiu, F. (2020). Chemical constituents of triterpenes from *Centipeda minima* and its anti-inflammatory activities. *Chinese Traditional and Herbal Drugs, 51*(19), 4907–4915.
Yan, Y. Y., Liu, G., Zhang, X. Y., & Hu, Y. T. (2020). A new monoterpene glycoside compound from roots of *Paeonia lactiflora*. *Chinese Traditional and Herbal Drugs, 51*(1), 5924–5928.
Yang, J. B., Sun, H., Ma, J., Song, Y. F., Liu, Y., Wang, Q., & Ma, S. C. (2020a). New phenolic constituents obtained from *Polygonum multiflorum*. *Chinese Herbal Medicines, 12*, 342–346.
Yang, Y. N., Huang, X. Y., Feng, Z. M., Jiang, J. S., & Zhang, P. C. (2014). Hepatoprotective activity of twelve novel 7'-hydroxy lignan glucosides from *Arctii Fructus*. *Journal of Agricultural and Food Chemistry, 62*, 9095–9102.
Yang, L. J., Ding, T., Zhou, Y., Xun, J. J., Shen, Y. H., & Zhang, W. D. (2020b). Study on chemical constituents of endophytic funfus *Aspergillus wentti* Y1 from *Ainsliaea macrocephala* and their bioactivities. *Chinese Traditional and Herbal Drugs, 51*(8), 2102–2106.
Yin, F., & Hu, L. H. (2005). Six new triterpene saponins with a 21,23-lactone skeleton from *Gynostemma pentaphyllum*. *Helvetica Chimica Acta, 88*, 1126–1134.
You, M., Chen, L., Wang, Q., Li, Z. F., Feng, Y. L., Zhong, G. Y., & Yang, S. L. (2020). Isolation and identification of chemical constituents from *Disporum cantoniense* (III). *Chinese Traditional and Herbal Drugs, 51*(7), 1814–1818.
Yu, H. M., Hou, Y. T., Zhu, L. J., Chen, Y. J., Chen, J. Y., Dong, M., ... Ye, Y. Q. (2020). Two new α-pyronoids from endophytic fungus *Aspergillus oryzae* derived from *Paris polyphylla* var. *yunnanensis*. *Chinese Traditional and Herbal Drugs, 51*(19), 4891–4895.
Yu, L., Tang, H., Chen, H. Y., Wang, X. Q., & Zhang, B. (2020). Pharmacodynamic evaluation and mechanism of methoxyflavone to promote melanin production in zebrafish. *Chinese Traditional and Herbal Drugs, 51*(23), 6023–6034.
Yue, G. J., Wang, C. X., Yu, M. Q., Qin, N. K., Wen, Y., Zhang, W. Q., ... Ma, Q. (2020). *In vitro* study of astragaloside IV on reversing multidrug resistance of human breast cancer cell MDA-MB-231 to doxorubicin. *Chinese Traditional and Herbal Drugs, 51*(20), 5237–5242.
Zhang, D. P., Zhou, X. L., Ma, G. X., Song, H. L., Shi, L. L., & Wei, H. Y. (2020b). A new lignan from stems of *Trigonostemon lutescens*. *Chinese Traditional and Herbal Drugs, 51*(14), 3633–3636.

Zhang, H. D., Xie, X., Liu, L. N., Ni, F. Y., Yin, H. M., Wang, Y. X., & Xiao, W. (2020c). Studies on chemical constituents in Guizhi Fuling Capsule (VII). *Chinese Traditional and Herbal Drugs, 51*(16), 4113–4116.
Zhang, H. W., Jiang, W., Huang, W. L., Yang, X. J., Deng, Y., Wang, W., & Song, X. M. (2020a). A new triterpenoid from leaves of *Panax japonicas* var. *major*. *Chinese Traditional and Herbal Drugs, 51*(1), 26–30.
Zhang, H. X., Xia, Z., Xu, T. Q., Chen, Y. M., & Zhou, G. X. (2020). Study on chemical constituents of *Gendarussa vulgaris*. *Chinese Traditional and Herbal Drugs, 51*(18), 4620–4626.
Zhang, Q. Y., Lin, C. Z., Yuan, Y., Ma, Y. X., & Zhu, C. Z. (2020). Chemical constituents of *Picrasma quassioides*. *Chinese Traditional and Herbal Drugs, 51*(19), 4884–4890.
Zhang, Y. Z. (2018). *The distribution patterns of secondary metabolites in the tree of life of the seed plants*. Yunnan University. PhD Dissertation.
Zhou, F. L., Hu, M., Hu, J., Lin, T., & He, Y. C. (2020). Maslinic acid induces autophagy through PI3K/Akt/mTOR pathway in human nasopharyngeal carcinoma cells. *Chinese Traditional and Herbal Drugs, 51*(9), 2481–2485.
Zhou, H. Z., Tang, L. J., Gong, Y., Luo, W., Li, L. M., & Chen, H. L. (2020). Chemical constituents from flowers of *Stellera chamaejasme* and their antioxidant activity. *Chinese Traditional and Herbal Drugs, 51*(9), 2395–2401.
Zhu, H., Zhang, Z., Huang, W. Z., Ye, Y., Zhou, Y., Liu, G. H., ... Gao, X. M. (2020). A new diphenylpropanoid from *Cassia floribunda*. *Chinese Traditional and Herbal Drugs, 51*(11), 2871–2877.
Zhu, P. H. (2011). Effect of isoflavone extract from *Cicer arietinum* on learning and memory abilities in senile mice induced by *D*-galactose. *Chinese Traditional and Herbal Drugs, 42*(5), 969–971.
Zou, J., Chen, G. D., Zhao, H., Huang, Y., Luo, X., Xu, W., & Gao, H. (2018). Triligustilides A and B: Two pairs of phthalide trimers from *Angelica sinensis* with a complex polycyclic skeleton and their activities. *Organic Letters, 20*, 884–887.
Zuo, T. T., Li, W. W., Li, X., Wang, H. D., & Yang, W. Z. (2020). A new oleanolic acid-type saponin from roots of *Panax ginseng*. *Chinese Traditional and Herbal Drugs, 51*(14), 3623–3632.

Further reading

Hao, Da-Cheng, & Xiao, Pei-Gen (2020b). Plant pharmacophylogeny: past, present and future. *Journal of Chinese Pharmaceutical Sciences, 29*(12), 831–854.
Li, Z., Chen, L., Zhao, H. W., Li, B., Wang, X., & Yan, H. J. (2020e). A new steroid from leaves of *Dysoxylum binectariferum*. *Chinese Traditional and Herbal Drugs, 51*(19), 4896–4901.
Li, H. W., Lan, T. J., Yun, C. X., Yang, K. D., Du, Z. C., Luo, X. F., ... Deng, J. G. (2020). Mangiferin exerts neuroprotective activity against lead-induced toxicity and oxidative stress via Nrf2 pathway. *Chinese Herbal Medicines, 12*, 36–46.
Zhang, X. S., Bi, X. L., Xiao, W., Cao, J. Q., Xia, X. C., Diao, Y. P., & Zhao, Y. Q. (2013). Protein tyrosine phosphatase 1B inhibitory effect by dammarane-type triterpenes from hydrolyzate of total *Gynostemma pentaphyllum* saponins. *Bioorganic & Medicinal Chemistry Letters, 23*, 297–300.
Yang, M. H., Ma, S. C., Zang, H., Li, F. F., & Ding, L. (2020). Mechanism of wangzaozin A, an ent-kaurane diterpene, on cytoskeletal rearrangement and migration inhibition of A549 cells. *Chinese Traditional and Herbal Drugs, 51*(24), 6229–6238.
Wang, Z., Yin, Y., Bian, Y. Y., Tian, J. L., & Shi, L. (2020). Triterpenoids from *Gynostemma pentaphyllum* and their inhibition activity to α-glycosidase and protein tyrosine phosphatase 1B. *Chinese Traditional and Herbal Drugs, 51*(24), 6142–6150.
Wang, X. J., Xie, Q., Liu, Y., Lu, S. Y., Daniyal, M., Li, B., & Wang, W. (2020c). Study on antitumor activity of triterpenoid saponins from Tujia ethnomedicine Kouziqi. *Chinese Traditional and Herbal Drugs, 51*(7), 1831–1838.
Tian, Y. M., Li, R., Zhu, R. Y., Bai, Y., Chen, B. B., Xia, B. K., ... Zhang, D. W. (2020). Effect of lycopene on glycolipid metabolism and pancreatic tissue through regulation of TLR4/MyD88/NF-kB signaling pathway in high-fat diet induced obese mice. *Chinese Traditional and Herbal Drugs, 51*(16), 4236–4243.
Sun, Y. J., Chen, H. J., Gao, M. L., Feng, W. S., Chen, H., & Bian, H. (2020b). Triterpenoids from aerial parts of *Gendarussa vulgaris*. *Chinese Traditional and Herbal Drugs, 51*(2), 293–298.
Liu, W. Y., Chen, L. Y., Huang, Y. Y., Fu, L., Song, L. Y., Wang, Y. Y., & Bi, Y. F. (2020a). Antioxidation and active constituents analysis of flower residue of *Rosa damascena*. *Chinese Herbal Medicines, 12*, 336–341.
Li, Z. G., Wu, J., Zhan, S. Q., Zhu, L., Jiang, R., & Cai, Y. S. (2020d). One new C_{21} steroid from *Cynanchum auriculatum*. *Chinese Traditional and Herbal Drugs, 51*(23), 5921–5933.