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Identification of metabolites in different parts of Juandan Baihe (*Lilium lancifolium*) by UPLC-Q-TOF-MS and their hypoglycemic activities

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ABSTRACT

Objective To identify the main components in the extracts of different parts of Juandan Baihe (*Lilium lancifolium*) by ultra-high performance liquid chromatography quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS) technology and investigate their hypoglycemic activities.

Methods The MS fragmentation pathways of the main types of compounds in Juandan Baihe (*Lilium lancifolium*) were studied, and the main components in the extracts were systematically identified using MS fragmentation pathways combined with MS mining technology. Based on the hyperglycemia male mouse model [specific pathogen free (SPF)-grade Kunming mice] induced by streptozotocin (intragastric administration of 80 mg/kg for 3 d), the hypoglycemic effects of extracts of Juandan Baihe (*Lilium lancifolium*) roots, stems, corms, leaves, and flowers were evaluated by measuring the changes of blood glucose, daily water consumption, daily food intake, and body weight.

Results The MS fragmentation pathways of regalosides, dioscins, phenylpropanoids, flavonoids, and chlorogenic acids in Juandan Baihe (*Lilium lancifolium*) were clarified, and a mining method for compounds in this plant was constructed. A total of 58 compounds, including 6 chlorogenic acids, 14 regalosides, 13 phenylpropanoids, 5 flavonoids, and 20 dioscins, were identified from the roots, stems, corms, leaves, and flowers of Juandan Baihe (*Lilium lancifolium*). Among them, 30 compounds were reported for the first time from this plant. The root and corm extracts demonstrated significant hypoglycemic activities by reducing blood glucose levels from 23.76 ± 1.21 and 24.29 ± 1.35 mmol/L to 17.21 ± 1.23 and 18.78 ± 1.49 mmol/L, respectively ($P < 0.05$). The roots and corms extracts could also attenuate the symptoms of polydipsia ($P < 0.01$), polyphagia ($P < 0.05$), and weight loss caused by diabetes.

Conclusion This study clarifies that the roots of Juandan Baihe (*Lilium lancifolium*) are rich in regalosides and dioscins for the first time, and have significant hypoglycemic activities, providing the foundation for the comprehensive utilization of this plant and the development of hypoglycemic drugs.

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1 Introduction

Baihe (Lilii Cormus), which belongs to the perennial Liliaceae family, is a dried fleshy corm derived from *Lilium lancifolium* Thunb., *Lilium broumii* F. E. Brown var. *viridulum* Baker, or *Lilium pumilum* DC.. It is a precious traditional Chinese herb, and has the effects of nourishing and moistening the lungs and removing cardiopyrexia for tranquilization. It has been used for Yin deficiency and dryness cough, hemoptysis, insomnia and dreaminess, restlessness, palpitations, and mental confusion [1, 2]. Modern pharmacological research has shown that Baihe (Lilii Cormus) has immunomodulatory, anti-hypoxic stress injury, anti-oxidant, anti-depressant, anti-inflammatory, anti-tumor, hypoglycemic, and anti-bacterial effects [3, 4]. Glycosides, polyphenols, flavonoids, steroidal saponins, and polysaccharide compounds are the main chemicals corresponding to their biological activities [5, 6]. Over the past decades, researchers mainly focused on the medicinal parts of the corms, while few studies concentrated on other non-medicinal parts [7]. The medicinal parts of Juandan Baihe (*Lilium lancifolium*) are the corms, while other parts are almost unused, resulting in a huge waste of resources. In this study, we used ultra-high performance liquid chromatograph/quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS) technology to analyze the components of extracts from the roots, stems, corms, leaves, and flowers of Juandan Baihe (*Lilium lancifolium*), and identified the main components in those parts. Additionally, we investigated the hypoglycemic activities of different parts of the Juandan Baihe (*Lilium lancifolium*) to clarify the active parts. Our research lays a foundation for comprehensive utilization and provides a preliminary basis for developing hypoglycemic drugs based on Baihe (Lilii Cormus) resources.

2 Materials and methods

2.1 Instruments

1290/6540 UPLC-Q-TOF-MS (Agilent Technologies Co., Ltd.), Milli-Q Advantage A10 system (Millpore Corporation), SKP-3150 Pulverizer (Hebei Benchen Technology Co., Ltd.), AR2140 electronic balance (OHAUS Corp), Heidolph rotary evaporator (Heidolph), blood glucose meters, and test strips (Wenze Easy Type, Shanghai Johnson & Johnson Medical Devices Co., Ltd.).

2.2 Drugs and reagents

Six standards including chlorogenic acid (≥ 98%), caffeic acid (≥ 98%), acroside A (≥ 98%), dioscin B (≥ 98%), rutin (≥ 98%), and dioscin A (≥ 98%) were purchased (Shanghai Shidande Biotechnology Co., Ltd., China) for studying the MS fragmentation patterns of compounds in Juandan Baihe (*Lilium lancifolium*). Streptozotocin (> 99%) and acarbose (≥ 95%) were purchased from Dalian Meilun Biotechnology Co., Ltd. and Shanghai Yuanye Biotechnology Co., Ltd., China, respectively. Acetonitrile and formic acid (chromatographically pure) were purchased from Sinopharm Chemical Reagent Co., Ltd., China.

2.3 Sample preparation

The roots, stems, corms, leaves, and flowers of Juandan Baihe (*Lilium lancifolium*) plants were collected from farmers' plantations in Longshan County, Hunan Province, and were identified by WANG Hong, deputy director of the Pharmacy Department of the National Hospital of Traditional Chinese Medicine of Xiangxi Tujia and Miao Autonomous Prefecture. About 3.0 kg of roots, stems, corms, leaves, and flowers were dried in an oven at 60 °C, and were crushed after drying, respectively. An amount of 10 L of 70% ethanol was added to the dried powder for reflux extraction, and the extraction was conducted twice. The extract solution was combined and then the solvent was recovered by the vacuum reduction concentration to produce five extracts.

2.4 Preparation of standards and extracted solution

10 mg of six standard substances and dried extract from different parts of Juandan Baihe (*Lilium lancifolium*) were weighed, respectively, and 10 mL of methanol solution was used as the solvent. The extracted solution was filtered by a 0.22 μm microporous filter and transferred into a liquid phase vial. The standard and extract solvents were employed to investigate the MS fragmentation patterns and structural identification of compounds in Juandan Baihe (*Lilium lancifolium*).

2.5 UPLC-Q-TOF-MS condition

Ultra-high-performance liquid chromatography (UPLC) was used to separate the compounds in Juandan Baihe (*Lilium lancifolium*), and quadrupole time-of-flight mass spectrometry (Q-TOF-MS) was used to detect separate compounds and obtain the mass spectrometry and tandem mass spectrometry (MS/MS) spectra of the compounds. UPLC and Q-TOF-MS conditions were as follows.

Chromatography was performed using an Agilent 1290 UPLC system; an ACQUITY UPLC® BEH-C18 (100 mm × 2.1 mm, 1.7 μm) was employed as a separation column; the elution solution consisted of 0.1% deionized water (A) and 0.1% acetonitrile (B). The elution program was as follows: 0 – 20 min, 5 – 50% B, 20 – 32 min, 50 – 72% B, 32 – 40 min, 72% – 90% B. The column temperature was kept at 30 °C and the detection wavelength

was set at 254 nm. The rate was set at 0.3 mL/min, and the injection volume was 3 μL.

Mass spectrometric experiments were performed using a 6540 Q-TOF/MS accurate mass spectrometer in a negative mode. The condition of Q-TOF-MS was as follows: drying gas flow rate 10 L/min; drying gas temperature 350 °C; sheath gas flow rate 12 L/min; sheath gas temperature 300 °C; atomizing gas pressure 55 psig; capillary tube Voltage 3 500 V; cone voltage 100 V; scanning range *m/z* 100 – 1 700; secondary fragmentation voltage 15 – 30 eV. The total ion chromatograms (TICs) of different parts of Juandan Baihe (*Lilium lancifolium*), such as roots, stems, corms, leaves, and flowers, and the compounds were identified.

2.6 Analytical methods for metabolite identification

Juandan Baihe (*Lilium lancifolium*) contains many compounds, and the complex matrix affects the MS response of compounds during the MS analysis process. Two methods were used to discover as many metabolites in Juandan Baihe (*Lilium lancifolium*) extracts as possible. The first method was a non-targeted strategy, namely, all high-abundance compounds present in the TICs of Juandan Baihe (*Lilium lancifolium*) extract were selected and their MS/MS were produced by the target-MS/MS. The structures of the obtained compounds were tentatively identified by their MS/MS and the fragmentation patterns of standards [8-10]. The second method was the precise-targeting method, which summarizes the compounds currently reported in the genus of Baihe (Lilii Cormus), and then searches the *m/z* of these reported compounds in the TICs. If the *m/z* presents in the TICs, the MS/MS of the candidate is produced to determine whether its structure is consistent with the MS/MS, and finally determining the structure [11-13].

2.7 Evaluation of the hypoglycemic activity *in vivo*

2.7.1 Experimental animals Specific pathogen free (SPF)-grade male Kunming mice were purchased from Hunan Slack Jingda Experimental Animal Co., Ltd., and the license number is SCXK (Xiang) 2019-0004. Mice were kept in a clean animal room at a temperature of 20 – 25 °C, a humidity of 50% – 70%, and with a 12 h light and dark cycle. During the experiment, the animals had free access to water and food. This experiment was approved by the Biomedical Ethics Committee of Jishou University (JSDX-2023-0001).

2.7.2 Establishment of the hyperglycemic mice and drug administration A total of 80 SPF male Kunming mice (20 – 24 g, four weeks) were adaptively fed for one week. Except for the normal group, the remaining 70 mice were intraperitoneally injected with streptozotocin for 3 d (80 mg/kg) after feeding with high-fat diet for 30 d. Normal group was injected intraperitoneally with an equal volume of distilled water for 3 d. The fasting blood glucose of mice was measured on day 3 after injection. Mice with fasting blood glucose under 11.1 mmol/L were injected with 30 mg/kg streptozotocin solution (other mice were fed normally). The fasting blood glucose was measured again on day 7 after injection, mice with fasting blood glucose over 11.1 mmol/L and under 33.3 mmol/L were considered successful models [8]. The mice that were successfully modeled were assigned to seven groups [model group, positive control group (acarbose), and extracts of the roots, stems, corms, leaves, and flowers groups] according to their body weight and fasting blood glucose concentration [8]. The normal group and model group received distilled water, and the positive control group was given acarbose (100 mg/kg, ig) [14]. The administration group received the corresponding medicinal solution (the dosage of extracts for the five groups was also 100 mg/kg) for 28 d continuously. The fasting blood glucose of mice in each group was measured at day 0, 7, 14, 21, and 28, respectively.

2.7.3 Measurement of the water consumption The water consumption of mice in each group was measured from day 1 of the 1st week of intragastric administration to day 7 of the 4th week. The water bottles for mice in each group were filled to 200 mL every day, and the remaining water volume was measured after 24 h. The volume of water consumption for each group was calculated using the following formula:

Water consumption (mL/kg) = (initial water volume – remaining water volume)/mice weight

2.7.4 Determination of feed intake The feed intake of mice in each group was measured from day 1 of the 1st week to day 7 of the 4th week. A certain amount of high-fat feed was supplemented daily based on the mice's daily feed intake, and the remaining feed mass was determined after 24 h. The daily feed intake of the mice was calculated using the following formula:

Feed intake (g/kg) = (initial feed mass – remaining feed mass)/mice weight

2.8 Statistical analysis

SPSS 16.0 was used for statistical analysis. Measurement data are expressed as mean ± standard deviation (SD). One-way analysis of variance (ANOVA) and the least significant difference (LSD) test were used for statistical analyses. Statistical differences and biological significance were considered in the evaluation. $P < 0.05$ was considered statistically significant.

3 Results

3.1 Identification of chlorogenic acid-type compounds from Juandan Baihe (*Lilium lancifolium*)

Chlorogenic acid-type compounds have rarely been reported from Juandan Baihe (*Lilium lancifolium*).

Currently, only one compound, chlorogenic acid, has been reported [2]. To systematically identify chlorogenic acid-type compounds in Juandan Baihe (*Lilium lancifolium*) extracts, an exploration of the MS fragmentation patterns of chlorogenic acid compounds is required. Two main fragmentation pathways were observed [12]. The main MS fragmentation pathway of chlorogenic acid compounds was to break the ester group between quinic acid and caffeic acid to form high-abundance fragment ions. The highly abundant fragment ions *m/z* 191.057 0 and 179.035 5 in the MS/MS of chlorogenic acid (compound **2**, *m/z* 353.087 1, $[M–H]^-$) were produced from the cleavage of the ester group. The other fragmentation pathway was that highly abundant fragment ions could continue to lose some small molecules, such as CO_2 or H_2O group, to form characteristic fragment ions. The fragment ions *m/z* 173.045 6 and 135.044 7 were formed by the loss of H_2O and CO_2 from the highly abundant fragment ions *m/z* 191.057 0 and 179.035 5 (Figure 1A).

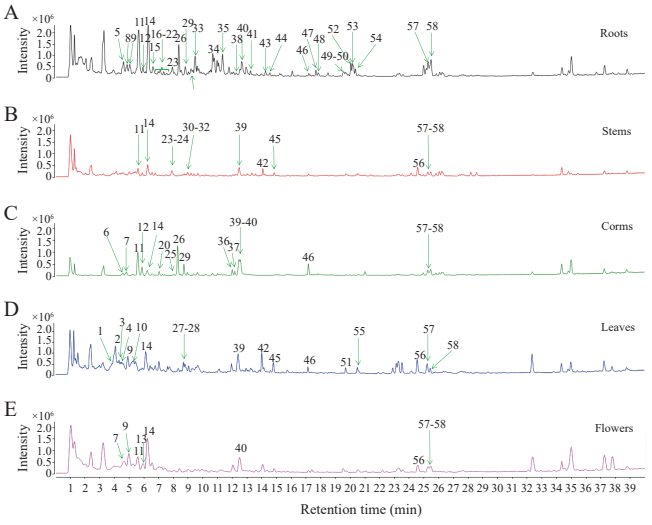

Figure 1 The total ion chromatograms of different parts of Juandan Baihe (*Lilium lancifolium*) and the peaks of metabolites **1** – **58**

A, roots. B, stems. C, corms. D, leaves. E, flowers.

Following the MS fragmentation pathways of chlorogenic acid-type compounds and the mass spectra of the candidates, compounds **1** – **4**, **10,** and **16** were identified as chlorogenic acid compounds, which were mainly detected from the leaves and stems of Juandan Baihe (*Lilium lancifolium*) (Figure 2). Taking compound **1** as an example, the MS/MS of compound **1** was very similar to that of the standard chlorogenic acid (compound **2**). The difference in *m/z* values between compound **1** and **2** was 15.991 8 Da, indicating that compound **1** had one less hydroxyl group than compound **2**. In addition, the characteristic fragment ion of *m/z* 163.041 0 (*m/z* 179.035 5 for compound **2**) in the MS/MS spectra of compound **1** showed that the benzene ring of compound **1** contains only one hydroxyl group. Therefore, compound **1** was preliminarily identified as 5-*O*-coumaroylquinic acid [12] (Figure 3A). In the same way, compounds **3** – **4**, **10,** and **16** were identified as chlorogenic acid-type compounds. Their structures are shown in Figure 4, and their MS information is shown in Table 1. Compounds **1**, **3**, **4**, **10,** and **16** were reported for the first time in Juandan Baihe (*Lilium lancifolium*).

3.2 Identification of caffeic acid-type compounds from Juandan Baihe (*Lilium lancifolium*)

Caffeic acid compounds are common chemical components in Juandan Baihe (*Lilium lancifolium*). The MS fragmentation pathways of caffeic acid-type compounds need to be studied to identify their structures in their extracts systematically. The main MS fragmentation pathway of caffeic acid-type compounds was the loss of substituent groups to form highly abundant fragment ions [12]. In the MS/MS of caffeic acid (compound **7**, *m/z* 179.034 2, $[M–H]^-$), the neutral loss of a CO_2 to form a high abundance ion at *m/z* 135.045 3 (carboxyl group present in the structure of compound **7**) was observed, and the molecular ion peak continued to lose H_2O or CO moiety thus forming the characteristic fragment ion at *m/z* 117.036 8 or 107.049 7 (Figure 1B).

According to the MS fragmentation pattern of caffeic acid-type compounds and the MS/MS spectra of the candidates, compounds **7**, **9**, **14**, **17**, **18**, **23**, **24**, **27**, **34**, **41** and **43** – **45** were identified as caffeic acid-type compounds. Taking compound **23** as an example, the MS/MS of compound **23** was very similar to that of the standard caffeic acid (compound **7**). The difference in the *m/z* values

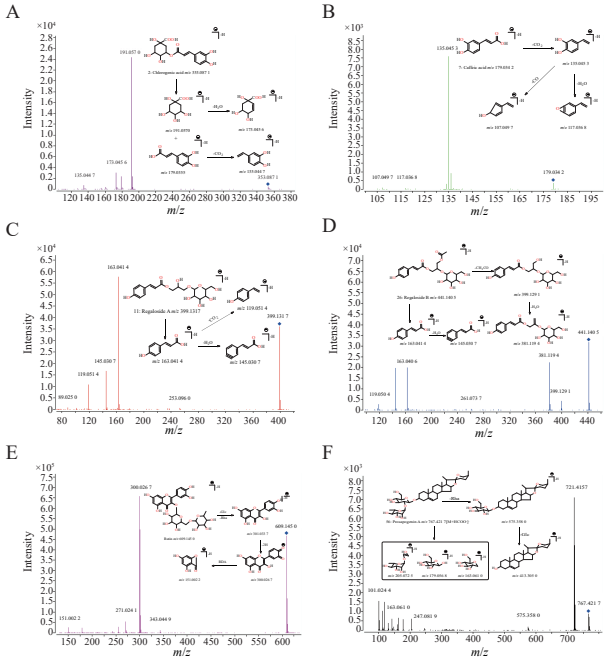

Figure 2 The fragmentation pathways and the corresponding MS/MS spectra of each standard substance

A, chlorogenic acid. B, caffeic acid. C, regaloside A. D, regaloside B. E, rutin. F, prosapogenin A.

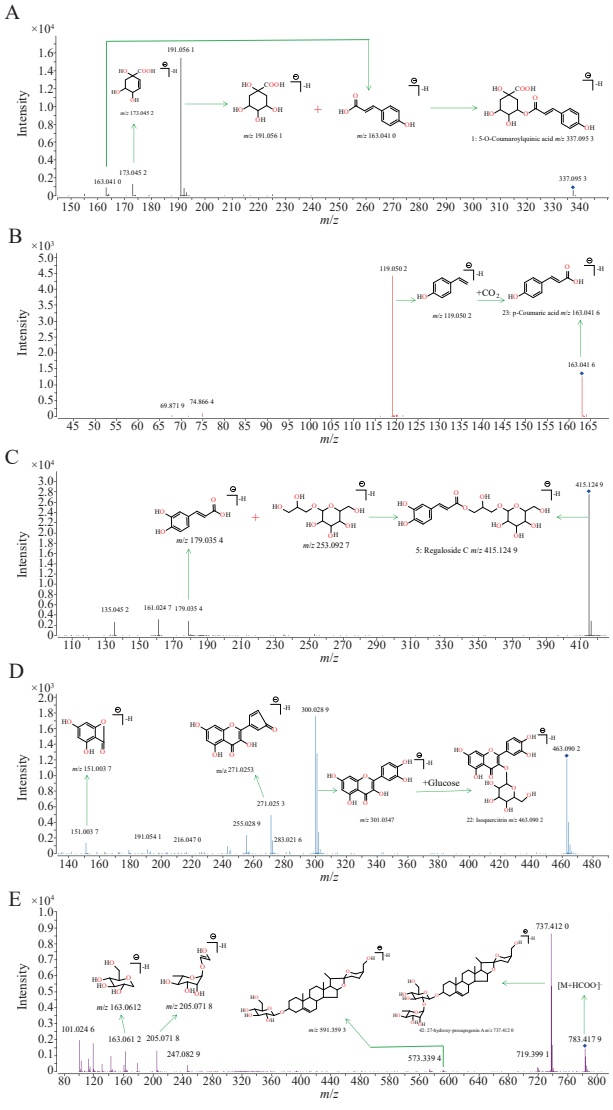

Figure 3 Identification of the structures of candidates and the corresponding MS/MS spectra

A, 5-*O*-coumaroylquinic acid. B, coumaric acid. C, regaloside C. D, isoquercitrin. E, 27-hydroxy-prosapogenin A.

between compound **23** and **7** was 15.992 6 Da, indicating that compound **23** had one less hydroxyl group than compound **7**. In addition, the fragment ion of *m/z* 119.050 2 (*m/z* 135.045 3 for compound **7**) in the mass spectrum of compound **23** indicated that the benzene ring of compound **23** contains only one hydroxyl group. Therefore, compound **23** was identified as *p*-coumaric acid (Figure 3B). In the same way, compounds **7**, **9**, **14**, **17**, **18**, **24**, **27**, **34**, **41** and **43** – **45** were identified as caffeic acid-type compounds. Their structures are shown in Figure 4, and their MS information is shown in Table 1. Compounds **17**, **18**, **24,** and **34** were reported for the first time in Juandan Baihe (*Lilium lancifolium*).

3.3 Identification of regalosides compounds from Juandan Baihe (*Lilium lancifolium*)

Regalosides are the main chemical components and active ingredients in Juandan Baihe (*Lilium lancifolium*). To systematically identify this type of compound from extracts, it is necessary to study their MS fragmentation patterns. Three main fragmentation pathways were observed for those compounds. First, regalosides lost the glycosyl moiety in the mass spectrum, thereby forming high-abundance characteristic ions [1]. Regaloside A (compound **11**, *m/z* 399.131 7, $[M-H]^-$) and regaloside B (compound **26**, *m/z* 441.140 5, $[M-H]^-$) are regaloside-type compounds, in their MS/MS spectra. The loss of glycosyl moiety from the parent ions resulted in the formation of highly abundant fragment ions at *m/z* 163.041 4 and 163.040 6 were observed (Figure 1C and 1D). The subsequent fragmentation behaviors of highly abundant fragment ions were consistent with that of phenylpropanoid compounds. Second, the loss of substituent groups to form a series of characteristic fragment ions presented in the mass spectrum. In the mass spectrum of regaloside B, the fragment ion *m/z* 399.129 1 was formed by the neutral loss of CH_2CO moiety from the parent ion at *m/z* 441.140 5 (Figure 1D), the ion *m/z* 399.129 1 continued to loss of H_2O moiety and formation of the fragment ions at *m/z* 381.119 4 [15, 16]. Third, if there is a sugar group in the structure of other regaloside, a series of fragment ions will be formed produced from the sugar group [17]; however, in the mass spectra of regaloside A and B, the characteristic fragment ions of sugar groups were not observed.

Compounds **5**, **6**, **8**, **11** – **13**, **20**, **25**, **26,** and **29** – **33** were identified as regalosides following the MS fragmentation patterns and the MS/MS of these compounds. Taking compound **5** as an example, the mass spectrum of compound **5** was similar to that of the standard regaloside A (compound **11**). The difference in *m/z* values between compounds **5** (*m/z* 415.124 9, Figure 3C) and **11** (*m/z* 399.131 7, Figure 1C) was 15.993 2 Da, indicating that compound **5** has one more hydroxyl group than compound **11**. Additionally, the fragment ion at *m/z* 179.035 4 in the mass spectrum of compound **5** (*m/z* 163.041 4 for compound **11**, Figure 1C) indicated that the benzene ring of compound **5** contains two hydroxyl groups. Therefore, compound **5** was tentatively identified as regaloside C (Figure 3C). This compound has been reported from Juandan Baihe (*Lilium lancifolium*), and its mass spectrum was consistent with previous research [1]. Similarly, compounds **6**, **8**, **11** – **13**, **20**, **25**, **26,** and **29** – **33** were preliminarily identified. Their structures are shown in Figure 4, and their MS information is shown in Table 1. Among them, compounds **25**, **29,** and **31** – **33** were reported for the first time from this medicinal plant. Those compounds are mainly present in the roots and corms of Juandan Baihe (*Lilium lancifolium*), and their content are higher than in other parts.

3.4 Identification of flavonoid glycosides from Juandan Baihe (*Lilium lancifolium*)

There are three main fragmentation pathways for flavonoid glycosides [16]. First, the compound lost all sugars in

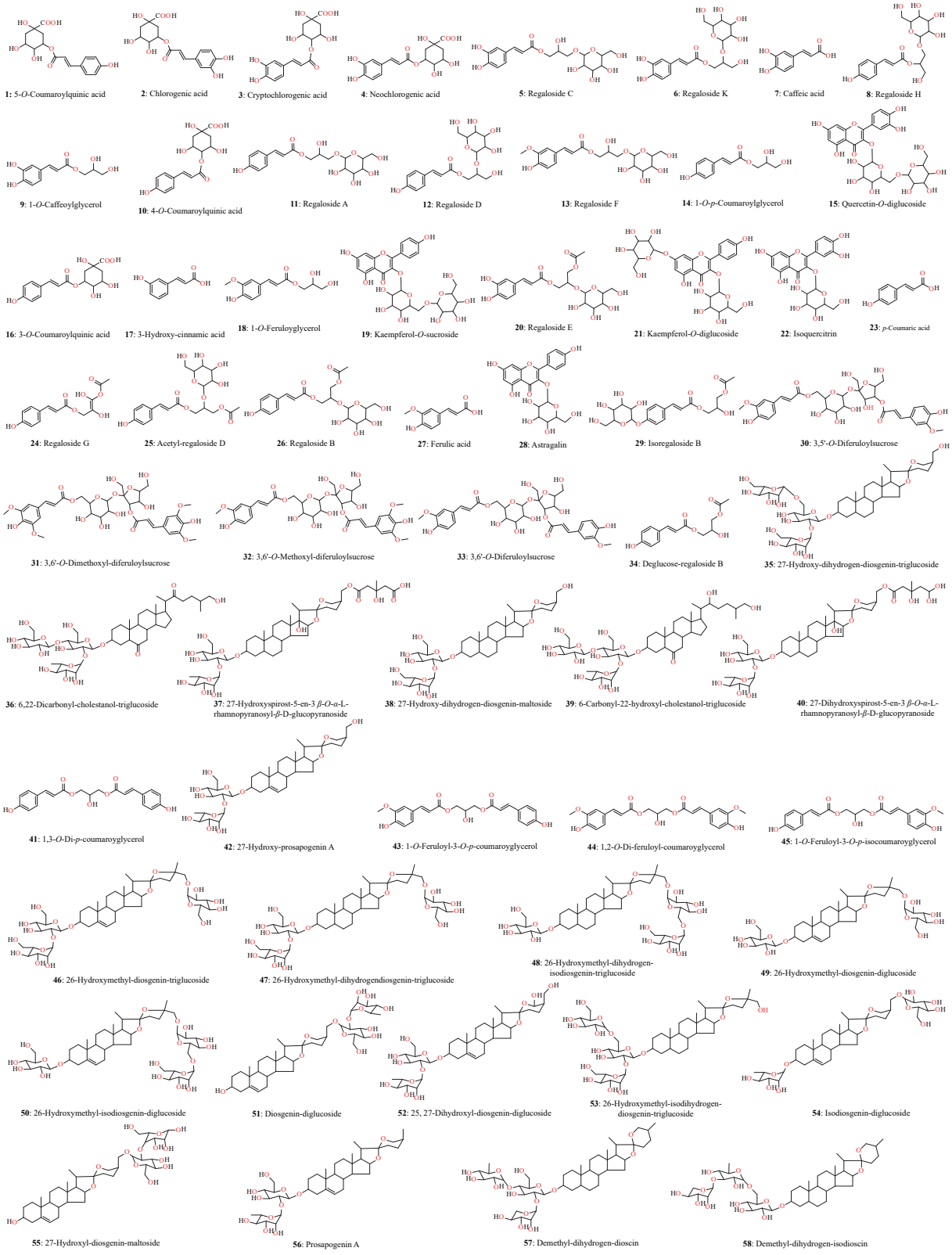

Figure 4 The structures of the identified compounds (**1** – **58**) from different parts of Juandan Baihe (*Lilium lancifolium*)

the mass spectrum, forming highly abundant skeleton ions. Rutin (*m/z* 609.145 0, $[M–H]^-$) is a flavonoid glycoside compound. In its MS/MS spectrum, the sugar group was lost to form a highly abundant skeleton fragment ion at *m/z* 300.027 9 (Figure 1E). Second, these compounds underwent cleavage of the middle oxygen ring to form a series of characteristic fragmentions. In the mass spectrum of rutin, the highly abundant skeleton ions underwent fragmentation of the C-ring to form the characteristic fragment ions of *m/z* 151.002 2 and 121.029 1 [11]. Third, flavonoids lost some substituent groups, such as CH_2O and H_2O, thus forming a series of characteristic fragment

Table 1 Phytochemical compounds identified in Juandan Baihe (*Lilium lancifolium*) by UPLC-Q-TOF-MS

Compound	t_R (min)	[M−H]⁻ (*m/z*)	Molecular formula	MS/MS (*m/z*)	Distribution	Tentatively identification
1[b]	3.87	337.0953	$C_{16}H_{18}O_8$	191.0561, 179.0452, 163.0410	L, S	5-*O*-Coumaroylquinic acid
2[*]	3.97	353.0868	$C_{16}H_{18}O_9$	191.0573, 173.0453, 135.0446	L, S, F	Chlorogenic acid
3[b]	4.09	353.0883	$C_{16}H_{18}O_9$	191.0572, 173.0456	L, S	Cryptochlorogenic acid
4[b]	4.24	353.0861	$C_{16}H_{18}O_9$	191.0568, 173.0463	L, S	Neochlorogenic acid
5	4.47	415.1249	$C_{18}H_{24}O_{11}$	179.0354, 161.0247, 135.0456	R, C	Regaloside C
6	4.56	415.1252	$C_{18}H_{24}O_{11}$	179.0354, 161.0246, 135.0457	R, C	Regaloside K
7[*]	4.75	179.0344	$C_9H_8O_4$	135.0456	C	Caffeic acid
8	4.80	399.1298	$C_{18}H_{24}O_{10}$	163.0404, 145.0295, 119.0508	R, C	Regaloside H
9	5.05	253.0733	$C_{12}H_{14}O_6$	179.0357, 161.0246, 135.0465	A	1-*O*-Caffeoylglycerol
10[b]	5.39	337.0962	$C_{16}H_{18}O_8$	191.0572, 173.0458, 163.0399	A	4-*O*-Coumaroylquinic acid
11[*]	5.61	399.1304	$C_{18}H_{24}O_{10}$	163.0404, 145.0297, 119.0504	A	Regaloside A
12	5.95	399.1277	$C_{18}H_{24}O_{10}$	163.0396, 145.0284, 119.0501	A	Regaloside D
13	6.25	429.1458	$C_{19}H_{26}O_{11}$	193.0506, 175.0450, 149.0625	A	Regaloside F
14	6.29	237.0774	$C_{12}H_{14}O_5$	163.0401, 145.0297, 119.0504	A	1-*O*-*p*-Coumaroyl-glycerol
15[b]	6.30	625.1431	$C_{27}H_{30}O_{17}$	301.0360, 300.0293, 151.0038	R, C	Quercetin-*O*-diglucoside
16[b]	6.45	337.0985	$C_{16}H_{18}O_8$	191.0577, 173.0496	A	3-*O*-Coumaroylquinic acid
17[b]	6.90	163.0375	$C_9H_8O_3$	119.0509	R, C	3-Hydroxy-Cinnamic acid
18[b]	6.94	267.0888	$C_{13}H_{16}O_6$	252.0643, 193.0500, 175.0409	A	1-*O*-Feruloylglycerol
19[b]	6.98	609.1449	$C_{27}H_{30}O_{16}$	285.0417, 284.0336, 255.0278	R, L, F	Kaempferol-*O*-sucroside
20	7.02	457.1359	$C_{20}H_{26}O_{12}$	397.1146, 219.0651, 161.0245, 135.0452	A	Regaloside E
21[b]	7.34	609.1457	$C_{27}H_{30}O_{16}$	285.0409, 284.0327, 255.0296	R, C	Kaempferol-*O*-diglucoside
22[b]	7.60	463.0902	$C_{21}H_{20}O_{12}$	301.0347, 300.0289, 271.0253, 255.0289, 151.0037	R, L, F	Isoquercitrin
23	7.75	163.0416	$C_9H_8O_3$	119.0502	R, L	*p*-Coumaric acid
24[b]	7.88	293.0657	$C_{14}H_{14}O_7$	163.0407, 147.0317, 119.0498	A	Regaloside G
25[b]	8.05	441.1354	$C_{20}H_{26}O_{11}$	399.1283, 163.0407, 145.0272, 119.0512	A	Acetyl-regaloside D
26[*]	8.33	441.1414	$C_{20}H_{26}O_{11}$	381.1192, 163.0404, 145.0298	A	Regaloside B
27	8.47	193.0503	$C_{10}H_{10}O_4$	149.0572, 134.0375	R, L, F	Ferulic acid
28[b]	8.50	447.0935	$C_{21}H_{20}O_{11}$	285.0401, 284.0324, 255.0298 227.0353, 151.0016	R, L, F	Astragalin
29[b]	8.73	441.1414	$C_{20}H_{26}O_{11}$	399.1310, 381.1204, 163.0417, 145.0313	A	Isoregaloside B
30	8.90	693.2045	$C_{32}H_{38}O_{17}$	487.1478, 223.0618, 205.0513	S, L, F	3,5'-*O*-Diferuloylsucrose
31[b]	9.03	753.2246	$C_{34}H_{42}O_{19}$	547.1658, 223.0624, 205.0511	S, L, F	3,6'-*O*-Dimethoxyl-diferuloylsucrose
32[b]	9.31	723.2127	$C_{33}H_{40}O_{18}$	517.1545, 223.0611, 205.0516	S, L, F	3,6'-*O*-Methoxyl-diferuloylsucrose
33[b]	9.39	693.2055	$C_{32}H_{38}O_{17}$	517.1573, 193.0509, 175.0412	S, L, F	3,6'-*O*-Diferuloylsucrose
34[b]	10.70	279.0872	$C_{14}H_{16}O_6$	219.0680, 163.0396, 145.0291, 119.0516	A	Deglucose-regaloside B
35[b]	11.34	963.4728	$C_{45}H_{74}O_{19}$	917.4693, 755.4166, 431.3108	R, C	27-Hydroxy-dihydrogen-diosgenin-triglucoside
36	11.93	947.4751[a]	$C_{45}H_{74}O_{18}$	901.4810, 755.4233, 593.3731 431.3203	R, C	6,22-Dicarbonyl-Cholestanol-triglucoside
37	12.10	945.4334[a]	$C_{45}H_{72}O_{18}$	899.4676, 753.4032, 591.3569	R, C	27-Hydroxyspirost-5-en-3*β*-*O*-*α*-L-rhamnopyranosyl-*β*-D-glucopyranoside
38[b]	12.48	801.4270[a]	$C_{39}H_{64}O_{14}$	755.4210, 593.3677, 429.2991	R	27-Hydroxy-dihydrogen-diosgenin-maltoside
39[b]	12.57	949.4976[a]	$C_{45}H_{76}O_{18}$	903.4935, 757.4174, 433.3387	A	6-Carbonyl-22-hydroxyl-cholestanol-triglucoside

Table 1 Continued

Compound	t_R (min)	$[M-H]^-$ (*m/z*)	Molecular formula	MS/MS (*m/z*)	Distribution	Tentatively identification
40	12.59	947.481 4	$C_{45}H_{74}O_{18}$	901.481 5, 755.421 2, 593.372 5	A	27-Dihydroxyspirost-5-en-3*β*-*O*-*α*-L-rhamnopyranosyl-*β*-D-glucopyranoside
41	13.60	383.114 9	$C_{21}H_{20}O_7$	163.040 9, 119.051 8	R, S, L	1,3-*O*-Di-*p*-coumaroylglycerol
42	14.10	783.417 9[a]	$C_{39}H_{62}O_{13}$	737.412 0, 591.359 3, 429.306 6, 205.071 8, 163.061 2, 101.024 6	S, L, F	27-Hydroxy-prosapogenin A
43	14.23	413.125 1	$C_{22}H_{22}O_8$	193.050 9, 177.057 7, 163.040 5	R, S, L, F	1-*O*-Feruloyl-3-*O*-*p*-coumaroylglycerol
44	14.52	443.135 6	$C_{23}H_{24}O_9$	249.081 6, 233.061 7, 193.050 5	R, S, L, F	1,2-*O*-Di-feruloyl-coumaroylglycerol
45	14.67	413.122 5	$C_{22}H_{22}O_8$	193.050 7, 177.055 5, 163.039 3, 134.039 0	R, S, L, F	1-*O*-Feruloyl-3-*O*-*p*-isocoumaroylglycerol
46	17.19	799.409 8[a]	$C_{39}H_{62}O_{14}$	753.406 0, 429.297 0, 163.063 0	A	26-Hydroxymethyl-diosgenin-triglucoside
47[b]	17.64	917.473 2	$C_{45}H_{74}O_{19}$	871.468 3, 739.426 4, 431.311 8	R, C	26-Hhydroxymethyl-dihydrogendiosgenin-triglucoside
48[b]	17.82	917.467 3	$C_{45}H_{74}O_{19}$	871.465 0, 739.426 3, 431.314 5	R	26-Hydroxymethyl-dihydrogen-isodiosgenin-triglucoside
49	19.54	915.455 7	$C_{45}H_{72}O_{19}$	869.449 6, 737.408 3, 429.292 3	R, C	26-Hydroxymethyl-diosgenin-diglucoside
50	19.69	915.462 6	$C_{45}H_{72}O_{19}$	869.453 0, 737.407 1, 429.293 0	R, C	26-Hydroxymethyl-isodiosgenin-diglucoside
51	19.71	783.413 2[a]	$C_{39}H_{62}O_{13}$	737.409 1, 591.352 6, 429.298 8, 247.082 3, 205.072 2	R, C, L	Diosgenin-diglucoside
52[b]	19.80	799.412 8	$C_{39}H_{62}O_{14}$	753.406 7, 607.352 8, 445.300 9	R, C	25,27-Dihydroxyl-diosgenin-diglucoside
53[b]	20.04	917.475 6	$C_{45}H_{74}O_{19}$	871.470 1, 739.424 1, 431.316 7	R, C	26-Hydroxymethyl-isodihydrogen-diosgenin-triglucoside
54[b]	20.47	783.413 2[a]	$C_{39}H_{62}O_{13}$	737.411 6, 591.348 9, 429.297 8, 247.081 3, 205.071 5, 163.060 3	R, C	Isodiosgenin-diglucoside
55	20.70	799.410 8	$C_{39}H_{62}O_{14}$	753.404 7, 607.343 6, 429.301 2 247.083 1, 205.072 9, 163.061 3	S, L, F	27-Hydroxyl-diosgenin-maltoside
56[*]	24.56	767.421 7	$C_{39}H_{62}O_{12}$	721.415 6, 575.358 0, 413.304 2, 247.081 9, 205.072 5, 163.061 0	A	Prosapogenin A
57[b]	24.98	901.478 7[a]	$C_{44}H_{72}O_{16}$	855.472 3, 723.422 3, 415.324 1	A	Demethyl-dihydrogen-dioscin
58[b]	25.48	901.479 0[a]	$C_{44}H_{72}O_{16}$	855.474 4, 723.433 0, 415.321 7	A	Demethyl-dihydrogen-isodioscin

[a]$[M+HCOO^-]^-$ adduction. [b] This compound was reported for the first time in Juandan Baihe (*Lilium lancifolium*). [*] This compound was unambiguously identified compared with the standard. R, S, C, L, F, and A represent the roots, stem, corms, leaves, flowers, and whole plant of Juandan Baihe (*Lilium lancifolium*), respectively. t_R, the retation time. $[M-H]^-$, the deprotonated ion.

ions. In the mass spectrum of rutin, the fragment ions at *m/z* 271.024 0 and 255.029 9 were formed by the loss of a CH_2O and H_2O + CO, respectively, from the skeleton ion at *m/z* 301.034 4.

According to the MS fragmentation patterns of flavonoid glycosides and the mass spectrum of the candidates, compounds **15**, **19**, **21**, **22,** and **28** were identified as flavonoid glycosides. For example, in the MS/MS spectra of compound **22**, the characteristic fragment ions at *m/z* 301.034 7, 300.028 9, 271.025 3, 255.028 9, and 151.003 7 indicated that compound **22** was a flavonoid glycoside with the quercetin as the skeleton. The difference in *m/z* values between compound **22** and the quercetin skeleton ion (*m/z* 301.034 7) was 162.055 5 Da, indicating that the structure of compound **22** contained a glucose moiety. Therefore, compound **22** was tentatively identified as isoquercetin glycoside (Figure 3D), and this compound was reported for the first time from Juandan Baihe (*Lilium lancifolium*). Using a similar method, compounds **15**, **19**, **21,** and **28** were identified as flavonoid glycosides. Their structures are shown in Figure 4, and their MS information is shown in Table 1. Among them, compounds **15**, **19**, **21**, **22,** and **28** were reported for the first time from Juandan Baihe (*Lilium lancifolium*).

3.5 Identification of dioscins from Juandan Baihe (*Lilium lancifolium*)

To systematically identify dioscins from Juandan Baihe (*Lilium lancifolium*) extracts, it is necessary to study the MS fragmentation rules of these compounds. Two main fragmentation pathways were observed for diosgenins [1, 15, 16]. First, diosgenins gradually lost all sugars to form a series of characteristic ions and skeleton ions. Dioscin A (compound **56**, *m/z* 767.421 7, $[M+HCOO^-]^-$) is a dioscin compound. In its mass spectrum, all sugar groups were lost to form fragment ions of *m/z* 575.358 0 and 413.305 0 (Figure 1F). Second, the sugar lost from dioscins formed a series of characteristic fragment ions. In the mass spectrum of dioscin A, the fragment ions *m/z* 205.072 5, 179.056 8, and 163.061 0 were formed by the cleavage of the sugar part (Figure 1F) [17].

Compounds **35** – **40**, **42,** and **46** – **58** were identified as dioscins following the MS fragmentation pattern and the mass spectra of the candidates. For example, the mass spectrum of compound **42** (Figure 3E) was similar to that of dioscin A (compound **56**; Figure 1E). The difference between compound **42** (*m/z* 783.417 9, $[M+HCOO^-]^-$) and **56** (*m/z* 767.421 7, $[M+HCOO^-]^-$) was 15.996 2 Da, indicating that compound **42** had one more hydroxyl group than compound **56**. In the mass spectrum of compound **42**, the parent ion (*m/z* 737.412 0, $[M-H]^-$) continuously lost rhamnose and glucose moiety to form fragment ions *m/z* 591.359 3 and 429.306 6, indicating that the extra hydroxyl group of compound **42** was not in the sugar group. Instead, it was connected to dioscin. According to the structural characteristics of dioscinspreviouslyreportedfromthegenusofJuandanBaihe (*Lilium lancifolium*) [1, 2], the hydroxyl group was connected at position 27, and therefore, compound **42** was tentatively identified as 27-hydroxy-dioscin A (Figure 3E). By a similar method, compounds **35** – **40** and **46** – **58** were identified as dioscins. Their structures are shown in Figure 4, and their MS information is shown in Table 1. Among them, compounds **35**, **38**, **39**, **47**, **48**, **52** – **54,** and **56** – **58** were reported for the first time from this medicinal plant.

3.6 Hypoglycemic activities of Juandan Baihe (*Lilium lancifolium*) extracts

3.6.1 Effects of blood glucose of Juandan Baihe (*Lilium lancifolium*) extracts on hyperglycemic mice As shown in Figure 5A, the blood glucose levels of the mice in the model group were 23.14 ± 1.12, 24.26 ± 1.36, 25.78 ± 2.01, 28.79 ± 1.01, and 29.6 ± 1.56 mmol/L at day 0, 7, 14, 21, and 28, respectively. These levels were significantly higher than those of the normal group ($P < 0.01$), indicating that the hyperglycemia mouse model was successfully established. The blood glucose increased progressively over the duration of the model development, and on day 21

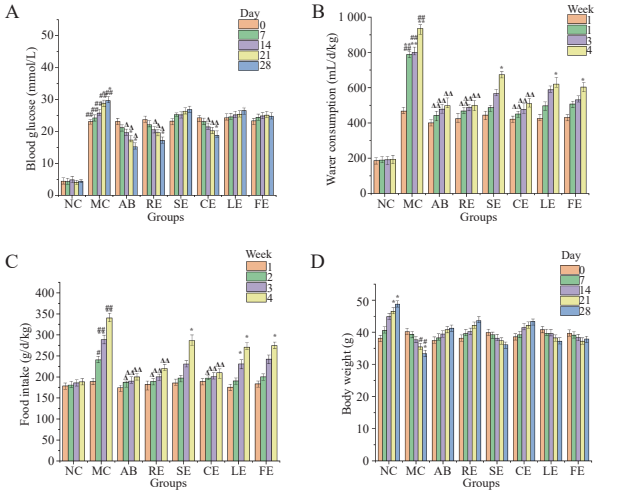

Figure 5 The hypoglycemic activities of different parts extracts of Juandan Baihe (*Lilium lancifolium*) of hyperglycemic mice

A, blood glucose. B, water consumption. C, food intake. D, body weight. $^*P < 0.05$ and $^{**}P < 0.01$, compared with day 0 or the first week. $^{\#\#}P < 0.01$, compared with the normal group. $^{\Delta}P < 0.05$ and $^{\Delta\Delta}P < 0.01$, compared with the model group in the same period. NC, normal group. MC, model group. AB, positive control group (acarbose). RE, extracts of roots. SE, extracts of stems. CE, extracts of corms. LE, extracts of leaves. FE, extracts of flowers.

and 28, the blood glucose levels were significantly higher than day 0 ($P < 0.05$). The positive control group (acarbose) has significant hypoglycemic activity by decreasing the glucose level from the initial 23.21 ± 0.98 mmol/L to 17.34 ± 0.78 mmol/L (day 21) and 15.23 ±1.27 mmol/L (day 28) ($P < 0.05$). For the roots, stems, corms, leaves, and flowers extracts, only roots and corms extracts showed significant hypoglycemic activity ($P < 0.05$), which could reduce the blood glucose concentration from 23.76 ± 1.21 and 24.29 ± 1.35 mmol/L to 17.21 ± 1.23 and 18.78 ± 1.49 mmol/L, respectively. However, other parts did not demonstrate significant hypoglycemic activity ($P > 0.05$). Compared with the model group, the positive control (acarbose), roots, and corms extract groups showed significant hypoglycemic activity at day 14, 21, and 28 ($P < 0.05$). The above experimental results show that the extracts of Juandan Baihe (*Lilium lancifolium*) roots and corms have significant hypoglycemic activity.

3.6.2 Effects of water consumption of Juandan Baihe (*Lilium lancifolium*) extracts on hyperglycemic mice As shown in Figure 5B, compared with the normal group, the water consumption of mice in the model group increased significantly ($P < 0.01$). The water consumption of the stem [631.45 ± 56.27 mL/(kg·d)], leaf [620.23 ± 58.67 mL/(kg·d)], and flower [603.22 ± 40.78 mL/(kg·d)] extracts was significantly increased compared with the first week [444.21 ± 40.12, 425.23 ± 30.23, and 431.45 ± 50.45 mL/(kg·d), respectively] ($P < 0.05$), while the positive control group (acarbose), root extracts, and corm

extracts could alleviate the increase in water consumption. Compared with the model group, the positive control (acarbose), roots, and corms extracts groups could significantly reduce the water consumption of mice on day 14, 21, and 28 ($P < 0.01$).

3.6.3 Effects of food intake of Juandan Baihe (*Lilium lancifolium*) extracts on hyperglycemic mice As shown in Figure 5C, compared with the normal group, the food intake of mice in the model group increased significantly from the second week ($P < 0.05$). The food intake of mice treated with the stem [286.54 ± 21.22 g/(kg·d)], leaf [270.56 ± 24.18 g/(kg·d)], and flower extracts [274.34 ± 28.21 g/(kg·d)] were significantly increased in the fourth week compared with the first week [185.67 ± 21.08, 175.34 ± 25.23, and 183.67 ± 19.34 g/(kg·d), respectively] ($P < 0.05$). While the root and corm extracts could alleviate the increase of food intake. Compared with the model group, the positive control (acarbose), roots, and corms extracts groups could significantly reduce the food intake of mice from the second week ($P < 0.05$).

3.6.4 Effects of body weight of Juandan Baihe (*Lilium lancifolium*) extracts on hyperglycemic mice As shown in Figure 5D, compared with the normal group, the body weight of mice in the model group decreased significantly on day 21 and 28 ($P < 0.05$). The weight of the mice treated with stem (36.12 ± 1.34 g), leaf (37.21 ± 1.09 g), and flower (37.89 ± 1.13 g) extracts was decreased on day 28, compared with the initial body weight (39.90 ± 1.45, 40.78 ± 1.27, and 39.67 ± 1.43 g, respectively), while the body weight increased slightly for the root and corm extracts groups.

Blood glucose concentration serves as a direct indicator for evaluating the hypoglycemic activities of Juandan Baihe (*Lilium lancifolium*) extracts. In addition, the clinical manifestations of diabetes include polydipsia, polyphagia, and weight loss. Therefore, the mice's water consumption, food intake, and body weight were further evaluated for the Juandan Baihe (*Lilium lancifolium*) extracts. The results proved that Juandan Baihe (*Lilium lancifolium*) roots and corm extracts demonstrated significant hypoglycemic activities.

4 Discussion

Research concerning medicinal parts mainly focuses on the corm of Juandan Baihe (*Lilium lancifolium*) in previous studies, while few studies concentrated on the chemical components of other parts [7]. The active ingredients of different parts of the same medicinal plant are different, resulting in significant differences in the efficacy of different medicinal parts [16, 18, 19]. This study used the UPLC-Q-TOF-MS technology to identify the chemical components from Juandan Baihe (*Lilium lancifolium*). Experimental results showed that the main components in this plant were dioscins, regalosides, caffeic acids, flavonoid glycosides, and chlorogenic acids. The roots of Juandan Baihe (*Lilium lancifolium*) were the most abundant compounds and contained a large amount of regalosides, dioscins, and caffeic acids. Among them, regalosides were the most abundant in the roots, such as regalosides A (compound **11**), 1-*O*-*p*-coumaroylglycerol (compound **14**), and regaloside B (compound **26**), which were much higher than those of other parts. Most flavonoids and chlorogenic acid compounds were concentrated in Juandan Baihe (*Lilium lancifolium*) leaves (such as compound **2** and chlorogenic acid), and their contents in other parts were relatively low. The roots and leaves of Juandan Baihe (*Lilium lancifolium*) contained a large amount of diosgenins. For example, the relative contents of compound **56** (dioscin A) in roots and leaves were significantly higher than that of other parts. The systematic identification and comparative analysis of the chemical components of different parts of Juandan Baihe (*Lilium lancifolium*) lay the foundation for the comprehensive utilization of this plant.

In previous studies, researchers adopted high performance liquid chromatograph/quadrupole time-of-flight mass spectrometry (HPLC-Q-TOF-MS) or UPLC-Q-TOF-MS technology to identify the chemical components in the corms of Juandan Baihe (*Lilium lancifolium*). However, the number of identified compounds was limited and they could not fully elucidate the material basis of this medicine [1, 7, 15, 16, 19, 20]. In this study, 58 high-content compounds were identified by the well-established UPLC-Q-TOF-MS technology, 30 of which were reported for the first time from this plant. This study further enriched the knowledge of compounds. Unfortunately, MS could not identify many compounds in this study. The MS fragmentation behaviors of these unknown compounds have not been reported, or they are new skeleton candidates. The MS cannot determine their structures. It is necessary to obtain its monomer compounds through phytochemical separation methods and identify their structures based on nuclear magnetic resonance, high-resolution mass spectrometry, and X-ray technology.

Research on the hypoglycemic activities of Juandan Baihe (*Lilium lancifolium*) mainly focuses on the polysaccha rides [20, 21] and steroidal saponins [22] extracted from the corms, while few studies concentrated on the hypoglycemic activities of other parts. The hypoglycemic effect mechanism of polysaccharides has been clarified. First, the polysaccharide has significant anti-oxidant activity and inhibits the damage of oxygen free radicals to pancreatic islet cells, thereby promoting insulin secretion to achieve hypoglycemic activity; second, polysaccharides can improve glucose metabolism enzymes' activity and promote glucose uptake and utilization to achieve hypoglycemic activity. Our study find that Juandan Baihe (*Lilium lancifolium*) root and corm extracts

(100 mg/kg) have significant hypoglycemic activities and can significantly reduce blood sugar in diabetic mice. It can also improve the symptoms of polydipsia, polyphagia, and weight loss caused by diabetes. The hypoglycemic activities of Juandan Baihe (*Lilium lancifolium*) root extract is more potent than corm extract. The hypoglycemic activities mechanism of the root and corm extracts may be related to stimulating glucose consumption [22]. A comparison of the high content of common components in the roots and corms indicates that the regalosides, such as regaloside A (compound **11**) and B (compound **26**), were the potentially active ingredients. According to previous study [23], regalosides have significant hypoglycemic activities, but the hypoglycemic activities of compounds **11** and **26** have yet to be reported and need further confirmation. The stem, leaves, and flower extracts of Juandan Baihe (*Lilium lancifolium*) did not show significant hypoglycemic activity.

5 Conclusion

This study primarily clarified the fragmentation pathways of regalosides, dioscins, phenylpropanoids, flavonoids, and chlorogenic acids in Juandan Baihe (*Lilium lancifolium*). A total of 58 compounds were identified from the roots, stems, corms, leaves, and flowers of Juandan Baihe (*Lilium lancifolium*) in accordance with the MS fragmentation rules. Among them, 30 compounds from this plant were reported for the first time. This study clarifies that the roots of Juandan Baihe (*Lilium lancifolium*) are rich in regalosides and dioscins. In addition, the roots and corms extracts exhibit significant hypoglycemic activity. They can significantly reduce blood sugar levels in hyperglycemic model mice and improve the symptoms of polydipsia, polyphagia, and weight loss caused by diabetes. This study lays the foundation for the comprehensive utilization of Juandan Baihe (*Lilium lancifolium*) and the development of new hypoglycemic drugs.

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Competing interests

The authors declare no conflict of interest.

References

[1] LIN MX, YUAN ZY, ZENG Q, et al. Analysis of chemical constituent of *Lilium broumii* by UPLC-Q-TOF-MS^E. Journal of Hunan University of Chinese Medicine, 2020, 40(8): 964–973.

[2] LUO LM, PEI G, QIN L, et al. Research progress on chemical constituents and pharmacological effects of medicinal *Lilium* plants. Traditional Chinese Drug Research & Clinical Pharmacology, 2017, 28(6): 824–837.

[3] HU ZD, TIAN S, MIAO YY, et al. Chemical composition, pharmacological research, and clinical application of Baihe. Pharmacology and Clinics of Chinese Materia Medica, 2022, 38(4): 241–246.

[4] SU Q, WU P, XIA BH, et al. Advance in research on chemical constituents and pharmacological activities of *Lilium*. Chinese Pharmaceutical Journal, 2021, 56(11): 875–882.

[5] WANG PY, LI JA, ATTIA FAK, et al. A critical review on chemical constituents and pharmacological effects of *Lilium*. Food Science and Human Wellness, 2019, 8(4): 330–336.

[6] LUO LM, QIN L, PEI G, et al. Advances in studies on steroidal saponins and their pharmacological activities in genus *Lilium*. China Journal of Chinese Materia Medica, 2018, 43(7): 1416–1426.

[7] YUAN ZY, LUO LM, CHEN NH, et al. Rapid analysis of chemical constituents of Lily Bulbil by UPLC-Q-TOF-MS and the antitumor activity of diosgenin. Natural Product Research and Development, 2019, 31(5): 808–813.

[8] ZHOU QY, LIAO X, KUANG HM, et al. LC-MS metabolite profiling and the hypoglycemic activity of *Morus alba* L. extracts. Molecules, 2022, 27(17): 5360.

[9] CHEN JY, WANG WT, KONG JQ, et al. Application of UHPLC-Q-TOF MS based untargeted metabolomics reveals variation and correlation amongst different tissues of *Eucommia ulmoides* Oliver. Microchemical Journal, 2022, 172: 106919.

[10] LI XY, FU YJ, FU YF, et al. Simultaneous quantification of fourteen characteristic active compounds in *Eucommia ulmoides* Oliver and its tea product by ultra-high performance liquid chromatography coupled with triple quadrupole mass spectrometry (UPLC-QqQ-MS/MS). Food Chemistry, 2022, 389: 133106.

[11] LIU T, CAO XZ, CAO DM. Combination of UHPLC-Q Exactive-Orbitrap MS and network pharmacology to reveal the mechanism of *Eucommia ulmoides* leaves in the treatment of osteoarthritis. Journal of Food Biochemistry, 2022, 46(8): e14204.

[12] LIU JH, ZHONG XH, JIANG YY, et al. Systematic identification metabolites of *Hemerocallis citrina* Borani by high-performance liquid chromatography/quadrupole-time-of-flight mass spectrometry combined with a screening method. Journal of Pharmaceutical and Biomedical Analysis, 2020, 186: 113314.

[13] YU LY, CHEN MF, LIU JH, et al. Systematic detection and identification of bioactive ingredients from *Citrus aurantium* L. var. amara using HPLC-Q-TOF-MS combined with a screening method. Molecules, 2020, 25(2): 357.

[14] ZHANG T, GAO J, JIN ZY, et al. Protective effects of polysaccharides from *Lilium lancifolium* on streptozotocin-induced diabetic mice. International Journal of Biological Macromolecules, 2014, 65: 436–440.

[15] ZHAO KH, ZHOU F, YAN SE, et al. The analysis of compounds from Longya lily via HPLC-Q- TOF-MS and HS-SPME-GC-MS. Natural Product Research and Development, 2020, 32(8): 1331–1342.

[16] ZHAO KH, YAN SE, HE YJ, et al. Analysis of phenolic compounds in lily by HPLC-Q-TOF-MS. Chinese Traditional Patent Medicine, 2019, 41(6): 1445–1450.

[17] QING ZX, ZHAO H, TANG Q, et al. Systematic identification of

flavonols, flavonol glycosides, triterpene and siraitic acid glycosides from *Siraitia grosvenorii* using high-performance liquid chromatography/quadrupole-time-of-flight mass spectrometry combined with a screening strategy. Journal of Pharmaceutical and Biomedical Analysis, 2017, 138: 240–248.

[18] TANG YC, LIU YJ, HE GR, et al. Comprehensive analysis of secondary metabolites in the extracts from different lily bulbs and their antioxidant ability. Antioxidants, 2021, 10(10): 1634.

[19] MUNAFO JP Jr, GIANFAGNA TJ. Quantitative analysis of steroidal glycosides in different organs of Easter lily (*Lilium longiflorum* Thunb.) by LC-MS/MS. Journal of Agricultural and Food Chemistry, 2011, 59(3): 995–1004.

[20] LI YP, PI XF, LIU CM, et al. Study on mechanism of hypoglycemic action of lily polysaccharide *in vitro*. Lishizhen Medicine and Materia Medica Research, 2012, 23(8): 1964–1966.

[21] LIU CM, FU GM, TU ZC, et al. Study on hypoglycemic function of lily polysaccharide. Food Science, 2002, 23(6): 113–114.

[22] ZHU MD, LUO JG, LV HW, et al. Determination of anti-hyperglycaemic activity in steroidal glycoside rich fraction of lily bulbs and characterization of the chemical profiles by LC-Q-TOF-MS/MS. Journal of Functional Foods, 2014, 6: 585–597.

[23] MURRAY AF, PALATINI K, KOMARNYTSKY S, et al. Phenylpropanoid glycerol glucosides attenuate glucose production in hepatocytes. ACS Omega, 2019, 4(6): 10670–10676.

基于 UPLC-Q-TOF-MS 技术鉴定卷丹百合不同部位中化学成分及其降血糖活性研究

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【摘要】目的 基于超高效液相色谱-四极杆飞行时间质谱（UPLC-Q-TOF-MS）技术鉴定卷丹百合不同部位提取物中的主要成分，并对其降血糖活性进行研究。**方法** 对百合中主要类型化合物的质谱裂解规律进行研究，基于质谱裂解规律结合质谱挖掘技术对卷丹百合不同部位提取物中的化学成分进行系统鉴定。并基于链脲佐菌素诱导（每天灌胃给药 80 mg/kg，连续给药 3 天）的高血糖雄性小鼠模型 [无特定病原体 (SPF) 昆明小鼠]，通过测量小鼠的血糖、日饮水量、日采食量及体重变化情况评价卷丹百合根、茎、球茎、叶和花提取物的降血糖活性。**结果** 本研究阐明了卷丹百合中王百合苷类、薯蓣皂苷类、咖啡酸类、黄酮苷类和绿原酸类化合物的质谱裂解规律，构建了百合植株中化合物的挖掘方法，从卷丹百合的根、茎、球茎、叶和花中共鉴定了 58 个化合物，包括绿原酸类化合物 6 个，王百合苷类化合物 14 个，咖啡酸类化合物 13 个，黄酮苷类化合物 5 个，薯蓣皂苷类化合物 20 个。其中 30 个化合物首次在百合中报道。卷丹百合根及球茎提取物表现出显著的降血糖活性，使高血糖模型小鼠血糖水平从最初的 23.76 ± 1.21 mmol/L 和 24.29 ± 1.35 mmol/L 下降到 17.21 ± 1.23 mmol/L 和 18.78 ± 1.49 mmol/L（$P < 0.05$）。卷丹百合根及球茎提取物还能改善糖尿病引起的多饮（$P < 0.01$）、多食（$P < 0.05$）及体重减轻的症状。**结论** 本研究首次阐明卷丹百合根含有丰富的王百合苷类和薯蓣皂苷类化合物，并具有显著的降血糖活性，为百合植株的综合利用及降血糖药物的开发奠定基础。

【关键词】卷丹百合；化学成分；降血糖活性；UPLC-Q-TOF-MS；结构鉴定；质谱裂解规律