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ORIGINAL ARTICLE

Simultaneously qualitative and quantitative analysis of the representative components in *Kadsura heteroclita* stem by UHPLC-Q-Orbitrap HRMS

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Abstract

***Kadsura heteroclita* (Roxb) Craib stem (KHS) is a medicinal plant used for the treatment of rheumatism arthritis diseases in Tujia ethnomedicine. Thus far, the complex chemical compositions in KHS are not clear, and the levels of the major compounds in KHS are not well understood. In this study, a novel UHPLC-Q-Orbitrap HRMS method was established for the simultaneous quali-quantitative analysis of KHS. A total of 204 compounds were identified, including triterpenoids, lignans, sesquiterpenes, fatty acids, phenolic acids, and flavonoids, more than 100 of which were first discovered in KHS. Using the same method, 12 representative bioactive components were successfully quantified. The method was fully validated by linearity, LOD, LOQ, precision, stability, recovery, and matrix effects, and it was applied to quantify the 12 representative compounds in 4 batches of KHS. As this method enables retrospective data analysis and has no upper limit to the number of analytes in a single run, it can be applied to quantify more active components of KHS in the future.**

Keywords: Identification, *Kadsura heteroclita*, Quantification, UHPLC-Q-Orbitrap HRMS

1. Introduction

Kadsura heteroclita (Roxb) Craib stem (KHS) belongs to the genus *Kadsura* of the schizandraceae family, a special folk medicine called Xuetong in Tujia ethnomedicine [1]. According to traditional Chinese medicine theories, KHS possesses the effects of expelling wind-evil, regulating Qi to alleviate pain, reinforcing vital energy and promoting blood circulation to relieve blood stasis, and eliminating wetness-evil [2]. The cold-humid natural environment, make Tujia people vulnerable to cold and dampness, which results in rheumatic arthralgia, articulation pain and other diseases. For the treatment of rheumatism arthralgia, Tujia people have accumulated rich experience in medicine. KHS has long been used for the prevention and treatment of wind-dampness, epigastric pain, bone pain, blood deficiency, numb hands and feet, irregular menstruation and rheumatoid arthritis in the Wuling Mountain area of China [3]. As an important local herb medicine, KHS presents strong pharmacological activity in the treatment of rheumatoid arthritis [4, 5]. These

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features triggered our research enthusiasm to explore the bioactive components in KHS.

At present, phytochemical isolation and HPLC analysis revealed that KHS contains diverse bioactive components, including triterpenoids, lignans, sesquiterpenes, fatty acid, volatile oil, and flavonoids [6-14]. Triterpenoids and lignans are the principal active components for the treatment of rheumatoid arthritis in KHS [4], and they also display multiple pharmacological activities. Currently, there are few researches on the determination of the components in KHS [15]. This is a barrier to the identification of the diversity and synergism of the chemical constituents of KHS, which has limited the understanding of its inherent qualities. Hence, there is an urgent need to conduct a study on the comprehensive quali-quantitative analysis of the bioactive constituents in KHS.

Today, ultra-high-performance liquid chromatography, coupled with hybrid quadrupole-Orbitrap HRMS (UHPLC-Q-Orbitrap HRMS) has been successfully used for rapid characterization of plant constituents with exact MS and MS^2 information [16, 17]. Orbitrap HRMS can generate full scan data over a wide range of masses while enabling qualitative and quantitative analysis of the components [18-21]. It has been successfully applied to the simultaneous qualitative and quantitative analysis of targeted compounds in areas such as food safety, pesticide and veterinary drug residues, and illegal addition of herbs [22-24]. But the composition of traditional Chinese medicine is complex: besides target components, the untargeted components are also worth exploring. Therefore, it is necessary to establish a new analytical method to identify both targeted and untargeted components and quantify the active ingredients in traditional Chinese medicine. In this study, a novel quali-quantitative analytical method by UHPLC-Q-Orbitrap HRMS was developed for rapid and systematic identification and quantification of the components in KHS. The method can fulfill the simultaneous quali-quantitative analysis of KHS in a single run. In addition, our method can be used as an extended application to quantify more potential active components of KHS in the future based on the exact MS data.

2. Materials and methods

2.1. Chemicals and reagents

Schisanlactone E (SE), heteroclitalactone F (HF), heteroclitalactone B (HB), schisanlactone B (SB), heteroclitalactone M (HM), heteroclitalactone D (HD), heteroclitalactone E (HE), schisandronic acid (SDA), 6-hydroxyhinokinin-6-*O*-β-D-glucopyranoside (6-H-6-glc), d-Epigalbacin (d-E), schizandriside (SZD) and kadsurarin (KDA) were separated and identified from the stem of *K. heteroclita* in our previous researches [6-9]. The purities of reference standards were over 95%. The structures of the 12 reference standards are shown in Fig. 1.

Acetonitrile, methanol, dimethyl sulfoxide (DMSO), and formic acid of HPLC grade were purchased from Merck (Darmstadt, Germany). Deionized water was produced with a Milli-Q system (Merck Millipore, USA). Four batches of Xuetong were collected in Shimen, Hunan, China in four different seasons during 2018-2019, and identified by Prof Wei Wang from Hunan University of Chinese Medicine.

2.2. Preparation of standards solutions and samples

The stock solutions of 12 reference standards (10.0 mg/mL) were prepared in DMSO and further diluted to 1.0 mg/mL with methanol. All stock solutions were stored at −20 °C until use. The working solution was freshly prepared by serial dilutions of mixed stock solution with 50% methanol to yield 1.0-2000.0 ng/mL for SZD, 6-H-6-glc, HM, HE, HD, SB, SE, HB, and HF; 1.0-200.0 ng/mL for KDA; 50.0-100,000.0 ng/mL for d-E; and 50.0-25,000.0 ng/mL for SDA.

0.5 g dried KHS powder was accurately weighed and placed into round-bottomed flask. And it was ultrasonically extracted with 15 mL of methanol for 15 min at room temperature. The solution was allowed to cool naturally and weighed again, and the lost weight was made up with methanol and shaken. The solution was centrifuged at 13,000 rpm for 10 min. The supernatant was used for the identification of KHS and quantification of HM, KDA, SB, HB, and HF, and the supernatant was diluted at 1:50 (v/v) with 50% methanol for the quantification analysis of the rest of the compounds. All samples were filtered (0.22 μm) before analyses.

2.3. Chromatographic and mass spectrometric conditions

UHPLC analysis was operated on a Waters Acquity H-Class UHPLC system (Waters, Milford, MA, USA). Sample separations were performed on an ACQUITY UPLC HSS T3 column (2.1 × 100 mm, 1.8 μm) and maintained at 40 °C. The mobile phase consisted of 0.1% formic acid aqueous solution (A) and acetonitrile/methanol (4:1, v/v) (B). The gradient elution conditions were: 0-6 min: 20-50% B; 6-14 min: 50-90% B; 14-18 min: 90% B. The column

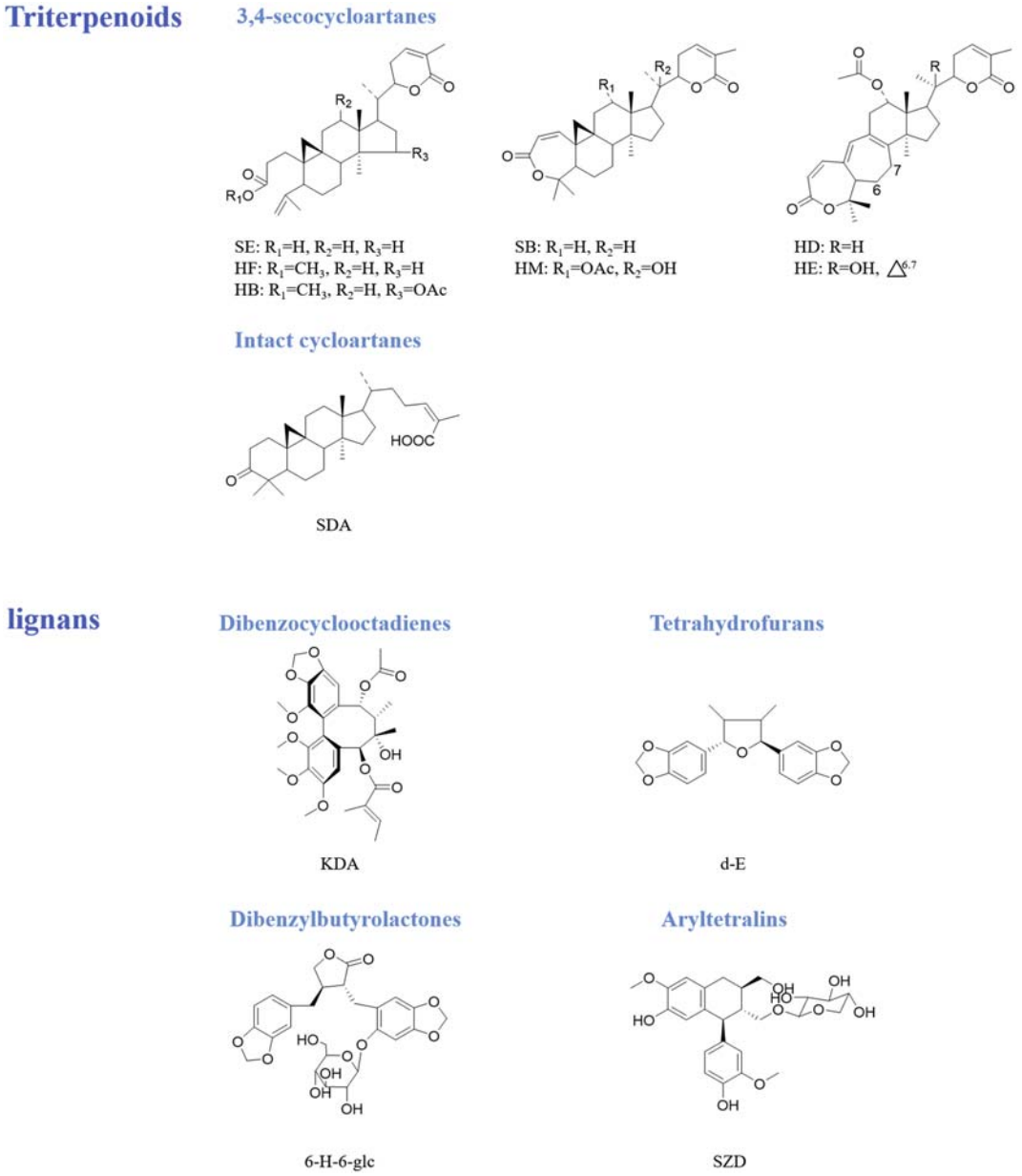

Fig. 1. Chemical structures of 12 reference standards in KHS.

was re-equilibrated for 1 min at 20% B prior to the next injection. Flow rate was 0.4 mL/min. The temperature of the autosampler was maintained at 4 °C, and the injection volume was 5 μL.

HRMS detection was conducted on a Q Exactive Orbitrap MS system (Thermo Scientific, Waltham, MA, USA) equipped with a heated electrospray ionization (HESI) source in both positive and negative ion modes. Spray voltages were +3.8 and −2.8 kV for positive and negative ion modes, respectively. Sheath gas flow rate, auxiliary gas flow rate, and sweep gas flow rate were set to 40, 10, and 0 arbitrary units, respectively. Capillary temperature and auxiliary gas heater temperature were maintained at 325 and 350 °C, respectively. The scan mode was full MS/dd-MS^2 (Top 5) with resolutions of 70,000 and 17,500 FWHM. Full MS scan was acquired in the m/z range of 100-1500 Da. The stepped normalized collision energies (NCE) were set to 20, 40, and 60 eV. Data acquisition was performed in positive and negative ion mode separately. Data acquisition and processing were executed with Xcalibur 4.1 and Compound Discover 3.0 (Thermo Scientific) software, respectively. The data of full MS and dd-MS^2 was used for qualitative analysis, and the peak areas of full MS were utilized for quantitative analysis.

2.4. Compound identification and validation

Compounds were verified with reference standards or tentatively identified by searching in various databases such as in-house genus Kadsura database, MassBank, mzCloud and ChemSpider. The method developed for the quantification of 12 active compounds in KHS was validated by linearity, LOD, LOQ, precision, stability, recovery, and matrix effects. They were described in detail in section 3.3 and 3.5, respectively.

3. Results and discussion

3.1. Optimization of the method

For Q-Orbitrap HRMS conditions, both positive and negative ion modes were used for qualitative analysis to obtain more components. The positive ion mode was used to quantify analytes with more compounds and higher response than negative ion mode. And the selection of 12 target compounds for quantification was based on the active ingredients for the treatment of rheumatoid arthritis in KHS, especially triterpenoids and lignans [4], and they also display multiple pharmacological activities [6, 25–31]. Cycloartane triterpenoids are the most abundant triterpenoids in KHS, so eight cycloartane triterpenoids (SE, HF, HB, SB, HM, HD, HE, and SDA) were chosen for the quantification study. Lignans in KHS mainly include four skeleton-types: dibenzocyclooctadienes, tetrahydrofurans, dibenzylbutyrolactones, and arylteralins, with KDA, d-E, 6-H-6-glc, and SZD as the respective representative compounds. The external standard method was used for quantification.

For UHPLC conditions, the type of column and the compositions of mobile phase were optimized to improve the sensitivity and resolution of the analytes. The ACQUITY UPLC HSS T3 column was selected based on the better peak shapes and improved analyte responses (Fig. S1). The best response and separation for most analytes were obtained when 0.1% formic acid aqueous solution (A) and acetonitrile/methanol (4:1, v/v) (B) were utilized as the mobile phases.

For the sample preparation conditions, the extraction solvent (methanol, 95% ethanol, and acetonitrile), solid-liquid ratio (1:10, 1:30, 1:50), and ultrasound extraction time (5, 15, 30 min) were examined according to the literatures [32–34] (Table S1–3). The extraction efficiency was assessed by comparing the total peak areas of each category components, respectively, and the most efficient extraction was considered as the one which extracted the highest amount of these components [35]. According to the peak shape and the extraction efficiency, the final sample preparation conditions were that 0.5 g KHS powder was ultrasonically extracted with 15 mL of methanol for 15 min at room temperature.

3.2. Advantages of our established analytical method

In recent years, there have been many qualitative and quantitative studies of traditional Chinese medicines. Most of them need to build different analytical methods for the identification and quantification researches, respectively [36, 37]. In our study, a simple and fast UHPLC-Q-Orbitrap HRMS method was developed for the simultaneous quali-quantitative analysis of KHS in a single run. In this study, the exact MS and MS^2 data were used for identification, and the peak areas of extracted ions were utilized to quantify the representative compounds in KHS, making results more accurate and reliable. This method simultaneously identified 204 targeted and untargeted components in a wide mass range and quantified 12 active components over a wide linear range. There was no need to enter precursor ions or ion transitions of the analytes in advance, nor did it need to optimize collision energy values, compared with the MRM mode of triple-quadrupole MS. But it can be comparable to triple-quadrupole MS quantitative performance [38]. In addition, the method can enable retrospective data analysis, and it has no upper limit to the number of analytes in a single run. The exact MS data of new active compound can be entered into Xcalibur to obtain the peak areas for quantitative analysis. So, our method can be used as an extended application to quantify more potential active components of KHS in the future.

3.3. A systematical quali-quantitative strategy for the components in KHS

A three-step analytical strategy (Fig. 2) was established to systematically identify and quantify the chemical components in KHS. Step 1, data acquisition: samples were analyzed by UHPLC-Q-Orbitrap HRMS with the full MS/dd-MS^2 scan mode. The exact MS data of reported compounds in KHS was imported in the "Inclusion list" (Table S4–S5) to acquire the MS^2 information of the targeted components. The function "If idle-pick others" in dd-MS^2 setting was enabled to simultaneously obtain the MS^2 information of the untargeted components. Step 2, compound identification: targeted compounds were verified with reference standards

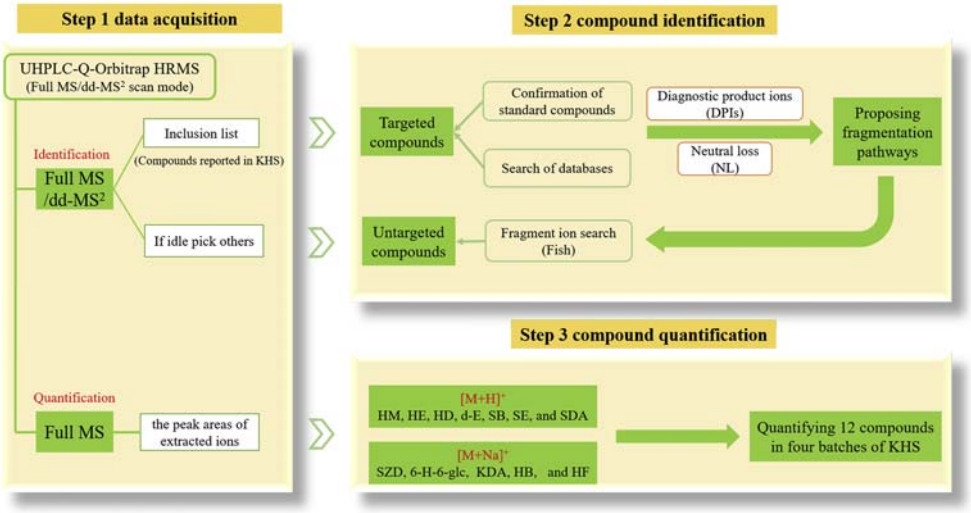

Fig. 2. A proposed integrated strategy for identification of the components in KHS.

or tentatively identified by in-house genus *Kadsura* database. For untargeted compounds, firstly, the molecular formula provided by Xcalibur was used to search in online databases such as MassBank (https://massbank.eu/MassBank/), mzCloud (https://www.mzcloud.org/) and ChemSpider (http://www.chemspider.com/). Then, the measured MS^2 spectrum was compared with the known MS^2 spectrum in databases or literature. Finally, the untargeted compounds were tentatively identified by comparing the measured spectrum with the known spectrum. The fragmentation pathways of triterpenoids and lignans in KHS could be proposed according to the neutral loss (NL) and diagnostic ions (DPIs), which would be applied to find untargeted compounds with similar structures. Moreover, the calculated log P (Clog P) obtained by ChemDraw 14.0 was utilized to estimate the retention time of the isomers, with larger Clog P indicating a longer retention time Clog P. Step 3, compound quantification: for each analyte, the exact masses of different adduct ions were imported into Xcalibur 4.1 to evaluate which generated the highest abundance in full MS scan spectrum. The $[M+Na]^+$ adducts were selected for the quantification of SZD, 6-H-6-glc, KDA, HB, and HF. And the $[M+H]^+$ adducts were utilized for the rest analytes. The method was successfully applied to quantify 12 representative compounds in four batches of KHS samples.

3.4. Characterization of components in KHS

We conducted two experiments to screen the compounds in KHS. A total of 204 compounds were successfully identified based on this strategy, including triterpenoids, lignans, sesquiterpenes, fatty acids, phenolic acids, and flavonoids, more than 100 of which were firstly discovered in KHS. Triterpenoids and lignans were the dominant compounds. Information of the identified compounds is summarized in Table S6. Total ion chromatograms in positive and negative ion modes of KHS extracts and blank solvent have been displayed in Fig. S2–S3, which suggested that there was no obvious interference for the detection of components in KHS.

3.4.1. Identification of triterpenoids

Triterpenoids were the most abundant in KHS. According to the fragmentation rules of the reference standards, it was found that the MS^2 spectrometry of triterpenoids in positive ion mode has the following characteristics: (1) the continuous NL of H_2O and CO_2 occurred in the high-mass fraction; (2) there were few fragment ions in the middle-mass fraction; (3) the fragment ions in the low mass fraction were densely clustered. Based on these typical features, triterpenoids can be quickly identified. Taking HD, SB, SE, and SDA as examples, the fragmentation pathways of triterpenoids were clarified.

3.4.1.1. 3,4-secocycloartane triterpenoids. This group of triterpenoids is abundant in genus *Kadsura*. Compound **114** displaying $[M+H]^+$ ion at m/z 523.0348, was verified as HD based on the reference standard. As shown in Fig. 3, the fragment ion at m/z 463.2831 derived from $[M+H]^+$ ion via the loss of an acetyl group, which further continuously lost H_2O to form m/z 445.2729 and 427.2618. The fragment ion at m/z 417.2793 derived from m/z 463.2831 via the loss of a carboxyl group (−46.0038 Da). The precursor ion at

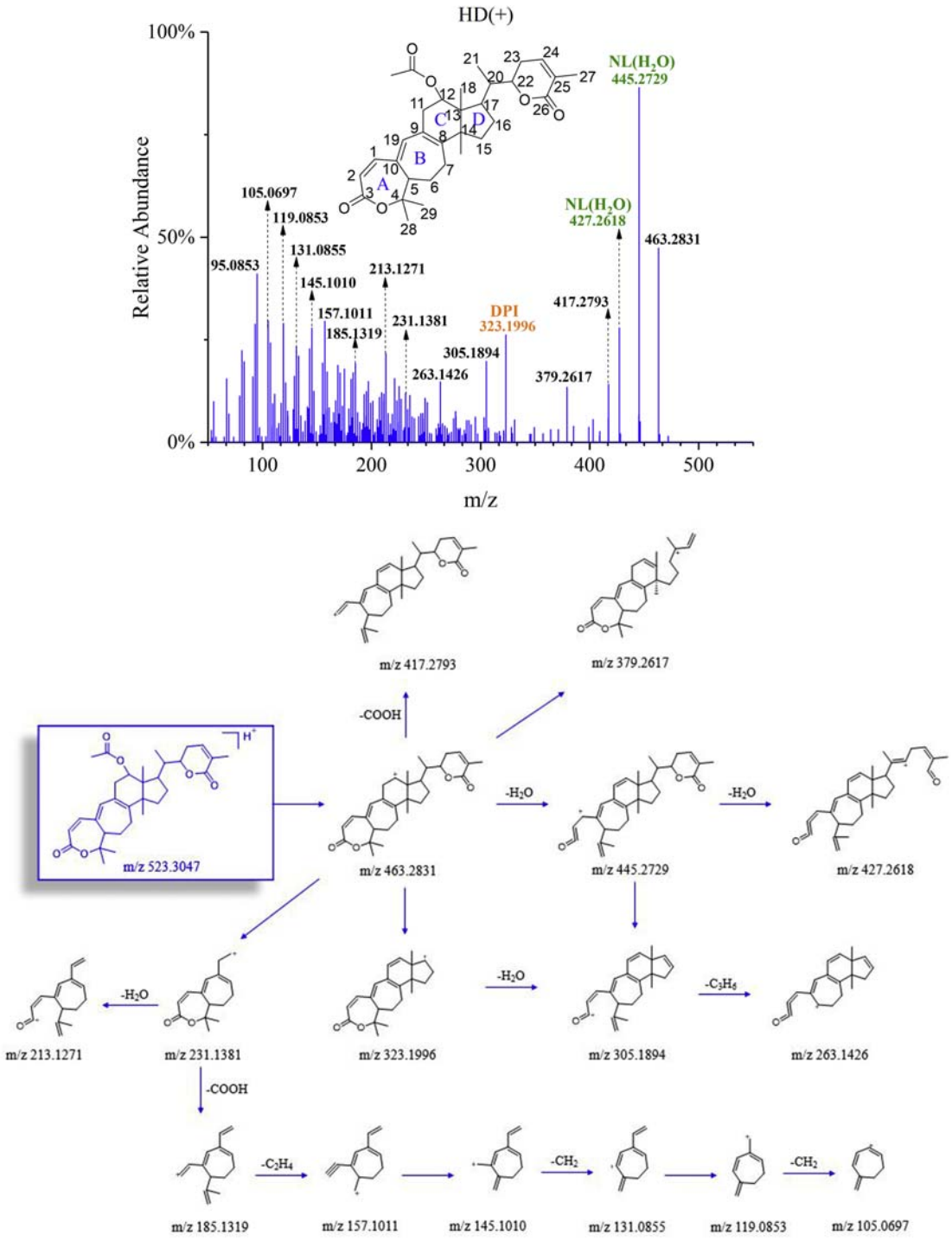

Fig. 3. The exact MS^2 spectrum and proposed fragmentation pathways of heteroclitalactone D (HD) in positive ion mode.

m/z 463.2831 generated DPI at m/z 323.1996 by breaking the bond between C-17 and C-20. This further successively formed m/z 305.1894 and 263.1426 by NL H_2O and breaking the bond between C-4 and C-5. The fragment ion at m/z 379.2617 derived from m/z 463.2831 via breaking the bond between C-23 and C-24 followed by opening the six membered α,β-unsaturated lactone ring. The fragment ion at m/z 463.2831 underwent a C-ring cleavage reaction, producing m/z 231.1381, which further generated m/z 213.1271 and 185.1319 via the loss of H_2O and carboxyl group, respectively. The latter sequentially lost a series of minor ions to yield the fragment ions at m/z 157.1011, 145.1010, 131.0855, 119.0853 and 105.0697. Compound 87 was "FIShed" by DPI at m/z 323.1996, displaying

$[M+H]^+$ ion at m/z 463.2836, and it had similar fragmentation pathways with HD. Compound **87** had one less acetyl group than HD, so it was tentatively identified as lancilactone B.

Compound **149** displayed $[M+H]^+$ ion at m/z 467.3153, verified as SB in accordance with the reference standard. The $[M+H]^+$ ion generated DPI at m/z 327.2315 via breaking the bond between C-17 and C-20, which further lost H_2O to produce m/z 309.2204. Compound **80** was "FIShed" by DPI at m/z 327.2315 and displayed $[M+H]^+$ ion at m/z 483.3092, suggesting that it has one more hydroxyl group than SB. The $[M+H]^+$ ion lost OH and H to produce double bond, which further underwent the same fragmentation pathways as SB. Compound **80** was tentatively identified as kadsulactone A.

Compound **177** possessed the typical MS^2 features of triterpenoids, displaying a $[M+H]^+$ ion at m/z 469.0036, which generated DPI at m/z 329.2477 by breaking the bond between C-17 and C-20. It underwent a C-ring cleavage reaction, producing DPIs at m/z 219.1378 and 249.1843. Compound **177** was verified as SE by comparison with the reference standard. The detailed fragmentation pathways of SE have been reported in our previous research [20].

3.4.1.2. Intact cycloartane triterpenoids. Compound **204**, showing $[M+H]^+$ ion at m/z 455.3515, was verified as SDA in accordance with the reference standard. As shown in Fig. S4, the $[M+H]^+$ ion continuously lost H_2O to form m/z 437.3405 and 419.3296, respectively. The fragment ion at m/z 409.3465 derived from $[M+H]^+$ ion via the loss of a carboxyl group, which further generated m/z 95.0854. The fragment ion at m/z 329.2464 derived from $[M+H]^+$ ion by the cleavage of A and B rings. The $[M+H]^+$ ion underwent a C-ring cleavage reaction, producing m/z 217.1592 and 235.1689. The former sequentially lost a series of minor ions to yield the fragment ions at m/z 201.1636, 187.1476, 173.1320, 161.1322, 147.1127, 133.1010, and 119.0854, and the latter lost a carboxyl group to generate the fragment ion at m/z 189.1633, which further cracked to yield m/z 121.1010 and 107.0854.

Compounds 39, 42, 46, 61, 94, 101 and 156 shared exactly the same precursor and almost the same fragments. Their MS^2 spectrums were in line with the typical characteristics of terpenoids: the fragment ions in the low mass fraction were densely clustered; there were few fragment ions in the middle-mass fraction; the NL of H_2O occurred in the high-mass fraction; the typical fragment ions at m/z 95, 119, 133 were observed. And the above characteristic spectrums haven't been observed in blank solvent. So, they were tentatively identified as cycloartenone isomers.

3.4.2. Identification of lignans

Lignans from KHS were mainly divided into four different skeletons, including dibenzocyclooctadienes, tetrahydrofurans, dibenzylbutyrolactones, and arylteralins. Taking KDA, d-E, 6-H-6-glc, and SZD as the respective representative compounds, the fragmentation pathways of four different skeletons of lignans were introduced.

3.4.2.1. Dibenzocyclooctadiene lignans. Compound **103** was verified as KDA in accordance with the reference standard. As shown in Fig. 4, the $[M+Na]^+$ ion at 595.2134 lost the acetyl group at C-7 to yield the fragment ion at m/z 535.1922. The fragment ion at m/z 435.1395 was produced by m/z 535.1922 via the loss of substituent at C-7′, which further lost Na^+ to form m/z 413.1584. The fragment ion at m/z 435.1395 broke the bond between C-7′ and C-8′ to yield m/z 371.1485. This further led to the loss of the methoxy group (−31.0184 Da) at C-5′ or methyl group (−15.0210 Da) at C-8 to form m/z 340.1301 or 356.1275, respectively. The fragment ion at m/z 329.1023 was produced by m/z 535.1922 via breaking the bond between C-2 and C-2′, and losing methyl group at C-8. The fragment ion at m/z 495.1599 derived from $[M+Na]^+$ ion via the loss of substituent at C-7′.

3.4.2.2. Tetrahydrofuran lignans. Compound **129** was verified as d-E on the basis of the reference standard. As shown in Fig. S5, the $[M+H]^+$ ion at m/z 341.1375 produced m/z 323.1281 via the loss of H_2O (−18.0094 Da). The fragment ion at m/z 219.1014 derived from the $[M+H]^+$ ion by breaking the bond between C-1 and C-7, which further generated m/z 201.0907 via the loss of H_2O (−18.0107 Da). The fragment ion at m/z 219.1014 underwent the furan ring cleavage to yield m/z 179.0699. This further resulted in the loss of OH (−15.9948 Da) to yield m/z 163.0751 or C_2H_4 (−28.0310 Da) to generate m/z 151.0389. The latter produced m/z 149.0232 through dehydrogenation (−2.0157 Da) or formed DPI at m/z 135.0439 via the loss of the hydroxyl group. The fragment ion at m/z 149.0232 sequentially lost minor ions to yield m/z 123.0440, 107.0490 and 93.0333. Compound **100** was "FIShed" by DPI at m/z 135.0439 of d-E, displaying $[M+H]^+$ ion at m/z 345.1695. The predicted MS^2 fragments of kadsurindutin E was consistent with the MS^2 spectrum of compound **100**. Therefore, compound **100** was tentatively identified as kadsurindutin E. Similarly, compound **48** was tentatively identified as coumarinlignan.

3.4.2.3. Dibenzylbutyrolactone lignans. Compound **33** displaying $[M+Na]^+$ ion at m/z 555.1468, was verified as 6-H-6-glc according to the reference

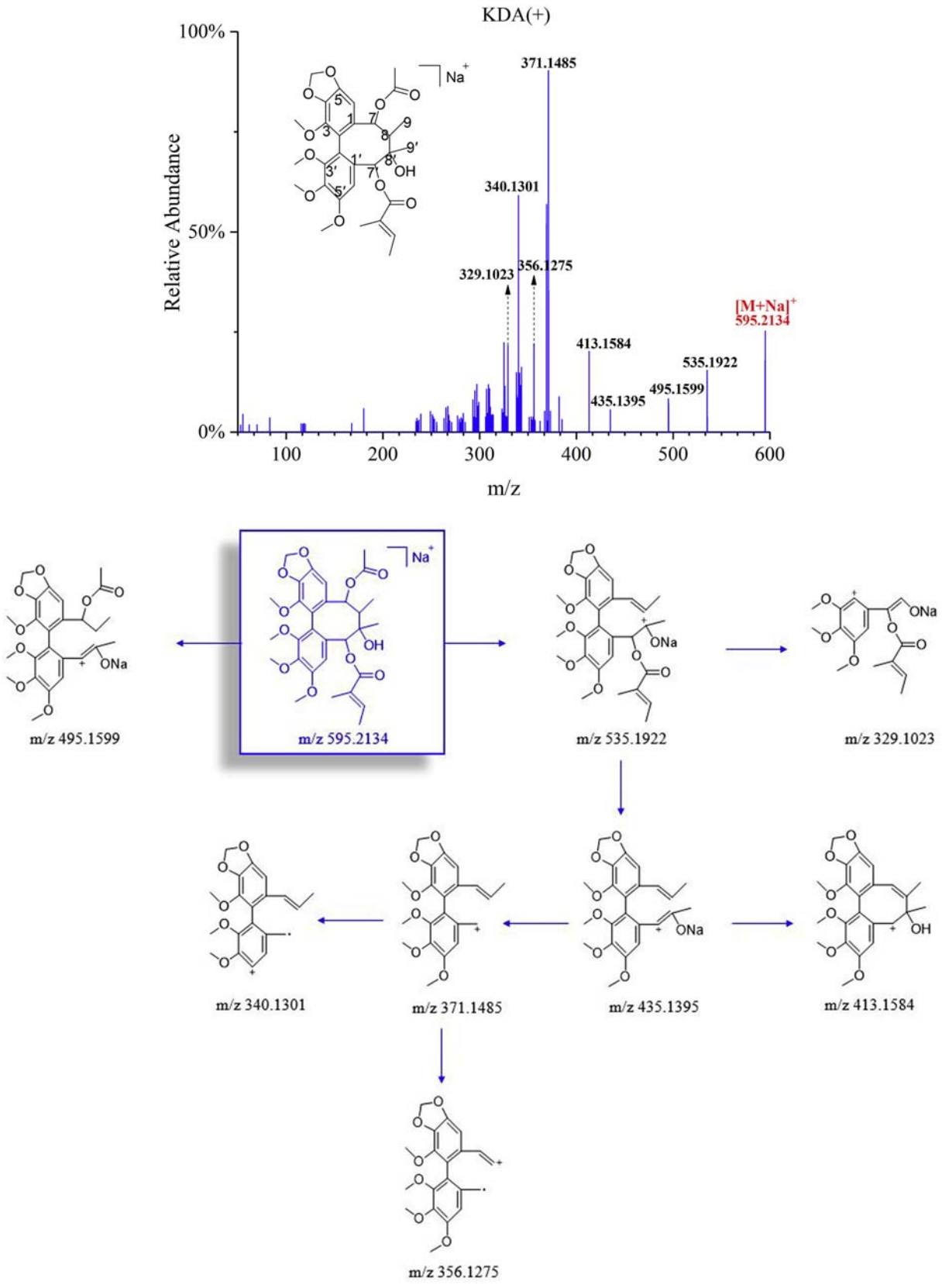

Fig. 4. The exact MS^2 spectrum and proposed fragmentation pathways of kadsurarin (KDA) in positive ion mode.

standard. As shown in Fig. S6, the $[M+Na]^+$ ion generated the fragment ion at m/z 392.0859 via losing a glucose (−163.0607 Da). The fragment ion at m/z 257.0423 was derived from m/z 392.0859 via breaking the bond between C-7 and C-8, which further produced m/z 107.0102 by breaking the bond between C-7′ and C-8′. The fragment ion at m/z 173.0207 was derived from $[M+Na]^+$ ion via losing a glucose and breaking the bond between C-7′and C-8′. Moreover, 6-H-6-glc is formed by the combination of the hydroxyl group of 6-hydroxyhinokinin with glucose. The MS and MS^2 data of compound **54** (235, 151, and 135) are consistent with those reported for 6-hydroxyhinokinin in the literature [9]; thus, it was tentatively identified as 6-hydroxyhinokinin.

3.4.2.4. Aryltetralin lignans. Compound **12** was verified as SZD according to the reference standard. In the MS spectrum, the response of $[M+Na]^+$ peak was higher than that of $[M+H]^+$ peak, but its MS^2 fragments were scarce, which made explaining the fragmentation pathways difficult. Therefore, the MS^2 data of the $[M+H]^+$ peak was used for the description of the fragmentation pathways (Fig. S7). The $[M+H]^+$ ion at m/z 493.0990 lost $C_5H_9O_4$ (−133.9515 Da) to yield m/z 359.1475, which further generated m/z 341.1376 through the loss of H_2O. The fragment ion at m/z 341.1376 successively lost CH_2O (−30.0104 Da), CH_4O (−32.0264 Da), and OH (−15.9953 Da) to yield m/z 311.1272, 279.1008, and 263.1055, respectively. The fragment ion at m/z 219.1017 was derived from m/z 341.1376 via breaking the bond between C-1 and C-7. This further formed m/z 201.0916 through the loss of H_2O (−18.0101 Da), and m/z 201.0916 could be further broken to generate m/z 137.0592.

Among the identified 204 compounds in KHS, only 12 of them were confirmed by reference standards. We will continue to separate and purify more reference standards to further verify our results in future studies.

3.5. Method validation for quantification of active compounds in KHS

The method developed for the quantification of compounds in KHS was validated by linearity, LOD, LOQ, precision, stability, recovery, and matrix effects.

Calibration curves were established by plotting the peak areas of reference standards (y-axis) against their concentration (x-axis), using squares linear regression with a weighting factor ($1/x^2$). All the calibration curves showed good linearity, with the coefficient of determination (r^2) higher than 0.992. The limit of detection (LOD) and the limit of quantification (LOQ) of each analyte were calculated at signal-to-signal (S/N) of 3 and 10 as criteria, respectively. The results are shown in Table 1.

Method precision was assessed by intra-day and inter-day precision. The intra-day precision was determined at the same concentration level with six replicates in one day. For inter-day precision, the above-mentioned experiment was repeated during three consecutive days. It indicated that this method had good intra-day and inter-day precisions with the RSDs within 1.5-4.7% and 0.2-4.9%, respectively. The stability of the analytes was tested by analyzing the same sample, which was stored at 4 °C, within 24 h. The result showed that the sample was stable within 24 h with the RSDs ranging from 1.1 to 4.7%. The results are shown in Table 2.

Recovery was used to evaluate the accuracy of the method. Recovery was assessed by adding 100% of the original concentration of each target compound into known amounts of a real sample. Then, the resultant samples were extracted and analyzed using the proposed method, and six experiments were repeated [35,39,40]. The recovery was calculated by the following formula: recovery (%) = (detected amount - original amount)/spiked amount × 100%. The recoveries of analytes varied from 89.5 to 114.1% with RSDs ranging from 2.3 to 5.0%, indicating that the method was accurate. The results are displayed in

Table 1. Quantitative ion, calibration curve, linear range, LOD and LOQ of 12 analytes.

Compounds	Quantitative ion (m/z)	Calibration curve	Linear range (ng/mL)	r^2	LOD (ng/mL)	LOQ (ng/mL)
Schizandriside	515.1888	y = 35502x-17373	1.0-2000.0	0.9963	0.2	0.5
6-hydroxyhinokinin-6-*O*-β-D-glucopyranoside	555.1473	y = 141801x-8809	1.0-2000.0	0.9987	0.2	0.5
Heteroclitalactone M	541.3160	y = 32851x-3532	1.0-2000.0	0.9957	0.2	0.5
Heteroclitalactone E	537.2847	y = 146324x-91350	1.0-2000.0	0.9978	0.2	0.5
Kadsurarin	595.2150	y = 286026x-13128	1.0-200.0	0.9948	0.5	1.0
Heteroclitalactone D	523.3054	y = 156394x-19223	1.0-2000.0	0.9996	0.2	0.5
d-Epigalbacin	341.1384	y = 6225x-113281	50.0-100000.0	0.9928	5.0	25.0
Schisanlactone B	467.3156	y = 394976x+287212	1.0-2000.0	0.9969	0.2	0.5
Schisanlactone E	469.3312	y = 410969x+2573740	1.0-2000.0	0.9970	0.5	1.0
Heteroclitalactone B	563.3343	y = 1134850x+91017	1.0-2000.0	0.9966	0.1	0.5
Heteroclitalactone F	505.3288	y = 569468x-144912	1.0-2000.0	0.9944	0.1	0.5
Schisandronic acid	455.3520	y = 5506x+382504	50.0-25000.0	0.9953	25.0	50.0

Table 2. Precision, stability, recovery and matrix effects of 12 analytes.

	Precision (n = 6)		Stability	Recovery (n = 6)					Matrix effects (n = 6)	
	Intra-day (RSD, %)	Inter-day (RSD, %)	(n = 6) (RSD, %)	Original amount (μg)	Spiked amount (μg)	Mean detected amount (μg)	Mean (%)	RSD (%)	Mean (%)	RSD (%)
Schizandriside	4.7%	3.0%	3.6%	135.5	135.5	273.3	101.8%	4.7%	98.0	10.0
6-hydroxyhinokinin-6-*O*-β-D-glucopyranoside	2.2%	0.2%	1.8%	40.5	40.5	80.7	99.2%	4.6%	101.9	5.3
Heteroclitalactone M	4.9%	2.8%	3.6%	7.8	7.8	15.6	100.2%	4.2%	100.6	5.2
Heteroclitalactone E	1.5%	2.1%	3.8%	27.8	27.8	57.7	107.9%	3.9%	102.6	4.7
Kadsurarin	2.0%	1.4%	3.0%	0.14	0.14	0.30	110.1%	2.5%	93.5	15.1
Heteroclitalactone D	1.8%	2.0%	3.1%	135.8	135.8	257.2	89.5%	4.6%	103.8	2.9
d-Epigalbacin	3.4%	2.7%	4.5%	214.5	214.5	459.3	114.1%	4.7%	102.3	8.6
Schisanlactone B	1.5%	1.8%	3.6%	5.2	5.2	10.7	107.0%	4.3%	105.9	7.1
Schisanlactone E	3.8%	4.0%	1.1%	1197.6	1197.6	2327.6	94.4%	4.5%	102.1	5.9
Heteroclitalactone B	2.3%	4.9%	4.7%	0.63	0.63	1.30	106.7%	2.3%	97.3	6.1
Heteroclitalactone F	3.5%	4.5%	3.5%	3.8	3.8	6.8	80.9%	4.7%	107.0	1.4
Schisandronic acid	2.9%	2.8%	4.3%	564.0	564.0	1191.0	111.2%	5.0%	110.6	3.0

Table 3. Contents of 12 compounds in four batches of KHS (μg/g of dry sample).

Compounds	Batch 1	Batch 2	Batch 3	Batch 4
Schizandriside	884.7	756.7	145.8	1121.4
6-hydroxyhinokinin-6-*O*-β-D-glucopyranoside	476.2	421.0	48.5	513.5
Heteroclitalactone M	8.2	7.2	10.3	18.7
Heteroclitalactone E	123.7	106.8	32.6	75.3
Kadsurarin	1.1	32.1	0.1	0.3
Heteroclitalactone D	50.2	41.5	144.7	54.7
d-Epigalbacin	115.5	111.4	346.5	176.0
Schisanlactone B	21.4	18.9	5.0	7.4
Schisanlactone E	2011.2	1424.7	1220.5	1817.4
Heteroclitalactone B	0.4	0.3	0.8	0.1
Heteroclitalactone F	2.5	1.6	5.2	0.8
Schisandronic acid	904.5	485.2	439.9	240.3
Total	4599.5	3407.3	2399.9	4025.8

Table 2. The matrix effect was evaluated by comparing the peak area response of the post-extracted spiked sample with the corresponding standard containing equivalent concentrations of the analytes in blank solvents. The matrix effect was measured as follows: [(peak area of post-extracted spiked sample) − (peak area of endogenous sample)]/(peak area of spiked standard solution) × 100% [41,42]. The matrix effect of analytes varied from 93.5 to 110.6% with RSDs ranging from 1.4 to 15.1%, indicating that the method was hardly interfered by matrix effects. The results are displayed in Table 2.

3.6. Quantification of components in KHS

The newly established and validated UHPLC-Q-Orbitrap HRMS method was applied to simultaneously quantify 12 representative compounds in four batches of KHS collected in Shimen, Hunan, China in four different seasons during 2018-2019. The extracted ion chromatogram of 12 mixed reference standards are displayed in Fig. S8, and the results of quantification are shown in Table 3.

The results revealed that the contents of these 12 bioactive compounds in KHS were significantly different. SE was the most abundant compound in KHS (1220.5-2011.2 μg/g), exhibiting anti-tumor activity [6] and inhibitory effect on the formation of P388 cells in leukemia [25]. In our previous study, SE exhibited a satisfactory oral bioavailability in rats (79.3%) [20]. HF, HB, SB, HM, HD, and HE, as the analogs of SE, displayed cytotoxic activity against cancer cell lines [6], with the levels of 0.8-5.2 μg/g, 0.1-0.8 μg/g, 5.0-21.4 μg/g, 7.2-18.7 μg/g, 41.5-144.7 μg/g, and 32.6-123.7 μg/g, respectively. SDA belongs to intact cycloartane triterpenoids that exhibit cytotoxic activity against leukemia and HeLa cells [26], at 240.3-904.5 μg/g in KHS. SZD, an aryltetralin lignan glycoside, displayed anti-tumor and antioxidant activities [27, 28, 30], present at a concentration of 145.8-1121.4 μg/g in KHS. d-E displayed anti-proliferative activity [31], and its content was in the range of 111.4-346.5 μg/g in our study. The content of KDA in four batches ranged from 0.1 to 32.1 μg/g, which affects HIV-1 reverse transcriptase [29].

4. Conclusion

A novel quali-quantitative method established here was able to simultaneously identify and quantify the compounds in KHS. This method proved to be simple, fast, sensitive, and efficient. As a result, 204 components were characterized, including triterpenoids, lignans, sesquiterpenes, fatty acids, phenolic acids, and flavonoids. Simultaneously, 12 representative triterpenoids and lignans were quantified successfully in KHS. This simple, fast, and sensitive method could also be used to quantify more potentially active components of KHS in the future.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgements

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Appendix A. Supplementary material

Table S1. Peak areas of 12 analytes in three different extraction solvents.

Compounds	MeOH	95%EtOH	ACN
Schizandriside	2.67E+08	2.34E+08	1.63E+08
6-hydroxyhinokinin-6-*O*-β-D-glucopyranoside	1.97E+09	2.28E+09	1.12E+09
Heteroclitalactone M	2.70E+07	2.70E+07	2.62E+07
Heteroclitalactone E	9.60E+08	9.46E+08	9.60E+08
Kadsurarin	1.45E+07	1.51E+07	1.56E+07
Heteroclitalactone D	6.44E+08	6.17E+08	6.66E+08
d-Epigalbacin	6.49E+07	6.05E+07	6.16E+07
Schisanlactone B	5.21E+08	5.10E+08	5.29E+08
Schisanlactone E	1.33E+10	1.31E+10	1.35E+10
Heteroclitalactone B	1.88E+07	1.83E+07	1.86E+07
Heteroclitalactone F	9.11E+07	8.32E+07	8.75E+07
Schisandronic acid	1.07E+09	1.02E+09	1.04E+09
Total	1.892E+10	1.891E+10	1.818E+10

Table S2. Peak areas of 12 analytes in different solid-liquid ratios.

Compounds	1:10	1:30	1:50
Schizandriside	1.13E+08	3.47E+08	4.27E+08
6-hydroxyhinokinin-6-*O*-β-D-glucopyranoside	9.49E+08	2.25E+09	1.93E+09
Heteroclitalactone M	1.61E+07	2.68E+07	1.59E+07
Heteroclitalactone E	5.90E+08	1.02E+09	6.87E+08
Kadsurarin	8.23E+06	1.39E+07	1.02E+07
Heteroclitalactone D	3.64E+08	6.29E+08	4.15E+08
d-Epigalbacin	3.84E+07	7.16E+07	4.01E+07
Schisanlactone B	3.19E+08	5.84E+08	3.68E+08
Schisanlactone E	6.39E+09	1.42E+10	1.49E+10
Heteroclitalactone B	1.27E+07	1.96E+07	9.38E+06
Heteroclitalactone F	4.24E+07	8.47E+07	5.99E+07
Schisandronic acid	5.29E+08	1.12E+09	8.46E+08
Total	9.37E+09	2.04E+10	1.97E+10

Table S3. Peak areas of 12 analytes in different ultrasound extraction time.

Compounds	5min	15min	30min
Schizandriside	3.14E+08	3.07E+08	2.99E+08
6-hydroxyhinokinin-6-*O*-β-D-glucopyranoside	2.12E+09	2.13E+09	1.94E+09
Heteroclitalactone M	2.41E+07	2.43E+07	2.49E+07
Heteroclitalactone E	9.29E+08	9.15E+08	8.70E+08
Kadsurarin	1.37E+07	1.36E+07	1.31E+07
Heteroclitalactone D	5.98E+08	6.15E+08	5.81E+08
d-Epigalbacin	5.38E+07	6.09E+07	5.63E+07
Schisanlactone B	5.11E+08	5.11E+08	4.90E+08
Schisanlactone E	1.31E+10	1.36E+10	1.33E+10
Heteroclitalactone B	1.69E+07	1.85E+07	1.74E+07
Heteroclitalactone F	8.03E+07	8.59E+07	8.43E+07
Schisandronic acid	1.02E+09	1.04E+09	1.05E+09
Total	1.883E+10	1.933E+10	1.870E+10

Table S4. The inclusion list in positive ion mode.

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
645.2694	C37H40O10	Chemical formula	$[M+H]^+$	1	Positive
639.2225	C37H34O10	Chemical formula	$[M+H]^+$	1	Positive
633.2694	C36H40O10	Chemical formula	$[M+H]^+$	1	Positive
643.2174	C36H34O11	Chemical formula	$[M+H]^+$	1	Positive
641.2017	C36H32O11	Chemical formula	$[M+H]^+$	1	Positive
577.4463	C35H60O6	Chemical formula	$[M+H]^+$	1	Positive
657.2906	C35H44O12	Chemical formula	$[M+H]^+$	1	Positive
657.2906	C35H44O12	Chemical formula	$[M+H]^+$	1	Positive
637.2643	C35H40O11	Chemical formula	$[M+H]^+$	1	Positive
635.2487	C35H38O11	Chemical formula	$[M+H]^+$	1	Positive
619.2538	C35H38O10	Chemical formula	$[M+H]^+$	1	Positive
557.3837	C34H52O6	Chemical formula	$[M+H]^+$	1	Positive
555.368	C34H50O6	Chemical formula	$[M+H]^+$	1	Positive
595.2902	C34H42O9	Chemical formula	$[M+H]^+$	1	Positive
623.2487	C34H38O11	Chemical formula	$[M+H]^+$	1	Positive
621.233	C34H36O11	Chemical formula	$[M+H]^+$	1	Positive
619.2174	C34H34O11	Chemical formula	$[M+H]^+$	1	Positive
617.2017	C34H32O11	Chemical formula	$[M+H]^+$	1	Positive
541.3524	C33H48O6	Chemical formula	$[M+H]^+$	1	Positive
563.3343	C33H48O6	Chemical formula	$[M+Na]^+$	1	Positive
599.2851	C33H42O10	Chemical formula	$[M+H]^+$	1	Positive
597.2694	C33H40O10	Chemical formula	$[M+H]^+$	1	Positive
627.2436	C33H38O12	Chemical formula	$[M+H]^+$	1	Positive
611.2487	C33H38O11	Chemical formula	$[M+H]^+$	1	Positive
607.2174	C33H34O11	Chemical formula	$[M+H]^+$	1	Positive
605.2017	C33H32O11	Chemical formula	$[M+H]^+$	1	Positive
515.3731	C32H50O5	Chemical formula	$[M+H]^+$	1	Positive
499.3782	C32H50O4	Chemical formula	$[M+H]^+$	1	Positive
529.3524	C32H48O6	Chemical formula	$[M+H]^+$	1	Positive
513.3575	C32H48O5	Chemical formula	$[M+H]^+$	1	Positive
535.3394	C32H48O5	Chemical formula	$[M+Na]^+$	1	Positive
497.3625	C32H48O4	Chemical formula	$[M+H]^+$	1	Positive
519.3445	C32H48O4	Chemical formula	$[M+Na]^+$	1	Positive
559.3265	C32H46O8	Chemical formula	$[M+H]^+$	1	Positive
581.3085	C32H46O8	Chemical formula	$[M+Na]^+$	1	Positive
543.3316	C32H46O7	Chemical formula	$[M+H]^+$	1	Positive
565.3136	C32H46O7	Chemical formula	$[M+Na]^+$	1	Positive
527.3367	C32H46O6	Chemical formula	$[M+H]^+$	1	Positive
549.3187	C32H46O6	Chemical formula	$[M+Na]^+$	1	Positive
511.3418	C32H46O5	Chemical formula	$[M+H]^+$	1	Positive
495.3469	C32H46O4	Chemical formula	$[M+H]^+$	1	Positive
573.3058	C32H44O9	Chemical formula	$[M+H]^+$	1	Positive
557.3109	C32H44O8	Chemical formula	$[M+H]^+$	1	Positive
541.316	C32H44O7	Chemical formula	$[M+H]^+$	1	Positive
571.2902	C32H42O9	Chemical formula	$[M+H]^+$	1	Positive
555.2952	C32H42O8	Chemical formula	$[M+H]^+$	1	Positive
577.2772	C32H42O8	Chemical formula	$[M+Na]^+$	1	Positive
539.3003	C32H42O7	Chemical formula	$[M+H]^+$	1	Positive
561.2823	C32H42O7	Chemical formula	$[M+Na]^+$	1	Positive
523.3054	C32H42O6	Chemical formula	$[M+H]^+$	1	Positive
553.2796	C32H40O8	Chemical formula	$[M+H]^+$	1	Positive
575.2615	C32H40O8	Chemical formula	$[M+Na]^+$	1	Positive
537.2847	C32H40O7	Chemical formula	$[M+H]^+$	1	Positive
559.2666	C32H40O7	Chemical formula	$[M+Na]^+$	1	Positive
521.2898	C32H40O6	Chemical formula	$[M+H]^+$	1	Positive
543.2717	C32H40O6	Chemical formula	$[M+Na]^+$	1	Positive
601.2643	C32H40O11	Chemical formula	$[M+H]^+$	1	Positive
585.2694	C32H40O10	Chemical formula	$[M+H]^+$	1	Positive
551.2639	C32H38O8	Chemical formula	$[M+H]^+$	1	Positive
573.2459	C32H38O8	Chemical formula	$[M+Na]^+$	1	Positive
599.2487	C32H38O11	Chemical formula	$[M+H]^+$	1	Positive

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Table S4. (continued)

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
583.2538	C32H38O10	Chemical formula	$[M+H]^+$	1	Positive
597.233	C32H36O11	Chemical formula	$[M+H]^+$	1	Positive
581.2381	C32H36O10	Chemical formula	$[M+H]^+$	1	Positive
547.2326	C32H34O8	Chemical formula	$[M+H]^+$	1	Positive
595.2174	C32H34O11	Chemical formula	$[M+H]^+$	1	Positive
617.1993	C32H34O11	Chemical formula	$[M+Na]^+$	1	Positive
579.2225	C32H34O10	Chemical formula	$[M+H]^+$	1	Positive
471.3833	C31H50O3	Chemical formula	$[M+H]^+$	1	Positive
439.3934	C31H50O	Chemical formula	$[M+H]^+$	1	Positive
501.3575	C31H48O5	Chemical formula	$[M+H]^+$	1	Positive
523.3394	C31H48O5	Chemical formula	$[M+Na]^+$	1	Positive
485.3625	C31H48O4	Chemical formula	$[M+H]^+$	1	Positive
507.3445	C31H48O4	Chemical formula	$[M+Na]^+$	1	Positive
515.3367	C31H46O6	Chemical formula	$[M+H]^+$	1	Positive
545.3109	C31H44O8	Chemical formula	$[M+H]^+$	1	Positive
497.3262	C31H44O5	Chemical formula	$[M+H]^+$	1	Positive
577.3007	C31H44O10	Chemical formula	$[M+H]^+$	1	Positive
599.2827	C31H44O10	Chemical formula	$[M+Na]^+$	1	Positive
509.2898	C31H40O6	Chemical formula	$[M+H]^+$	1	Positive
531.2717	C31H40O6	Chemical formula	$[M+Na]^+$	1	Positive
523.269	C31H38O7	Chemical formula	$[M+H]^+$	1	Positive
587.2487	C31H38O11	Chemical formula	$[M+H]^+$	1	Positive
609.2306	C31H38O11	Chemical formula	$[M+Na]^+$	1	Positive
571.2538	C31H38O10	Chemical formula	$[M+H]^+$	1	Positive
537.2483	C31H36O8	Chemical formula	$[M+H]^+$	1	Positive
535.2326	C31H34O8	Chemical formula	$[M+H]^+$	1	Positive
583.2174	C31H34O11	Chemical formula	$[M+H]^+$	1	Positive
567.2225	C31H34O10	Chemical formula	$[M+H]^+$	1	Positive
581.2017	C31H32O11	Chemical formula	$[M+H]^+$	1	Positive
603.1837	C31H32O11	Chemical formula	$[M+Na]^+$	1	Positive
565.2068	C31H32O10	Chemical formula	$[M+H]^+$	1	Positive
611.1759	C31H30O13	Chemical formula	$[M+H]^+$	1	Positive
579.1861	C31H30O11	Chemical formula	$[M+H]^+$	1	Positive
601.168	C31H30O11	Chemical formula	$[M+Na]^+$	1	Positive
563.1912	C31H30O10	Chemical formula	$[M+H]^+$	1	Positive
453.4666	C30H60O2	Chemical formula	$[M+H]^+$	1	Positive
445.404	C30H52O2	Chemical formula	$[M+H]^+$	1	Positive
475.3782	C30H50O4	Chemical formula	$[M+H]^+$	1	Positive
497.3601	C30H50O4	Chemical formula	$[M+Na]^+$	1	Positive
427.3934	C30H50O	Chemical formula	$[M+H]^+$	1	Positive
489.3575	C30H48O5	Chemical formula	$[M+H]^+$	1	Positive
473.3625	C30H48O4	Chemical formula	$[M+H]^+$	1	Positive
495.3445	C30H48O4	Chemical formula	$[M+Na]^+$	1	Positive
457.3676	C30H48O3	Chemical formula	$[M+H]^+$	1	Positive
479.3496	C30H48O3	Chemical formula	$[M+Na]^+$	1	Positive
441.3727	C30H48O2	Chemical formula	$[M+H]^+$	1	Positive
463.3547	C30H48O2	Chemical formula	$[M+Na]^+$	1	Positive
425.3778	C30H48O	Chemical formula	$[M+H]^+$	1	Positive
447.3597	C30H48O	Chemical formula	$[M+Na]^+$	1	Positive
487.3418	C30H46O5	Chemical formula	$[M+H]^+$	1	Positive
471.3469	C30H46O4	Chemical formula	$[M+H]^+$	1	Positive
493.3288	C30H46O4	Chemical formula	$[M+Na]^+$	1	Positive
455.352	C30H46O3	Chemical formula	$[M+H]^+$	1	Positive
477.3339	C30H46O3	Chemical formula	$[M+Na]^+$	1	Positive
439.3571	C30H46O2	Chemical formula	$[M+H]^+$	1	Positive
461.339	C30H46O2	Chemical formula	$[M+Na]^+$	1	Positive
549.3058	C30H44O9	Chemical formula	$[M+H]^+$	1	Positive
517.316	C30H44O7	Chemical formula	$[M+H]^+$	1	Positive
539.2979	C30H44O7	Chemical formula	$[M+Na]^+$	1	Positive
501.3211	C30H44O6	Chemical formula	$[M+H]^+$	1	Positive
523.303	C30H44O6	Chemical formula	$[M+Na]^+$	1	Positive

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Table S4. (continued)

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
485.3262	C30H44O5	Chemical formula	$[M+H]^+$	1	Positive
507.3081	C30H44O5	Chemical formula	$[M+Na]^+$	1	Positive
469.3312	C30H44O4	Chemical formula	$[M+H]^+$	1	Positive
491.3132	C30H44O4	Chemical formula	$[M+Na]^+$	1	Positive
453.3363	C30H44O3	Chemical formula	$[M+H]^+$	1	Positive
475.3183	C30H44O3	Chemical formula	$[M+Na]^+$	1	Positive
531.2952	C30H42O8	Chemical formula	$[M+H]^+$	1	Positive
553.2772	C30H42O8	Chemical formula	$[M+Na]^+$	1	Positive
515.3003	C30H42O7	Chemical formula	$[M+H]^+$	1	Positive
499.3054	C30H42O6	Chemical formula	$[M+H]^+$	1	Positive
505.2925	C30H42O5	Chemical formula	$[M+Na]^+$	1	Positive
467.3156	C30H42O4	Chemical formula	$[M+H]^+$	1	Positive
489.2975	C30H42O4	Chemical formula	$[M+Na]^+$	1	Positive
529.2796	C30H40O8	Chemical formula	$[M+H]^+$	1	Positive
513.2847	C30H40O7	Chemical formula	$[M+H]^+$	1	Positive
497.2898	C30H40O6	Chemical formula	$[M+H]^+$	1	Positive
481.2949	C30H40O5	Chemical formula	$[M+H]^+$	1	Positive
465.2999	C30H40O4	Chemical formula	$[M+H]^+$	1	Positive
494.2901	C30H39NO5	Chemical formula	$[M+H]^+$	1	Positive
511.269	C30H38O7	Chemical formula	$[M+H]^+$	1	Positive
533.251	C30H38O7	Chemical formula	$[M+Na]^+$	1	Positive
495.2741	C30H38O6	Chemical formula	$[M+H]^+$	1	Positive
517.2561	C30H38O6	Chemical formula	$[M+Na]^+$	1	Positive
479.2792	C30H38O5	Chemical formula	$[M+H]^+$	1	Positive
575.2487	C30H38O11	Chemical formula	$[M+H]^+$	1	Positive
559.2538	C30H38O10	Chemical formula	$[M+H]^+$	1	Positive
509.2534	C30H36O7	Chemical formula	$[M+H]^+$	1	Positive
493.2585	C30H36O6	Chemical formula	$[M+H]^+$	1	Positive
589.228	C30H36O12	Chemical formula	$[M+H]^+$	1	Positive
573.233	C30H36O11	Chemical formula	$[M+H]^+$	1	Positive
557.2381	C30H36O10	Chemical formula	$[M+H]^+$	1	Positive
507.2377	C30H34O7	Chemical formula	$[M+H]^+$	1	Positive
491.2428	C30H34O6	Chemical formula	$[M+H]^+$	1	Positive
571.2174	C30H34O11	Chemical formula	$[M+H]^+$	1	Positive
537.2119	C30H32O9	Chemical formula	$[M+H]^+$	1	Positive
521.217	C30H32O8	Chemical formula	$[M+H]^+$	1	Positive
415.3934	C29H50O	Chemical formula	$[M+H]^+$	1	Positive
443.352	C29H46O3	Chemical formula	$[M+H]^+$	1	Positive
457.3312	C29H44O4	Chemical formula	$[M+H]^+$	1	Positive
535.2902	C29H42O9	Chemical formula	$[M+H]^+$	1	Positive
503.3003	C29H42O7	Chemical formula	$[M+H]^+$	1	Positive
533.2745	C29H40O9	Chemical formula	$[M+H]^+$	1	Positive
517.2796	C29H40O8	Chemical formula	$[M+H]^+$	1	Positive
501.2847	C29H40O7	Chemical formula	$[M+H]^+$	1	Positive
485.2898	C29H40O6	Chemical formula	$[M+H]^+$	1	Positive
531.2589	C29H38O9	Chemical formula	$[M+H]^+$	1	Positive
545.2381	C29H36O10	Chemical formula	$[M+H]^+$	1	Positive
559.2174	C29H34O11	Chemical formula	$[M+H]^+$	1	Positive
589.1916	C29H32O13	Chemical formula	$[M+H]^+$	1	Positive
557.2017	C29H32O11	Chemical formula	$[M+H]^+$	1	Positive
541.2068	C29H32O10	Chemical formula	$[M+H]^+$	1	Positive
523.1963	C29H30O9	Chemical formula	$[M+H]^+$	1	Positive
507.2013	C29H30O8	Chemical formula	$[M+H]^+$	1	Positive
539.1912	C29H30O10	Chemical formula	$[M+H]^+$	1	Positive
521.1806	C29H28O9	Chemical formula	$[M+H]^+$	1	Positive
505.1857	C29H28O8	Chemical formula	$[M+H]^+$	1	Positive
537.1755	C29H28O10	Chemical formula	$[M+H]^+$	1	Positive
457.2949	C28H40O5	Chemical formula	$[M+H]^+$	1	Positive
501.2483	C28H36O8	Chemical formula	$[M+H]^+$	1	Positive
549.233	C28H36O11	Chemical formula	$[M+H]^+$	1	Positive
571.215	C28H36O11	Chemical formula	$[M+Na]^+$	1	Positive

(continued on next page)

Table S4. (continued)

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
533.2381	C28H36O10	Chemical formula	$[M+H]^+$	1	Positive
515.2276	C28H34O9	Chemical formula	$[M+H]^+$	1	Positive
537.2095	C28H34O9	Chemical formula	$[M+Na]^+$	1	Positive
499.2326	C28H34O8	Chemical formula	$[M+H]^+$	1	Positive
531.2225	C28H34O10	Chemical formula	$[M+H]^+$	1	Positive
553.2044	C28H34O10	Chemical formula	$[M+Na]^+$	1	Positive
511.1963	C28H30O9	Chemical formula	$[M+H]^+$	1	Positive
489.1544	C28H24O8	Chemical formula	$[M+H]^+$	1	Positive
429.2999	C27H40O4	Chemical formula	$[M+H]^+$	1	Positive
487.2326	C27H34O8	Chemical formula	$[M+H]^+$	1	Positive
509.2146	C27H34O8	Chemical formula	$[M+Na]^+$	1	Positive
501.2119	C27H32O9	Chemical formula	$[M+H]^+$	1	Positive
485.217	C27H32O8	Chemical formula	$[M+H]^+$	1	Positive
469.2221	C27H32O7	Chemical formula	$[M+H]^+$	1	Positive
533.2017	C27H32O11	Chemical formula	$[M+H]^+$	1	Positive
517.2068	C27H32O10	Chemical formula	$[M+H]^+$	1	Positive
499.1963	C27H30O9	Chemical formula	$[M+H]^+$	1	Positive
483.2013	C27H30O8	Chemical formula	$[M+H]^+$	1	Positive
505.1833	C27H30O8	Chemical formula	$[M+Na]^+$	1	Positive
515.1912	C27H30O10	Chemical formula	$[M+H]^+$	1	Positive
537.1731	C27H30O10	Chemical formula	$[M+Na]^+$	1	Positive
497.1806	C27H28O9	Chemical formula	$[M+H]^+$	1	Positive
541.228	C26H36O12	Chemical formula	$[M+H]^+$	1	Positive
473.217	C26H32O8	Chemical formula	$[M+H]^+$	1	Positive
521.2017	C26H32O11	Chemical formula	$[M+H]^+$	1	Positive
471.2013	C26H30O8	Chemical formula	$[M+H]^+$	1	Positive
533.1654	C26H28O12	Chemical formula	$[M+H]^+$	1	Positive
555.1473	C26H28O12	Chemical formula	$[M+Na]^+$	1	Positive
477.2119	C25H32O9	Chemical formula	$[M+H]^+$	1	Positive
429.2272	C25H32O6	Chemical formula	$[M+H]^+$	1	Positive
493.2068	C25H32O10	Chemical formula	$[M+H]^+$	1	Positive
475.1963	C25H30O9	Chemical formula	$[M+H]^+$	1	Positive
497.1782	C25H30O9	Chemical formula	$[M+Na]^+$	1	Positive
459.2013	C25H30O8	Chemical formula	$[M+H]^+$	1	Positive
481.1833	C25H30O8	Chemical formula	$[M+Na]^+$	1	Positive
473.1806	C25H28O9	Chemical formula	$[M+H]^+$	1	Positive
457.1857	C25H28O8	Chemical formula	$[M+H]^+$	1	Positive
433.2221	C24H32O7	Chemical formula	$[M+H]^+$	1	Positive
455.204	C24H32O7	Chemical formula	$[M+Na]^+$	1	Positive
417.2272	C24H32O6	Chemical formula	$[M+H]^+$	1	Positive
439.2091	C24H32O6	Chemical formula	$[M+Na]^+$	1	Positive
447.2013	C24H30O8	Chemical formula	$[M+H]^+$	1	Positive
431.2064	C24H30O7	Chemical formula	$[M+H]^+$	1	Positive
453.1884	C24H30O7	Chemical formula	$[M+Na]^+$	1	Positive
415.2115	C24H30O6	Chemical formula	$[M+H]^+$	1	Positive
461.1806	C24H28O9	Chemical formula	$[M+H]^+$	1	Positive
445.1857	C24H28O8	Chemical formula	$[M+H]^+$	1	Positive
467.1676	C24H28O8	Chemical formula	$[M+Na]^+$	1	Positive
477.1755	C24H28O10	Chemical formula	$[M+H]^+$	1	Positive
443.17	C24H26O8	Chemical formula	$[M+H]^+$	1	Positive
465.152	C24H26O8	Chemical formula	$[M+Na]^+$	1	Positive
359.2581	C23H34O3	Chemical formula	$[M+H]^+$	1	Positive
419.2064	C23H30O7	Chemical formula	$[M+H]^+$	1	Positive
403.2115	C23H30O6	Chemical formula	$[M+H]^+$	1	Positive
425.1935	C23H30O6	Chemical formula	$[M+Na]^+$	1	Positive
441.1884	C23H30O7	Chemical formula	$[M+H]^+$	1	Positive
433.1857	C23H28O8	Chemical formula	$[M+H]^+$	1	Positive
417.1908	C23H28O7	Chemical formula	$[M+H]^+$	1	Positive
439.1727	C23H28O7	Chemical formula	$[M+Na]^+$	1	Positive
401.1959	C23H28O6	Chemical formula	$[M+H]^+$	1	Positive
423.1778	C23H28O6	Chemical formula	$[M+Na]^+$	1	Positive

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Table S4. (continued)

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
415.1751	C23H26O7	Chemical formula	$[M+H]^+$	1	Positive
437.1571	C23H26O7	Chemical formula	$[M+Na]^+$	1	Positive
345.2424	C22H32O3	Chemical formula	$[M+H]^+$	1	Positive
367.2244	C22H32O3	Chemical formula	$[M+Na]^+$	1	Positive
407.2064	C22H30O7	Chemical formula	$[M+H]^+$	1	Positive
429.1884	C22H30O7	Chemical formula	$[M+Na]^+$	1	Positive
389.1959	C22H28O6	Chemical formula	$[M+H]^+$	1	Positive
373.201	C22H28O5	Chemical formula	$[M+H]^+$	1	Positive
395.1829	C22H28O5	Chemical formula	$[M+Na]^+$	1	Positive
403.1751	C22H26O7	Chemical formula	$[M+H]^+$	1	Positive
425.1571	C22H26O7	Chemical formula	$[M+Na]^+$	1	Positive
387.1802	C22H26O6	Chemical formula	$[M+H]^+$	1	Positive
409.1622	C22H26O6	Chemical formula	$[M+Na]^+$	1	Positive
417.1544	C22H24O8	Chemical formula	$[M+H]^+$	1	Positive
439.1363	C22H24O8	Chemical formula	$[M+Na]^+$	1	Positive
401.1595	C22H24O7	Chemical formula	$[M+H]^+$	1	Positive
423.1414	C22H24O7	Chemical formula	$[M+Na]^+$	1	Positive
385.1646	C22H24O6	Chemical formula	$[M+H]^+$	1	Positive
407.1465	C22H24O6	Chemical formula	$[M+Na]^+$	1	Positive
431.1337	C22H22O9	Chemical formula	$[M+H]^+$	1	Positive
415.1387	C22H22O8	Chemical formula	$[M+H]^+$	1	Positive
399.1438	C22H22O7	Chemical formula	$[M+H]^+$	1	Positive
493.0977	C22H20O13	Chemical f			

Table S5. The inclusion list in negative ion mode.

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
643.2549	C37H40O10	Chemical formula	$[M-H]^-$	1	Negative
637.2079	C37H34O10	Chemical formula	$[M-H]^-$	1	Negative
631.2549	C36H40O10	Chemical formula	$[M-H]^-$	1	Negative
641.2028	C36H34O11	Chemical formula	$[M-H]^-$	1	Negative
639.1872	C36H32O11	Chemical formula	$[M-H]^-$	1	Negative
575.4317	C35H60O6	Chemical formula	$[M-H]^-$	1	Negative
655.276	C35H44O12	Chemical formula	$[M-H]^-$	1	Negative
655.276	C35H44O12	Chemical formula	$[M-H]^-$	1	Negative
635.2498	C35H40O11	Chemical formula	$[M-H]^-$	1	Negative
633.2341	C35H38O11	Chemical formula	$[M-H]^-$	1	Negative
617.2392	C35H38O10	Chemical formula	$[M-H]^-$	1	Negative
555.3691	C34H52O6	Chemical formula	$[M-H]^-$	1	Negative
553.3535	C34H50O6	Chemical formula	$[M-H]^-$	1	Negative
593.2756	C34H42O9	Chemical formula	$[M-H]^-$	1	Negative
621.2341	C34H38O11	Chemical formula	$[M-H]^-$	1	Negative
617.2028	C34H34O11	Chemical formula	$[M-H]^-$	1	Negative
615.1872	C34H32O11	Chemical formula	$[M-H]^-$	1	Negative
539.3378	C33H48O6	Chemical formula	$[M-H]^-$	1	Negative
597.2705	C33H42O10	Chemical formula	$[M-H]^-$	1	Negative
595.2549	C33H40O10	Chemical formula	$[M-H]^-$	1	Negative
625.2291	C33H38O12	Chemical formula	$[M-H]^-$	1	Negative
609.2341	C33H38O11	Chemical formula	$[M-H]^-$	1	Negative
603.1872	C33H32O11	Chemical formula	$[M-H]^-$	1	Negative
513.3586	C32H50O5	Chemical formula	$[M-H]^-$	1	Negative
497.3636	C32H50O4	Chemical formula	$[M-H]^-$	1	Negative
527.3378	C32H48O6	Chemical formula	$[M-H]^-$	1	Negative
511.3429	C32H48O5	Chemical formula	$[M-H]^-$	1	Negative
495.348	C32H48O4	Chemical formula	$[M-H]^-$	1	Negative
557.312	C32H46O8	Chemical formula	$[M-H]^-$	1	Negative
541.3171	C32H46O7	Chemical formula	$[M-H]^-$	1	Negative
525.3222	C32H46O6	Chemical formula	$[M-H]^-$	1	Negative
509.3273	C32H46O5	Chemical formula	$[M-H]^-$	1	Negative
493.3323	C32H46O4	Chemical formula	$[M-H]^-$	1	Negative
571.2913	C32H44O9	Chemical formula	$[M-H]^-$	1	Negative
555.2963	C32H44O8	Chemical formula	$[M-H]^-$	1	Negative
539.3014	C32H44O7	Chemical formula	$[M-H]^-$	1	Negative
569.2756	C32H42O9	Chemical formula	$[M-H]^-$	1	Negative
553.2807	C32H42O8	Chemical formula	$[M-H]^-$	1	Negative
537.2858	C32H42O7	Chemical formula	$[M-H]^-$	1	Negative
521.2909	C32H42O6	Chemical formula	$[M-H]^-$	1	Negative
551.265	C32H40O8	Chemical formula	$[M-H]^-$	1	Negative
535.2701	C32H40O7	Chemical formula	$[M-H]^-$	1	Negative
519.2752	C32H40O6	Chemical formula	$[M-H]^-$	1	Negative
599.2498	C32H40O11	Chemical formula	$[M-H]^-$	1	Negative
583.2549	C32H40O10	Chemical formula	$[M-H]^-$	1	Negative
549.2494	C32H38O8	Chemical formula	$[M-H]^-$	1	Negative
597.2341	C32H38O11	Chemical formula	$[M-H]^-$	1	Negative
581.2392	C32H38O10	Chemical formula	$[M-H]^-$	1	Negative
595.2185	C32H36O11	Chemical formula	$[M-H]^-$	1	Negative
579.2236	C32H36O10	Chemical formula	$[M-H]^-$	1	Negative
545.2181	C32H34O8	Chemical formula	$[M-H]^-$	1	Negative
593.2028	C32H34O11	Chemical formula	$[M-H]^-$	1	Negative
577.2079	C32H34O10	Chemical formula	$[M-H]^-$	1	Negative
469.3687	C31H50O3	Chemical formula	$[M-H]^-$	1	Negative
437.3789	C31H50O	Chemical formula	$[M-H]^-$	1	Negative
499.3429	C31H48O5	Chemical formula	$[M-H]^-$	1	Negative
483.348	C31H48O4	Chemical formula	$[M-H]^-$	1	Negative
513.3222	C31H46O6	Chemical formula	$[M-H]^-$	1	Negative
543.2963	C31H44O8	Chemical formula	$[M-H]^-$	1	Negative
495.3116	C31H44O5	Chemical formula	$[M-H]^-$	1	Negative

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Table S5. (continued)

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
575.2862	C31H44O10	Chemical formula	$[M-H]^-$	1	Negative
507.2752	C31H40O6	Chemical formula	$[M-H]^-$	1	Negative
521.2545	C31H38O7	Chemical formula	$[M-H]^-$	1	Negative
585.2341	C31H38O11	Chemical formula	$[M-H]^-$	1	Negative
569.2392	C31H38O10	Chemical formula	$[M-H]^-$	1	Negative
535.2337	C31H36O8	Chemical formula	$[M-H]^-$	1	Negative
581.2028	C31H34O11	Chemical formula	$[M-H]^-$	1	Negative
565.2079	C31H34O10	Chemical formula	$[M-H]^-$	1	Negative
579.1872	C31H32O11	Chemical formula	$[M-H]^-$	1	Negative
563.1923	C31H32O10	Chemical formula	$[M-H]^-$	1	Negative
609.1614	C31H30O13	Chemical formula	$[M-H]^-$	1	Negative
577.1715	C31H30O11	Chemical formula	$[M-H]^-$	1	Negative
561.1766	C31H30O10	Chemical formula	$[M-H]^-$	1	Negative
451.4521	C30H60O2	Chemical formula	$[M-H]^-$	1	Negative
473.3636	C30H50O4	Chemical formula	$[M-H]^-$	1	Negative
425.3789	C30H50O	Chemical formula	$[M-H]^-$	1	Negative
487.3429	C30H48O5	Chemical formula	$[M-H]^-$	1	Negative
471.348	C30H48O4	Chemical formula	$[M-H]^-$	1	Negative
455.3531	C30H48O3	Chemical formula	$[M-H]^-$	1	Negative
439.3582	C30H48O2	Chemical formula	$[M-H]^-$	1	Negative
423.3632	C30H48O	Chemical formula	$[M-H]^-$	1	Negative
485.3273	C30H46O5	Chemical formula	$[M-H]^-$	1	Negative
469.3323	C30H46O4	Chemical formula	$[M-H]^-$	1	Negative
453.3374	C30H46O3	Chemical formula	$[M-H]^-$	1	Negative
437.3425	C30H46O2	Chemical formula	$[M-H]^-$	1	Negative
547.2913	C30H44O9	Chemical formula	$[M-H]^-$	1	Negative
515.3014	C30H44O7	Chemical formula	$[M-H]^-$	1	Negative
499.3065	C30H44O6	Chemical formula	$[M-H]^-$	1	Negative
483.3116	C30H44O5	Chemical formula	$[M-H]^-$	1	Negative
467.3167	C30H44O4	Chemical formula	$[M-H]^-$	1	Negative
451.3218	C30H44O3	Chemical formula	$[M-H]^-$	1	Negative
529.2807	C30H42O8	Chemical formula	$[M-H]^-$	1	Negative
513.2858	C30H42O7	Chemical formula	$[M-H]^-$	1	Negative
497.2909	C30H42O6	Chemical formula	$[M-H]^-$	1	Negative
481.296	C30H42O5	Chemical formula	$[M-H]^-$	1	Negative
465.301	C30H42O4	Chemical formula	$[M-H]^-$	1	Negative
527.265	C30H40O8	Chemical formula	$[M-H]^-$	1	Negative
511.2701	C30H40O7	Chemical formula	$[M-H]^-$	1	Negative
495.2752	C30H40O6	Chemical formula	$[M-H]^-$	1	Negative
479.2803	C30H40O5	Chemical formula	$[M-H]^-$	1	Negative
463.2854	C30H40O4	Chemical formula	$[M-H]^-$	1	Negative
492.2756	C30H39NO5	Chemical formula	$[M-H]^-$	1	Negative
509.2545	C30H38O7	Chemical formula	$[M-H]^-$	1	Negative
493.2596	C30H38O6	Chemical formula	$[M-H]^-$	1	Negative
477.2647	C30H38O5	Chemical formula	$[M-H]^-$	1	Negative
573.2341	C30H38O11	Chemical formula	$[M-H]^-$	1	Negative
557.2392	C30H38O10	Chemical formula	$[M-H]^-$	1	Negative
507.2388	C30H36O7	Chemical formula	$[M-H]^-$	1	Negative
491.2439	C30H36O6	Chemical formula	$[M-H]^-$	1	Negative
587.2134	C30H36O12	Chemical formula	$[M-H]^-$	1	Negative
571.2185	C30H36O11	Chemical formula	$[M-H]^-$	1	Negative
555.2236	C30H36O10	Chemical formula	$[M-H]^-$	1	Negative
505.2232	C30H34O7	Chemical formula	$[M-H]^-$	1	Negative
489.2283	C30H34O6	Chemical formula	$[M-H]^-$	1	Negative
569.2028	C30H34O11	Chemical formula	$[M-H]^-$	1	Negative
535.1974	C30H32O9	Chemical formula	$[M-H]^-$	1	Negative
519.2024	C30H32O8	Chemical formula	$[M-H]^-$	1	Negative
413.3789	C29H50O	Chemical formula	$[M-H]^-$	1	Negative
441.3374	C29H46O3	Chemical formula	$[M-H]^-$	1	Negative
455.3167	C29H44O4	Chemical formula	$[M-H]^-$	1	Negative

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Table S5. (continued)

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
533.2756	C29H42O9	Chemical formula	$[M-H]^-$	1	Negative
501.2858	C29H42O7	Chemical formula	$[M-H]^-$	1	Negative
531.26	C29H40O9	Chemical formula	$[M-H]^-$	1	Negative
515.265	C29H40O8	Chemical formula	$[M-H]^-$	1	Negative
499.2701	C29H40O7	Chemical formula	$[M-H]^-$	1	Negative
483.2752	C29H40O6	Chemical formula	$[M-H]^-$	1	Negative
529.2443	C29H38O9	Chemical formula	$[M-H]^-$	1	Negative
543.2236	C29H36O10	Chemical formula	$[M-H]^-$	1	Negative
557.2028	C29H34O11	Chemical formula	$[M-H]^-$	1	Negative
587.177	C29H32O13	Chemical formula	$[M-H]^-$	1	Negative
555.1872	C29H32O11	Chemical formula	$[M-H]^-$	1	Negative
539.1923	C29H32O10	Chemical formula	$[M-H]^-$	1	Negative
521.1817	C29H30O9	Chemical formula	$[M-H]^-$	1	Negative
505.1868	C29H30O8	Chemical formula	$[M-H]^-$	1	Negative
537.1766	C29H30O10	Chemical formula	$[M-H]^-$	1	Negative
519.1661	C29H28O9	Chemical formula	$[M-H]^-$	1	Negative
503.1711	C29H28O8	Chemical formula	$[M-H]^-$	1	Negative
535.161	C29H28O10	Chemical formula	$[M-H]^-$	1	Negative
455.2803	C28H40O5	Chemical formula	$[M-H]^-$	1	Negative
499.2337	C28H36O8	Chemical formula	$[M-H]^-$	1	Negative
547.2185	C28H36O11	Chemical formula	$[M-H]^-$	1	Negative
531.2236	C28H36O10	Chemical formula	$[M-H]^-$	1	Negative
513.213	C28H34O9	Chemical formula	$[M-H]^-$	1	Negative
497.2181	C28H34O8	Chemical formula	$[M-H]^-$	1	Negative
529.2079	C28H34O10	Chemical formula	$[M-H]^-$	1	Negative
509.1817	C28H30O9	Chemical formula	$[M-H]^-$	1	Negative
487.1398	C28H24O8	Chemical formula	$[M-H]^-$	1	Negative
427.2854	C27H40O4	Chemical formula	$[M-H]^-$	1	Negative
485.2181	C27H34O8	Chemical formula	$[M-H]^-$	1	Negative
499.1974	C27H32O9	Chemical formula	$[M-H]^-$	1	Negative
483.2024	C27H32O8	Chemical formula	$[M-H]^-$	1	Negative
467.2075	C27H32O7	Chemical formula	$[M-H]^-$	1	Negative
531.1872	C27H32O11	Chemical formula	$[M-H]^-$	1	Negative
515.1923	C27H32O10	Chemical formula	$[M-H]^-$	1	Negative
497.1817	C27H30O9	Chemical formula	$[M-H]^-$	1	Negative
481.1868	C27H30O8	Chemical formula	$[M-H]^-$	1	Negative
513.1766	C27H30O10	Chemical formula	$[M-H]^-$	1	Negative
495.1661	C27H28O9	Chemical formula	$[M-H]^-$	1	Negative
539.2134	C26H36O12	Chemical formula	$[M-H]^-$	1	Negative
471.2024	C26H32O8	Chemical formula	$[M-H]^-$	1	Negative
519.1872	C26H32O11	Chemical formula	$[M-H]^-$	1	Negative
469.1868	C26H30O8	Chemical formula	$[M-H]^-$	1	Negative
531.1508	C26H28O12	Chemical formula	$[M-H]^-$	1	Negative
475.1974	C25H32O9	Chemical formula	$[M-H]^-$	1	Negative
427.2126	C25H32O6	Chemical formula	$[M-H]^-$	1	Negative
491.1923	C25H32O10	Chemical formula	$[M-H]^-$	1	Negative
473.1817	C25H30O9	Chemical formula	$[M-H]^-$	1	Negative
457.1868	C25H30O8	Chemical formula	$[M-H]^-$	1	Negative
471.1661	C25H28O9	Chemical formula	$[M-H]^-$	1	Negative
455.1711	C25H28O8	Chemical formula	$[M-H]^-$	1	Negative
431.2075	C24H32O7	Chemical formula	$[M-H]^-$	1	Negative
415.2126	C24H32O6	Chemical formula	$[M-H]^-$	1	Negative
445.1868	C24H30O8	Chemical formula	$[M-H]^-$	1	Negative
429.1919	C24H30O7	Chemical formula	$[M-H]^-$	1	Negative
413.197	C24H30O6	Chemical formula	$[M-H]^-$	1	Negative
459.1661	C24H28O9	Chemical formula	$[M-H]^-$	1	Negative
443.1711	C24H28O8	Chemical formula	$[M-H]^-$	1	Negative
475.161	C24H28O10	Chemical formula	$[M-H]^-$	1	Negative
441.1555	C24H26O8	Chemical formula	$[M-H]^-$	1	Negative
357.2435	C23H34O3	Chemical formula	$[M-H]^-$	1	Negative

(continued on next page)

Table S5. (continued)

Mass [m/z]	Formula [M]	Formula type	Species	CS [z]	Polarity
417.1919	C23H30O7	Chemical formula	$[M-H]^-$	1	Negative
401.197	C23H30O6	Chemical formula	$[M-H]^-$	1	Negative
431.1711	C23H28O8	Chemical formula	$[M-H]^-$	1	Negative
415.1762	C23H28O7	Chemical formula	$[M-H]^-$	1	Negative
399.1813	C23H28O6	Chemical formula	$[M-H]^-$	1	Negative
413.1606	C23H26O7	Chemical formula	$[M-H]^-$	1	Negative
343.2279	C22H32O3	Chemical formula	$[M-H]^-$	1	Negative
405.1919	C22H30O7	Chemical formula	$[M-H]^-$	1	Negative
387.1813	C22H28O6	Chemical formula	$[M-H]^-$	1	Negative
371.1864	C22H28O5	Chemical formula	$[M-H]^-$	1	Negative
401.1606	C22H26O7	Chemical formula	$[M-H]^-$	1	Negative
385.1657	C22H26O6	Chemical formula	$[M-H]^-$	1	Negative
415.1398	C22H24O8	Chemical formula	$[M-H]^-$	1	Negative
399.1449	C22H24O7	Chemical formula	$[M-H]^-$	1	Negative
383.15	C22H24O6	Chemical formula	$[M-H]^-$	1	Negative
429.1191	C22H22O9	Chemical formula	$[M-H]^-$	1	Negative
413.1242	C22H22O8	Chemical formula	$[M-H]^-$	1	Negative
397.1293	C22H22O7	Chemical formula	$[M-H]^-$	1	Negative
491.0831	C22H20O13	Chemical formula	$[M-H]^-$	1	Negative
357.1708	C21H26O5	Chemical formula	$[M-H]^-$	1	Negative
401.1242	C21H22O8	Chemical formula	$[M-H]^-$	1	Negative
337.2384	C20H34O4	Chemical formula	$[M-H]^-$	1	Negative
329.1758	C20H26O4	Chemical formula	$[M-H]^-$	1	Negative
343.1551	C20H24O5	Chemical formula	$[M-H]^-$	1	Negative
327.1602	C20H24O4	Chemical formula	$[M-H]^-$	1	Negative
357.1344	C20H22O6	Chemical formula	$[M-H]^-$	1	Negative
339.1238	C20H20O5	Chemical formula	$[M-H]^-$	1	Negative
369.098	C20H18O7	Chemical formula	$[M-H]^-$	1	Negative
367.0823	C20H16O7	Chemical formula	$[M-H]^-$	1	Negative
217.1962	C16H26	Chemical formula	$[M-H]^-$	1	Negative
239.2017	C15H28O2	Chemical formula	$[M-H]^-$	1	Negative
237.186	C15H26O2	Chemical formula	$[M-H]^-$	1	Negative
221.1911	C15H26O	Chemical formula	$[M-H]^-$	1	Negative
251.1653	C15H24O3	Chemical formula	$[M-H]^-$	1	Negative
219.1754	C15H24O	Chemical formula	$[M-H]^-$	1	Negative
203.1805	C15H24	Chemical formula	$[M-H]^-$	1	Negative
265.1445	C15H22O4	Chemical formula	$[M-H]^-$	1	Negative
249.1496	C15H22O3	Chemical formula	$[M-H]^-$	1	Negative
233.1547	C15H22O2	Chemical formula	$[M-H]^-$	1	Negative
289.0718	C15H14O6	Chemical formula	$[M-H]^-$	1	Negative
303.051	C15H12O7	Chemical formula	$[M-H]^-$	1	Negative
301.0354	C15H10O7	Chemical formula	$[M-H]^-$	1	Negative
285.0405	C15H10O6	Chemical formula	$[M-H]^-$	1	Negative

Table S6. Characterization of the components in KHS by UHPLC-Q-Orbitrap HRMS.

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
1	0.58	$C_{12}H_{22}O_{11}$	-	341.1086	−0.9	341.1086(6), 179.0555(5), 119.0340(10), 101.0231(14), 89.0232(51), 71.0126(54), 59.0127(100)	Trehalose	MassBank
2	0.58	$C_6H_{12}O_6$	-	179.0553	−4.5	179.0562(2), 161.0453(1), 113.0233(6), 101.0230(6), 89.0233(22), 71.0127(58), 59.0127(100)	Glucose	MassBank
3	0.63	$C_8H_8O_4$	-	167.0342	−4.8	167.0342(16), 152.0105(100), 124.0141(32), 108.0205(76), 96.9588(17)	5-Methoxysalicylic Acid isomer	MassBank
4	0.63	$C_{15}H_{14}O_6$	+	291.0863	0.0	291.0820(6), 165.0547(13), 139.0388(100), 123.0439(68)	Catechin isomer	mzCloud
5	0.64	$C_{15}H_{12}O_7$	+	305.0657	0.3	305.1592(67), 151.0388(100), 139.0389(67), 127.0389(48), 123.1164(30), 102.0912(51)	Taxifolin isomer	mzCloud
6	0.84	$C_8H_8O_4$	-	167.0343	−4.2	167.0341(15), 152.0105(100), 123.0440(11), 108.0205(82)	5-Methoxysalicylic Acid isomer	MassBank
7	1.02	$C_7H_6O_4$	-	153.0186	−4.6	153.0184(14), 110.0318(5), 109.0283(100), 108.0204(10)	Gentisic acid	MassBank
8	1.12	$C_{15}H_{14}O_6$	+	291.0859	−1.4	291.0866(7), 165.0544(13), 139.0388(100), 123.0439(65)	Catechin isomer	mzCloud
9	2.26	$C_9H_{10}O_3$	-	165.0550	−4.2	165.0545(9), 164.8946(11), 121.0284(18), 96.9588(20), 78.9577(6), 59.0127(100)	3-Ethoxybenzoic acid	mzCloud
10	2.26	$C_{10}H_{18}O_5$	-	217.1077	−1.8	217.1075(15), 155.1069(22), 143.0703(100), 125.0597(31), 97.0647(17), 73.0823(47)	Diethylene glycol diglycidyl ether isomer	ChemSpider
11	2.41	$C_8H_{14}O_4$	-	173.0812	−4.0	173.0810(26), 128.8769(31), 111.0804(100), 83.0491(24), 61.9871(14)	Suberic acid	MassBank
12	2.57	$C_{25}H_{32}O_{10}$	+	493.2044	−4.9	341.1361(98), 311.1272(54), 279.1018(48), 219.1008(100), 137.0599(42)	Schizandriside	Standard
13	2.58	$C_{26}H_{34}O_{12}$	-	537.1975	−0.4	511.0048(6), 491.1945(27), 359.1492(68), 344.1263(43), 341.1385(12), 313.1090(17), 299.0915(11), 295.0998(15), 241.0500(18), 173.0597(24), 159.0444(27), 129.9748(21), 109.0283(66)	Diosbulbinoside F isomer	ChemSpider
14	2.94	$C_{22}H_{24}O_6$	+	385.1642	−1.0	385.0903(18), 311.1260(20), 207.1014(40), 189.0908(48), 180.0063(10), 175.0755(33), 161.0594(100), 137.0599(14)	Schizandrin C isomer	in-house database
15	3.31	$C_{15}H_{24}O$	+	221.1900	0.0	221.1897(83), 203.1792(95), 161.1323(22), 147.1166(100), 133.1010(20), 123.1166(21), 121.1010(43), 119.0854(51), 109.1011(29), 107.0854(40), 105.0697(61), 95.0854(31), 81.0697(27)	(−)-Caryophyllene oxide isomer	mzCloud
16	3.33	$C_{20}H_{24}O_5$	+	345.1692	−1.4	253.8806(10), 236.9070(13), 226.8927(17), 201.0659(24), 177.0903(59), 163.0752(40), 137.0599(62), 90.9766(100)	Kadsurindutin E isomer	in-house database

17	3.38	$C_{10}H_{10}O_3$	+	179.0703	0.0	179.0704(30), 178.1587(100), 161.0596(26), 147.0439(49), 133.0646(11), 119.0491(31), 91.0541(17)	4-methyoxycinnamic acid isomer	MassBank
18	3.56	$C_9H_{16}O_4$	-	187.0969	−3.7	187.0969(32), 125.0960(100), 97.0647(20)	Azelaic acid	MassBank
19	3.59	$C_{15}H_{12}O_6$	-	287.0561	0.0	287.0568(10), 259.0605(18), 243.0322(32), 195.0111(13), 179.1673(10), 177.0547(15), 151.0027(14), 125.0233(100)	Maesopsin	mzCloud
20	3.70	$C_{20}H_{24}O_5$	+	345.1694	−0.9	304.8900(12), 236.9052(25), 226.8929(23), 177.0905(100), 163.0754(45), 137.0596(58), 90.9765(98)	Kadsurindutin E isomer	in-house database
21	3.72	$C_{25}H_{32}O_{10}$	+	515.1882	−1.2	515.1882 (100)	Schizandriside isomer	in-house database
22	3.73	$C_{26}H_{34}O_{12}$	-	537.1973	−0.8	419.5065(7), 326.1162(37), 311.0923(60), 283.0968(30), 129.9747(37), 112.9844(19), 89.0232(22), 61.9871(100)	Diosbulbinoside F isomer	ChemSpider
23	3.86	$C_{15}H_{26}O_2$	+	239.2005	−0.4	239.1999(46), 221.1894(56), 203.1796(100), 174.9639(57), 147.1169(58), 133.1012(36), 119.0854(45), 109.1012(41), 107.0853(49), 95.0853(71), 81.0699(62)	Oplodiol isomer	DPI
24	3.96	$C_{30}H_{48}O_2$	+	441.3723	−0.9	441.3719(100), 423.3612(21), 405.3519(8), 221.1901(9), 203.1790(21), 161.1322(14), 147.1167(21), 133.1010(24), 121.1010(27), 95.0854(50)	Kadsuracoccinic acid B isomer	in-house database
25	4.02	$C_{15}H_{20}O_4$	-	263.1286	−1.1	263.1288(59), 219.1385(61), 204.1146(100), 203.1069(78), 189.0901(25), 185.0963(17), 161.0963(16), 136.0519(32)	Abscisic acid isomer	MassBank
26	4.38	$C_{30}H_{48}O_2$	+	441.3720	−1.6	441.3721(100), 423.3619(22), 405.3514(8), 221.1891(8), 203.1792(21), 161.1322(13), 147.1167(18), 133.1010(20), 121.1010(22), 95.0854(45)	Kadsuracoccinic acid B isomer	in-house database
27	4.58	$C_{15}H_{20}O_4$	-	263.1287	−0.8	263.1291(37), 219.1387(96), 204.1148(63), 203.1063(50), 201.1277(74), 180.6831(67), 139.0750(33)	Abscisic acid isomer	MassBank
28	4.78	$C_{10}H_{18}O_4$	-	201.1127	−2.5	201.1125(58), 183.1014(41), 139.1118(100), 116.9272(45)	Sebacic acid	MassBank
29	4.79	$C_{20}H_{18}O_7$	+	371.1123	−0.5	371.1100(1), 233.0807(5), 215.0699(11), 157.0646(5), 151.0389(100), 129.0696(5)	6-hydroxyhinokinin isomer	DPI
30	4.94	$C_{30}H_{48}O_2$	+	441.3723	−0.9	441.3719(100), 423.3608(25), 405.3512(10), 221.1898(9), 203.1789(20), 161.1323(14), 147.1167(25), 133.1010(25), 121.1010(30), 95.0854(46)	Kadsuracoccinic acid B isomer	in-house database
31	4.95	$C_{15}H_{20}O_4$	+	267.1590	−0.4	267.1577(27), 231.1376(100), 203.1425(20), 191.1064(31), 175.1118(20), 90.9764(42)	Verrucarol isomer	MassBank
32	5.28	$C_{26}H_{28}O_{12}$	+	555.1465	−1.4	555.1458(100), 434.8627(5), 318.5458(6), 157.1312(5), 135.0438(15)	6-hydroxyhinokinin- 6-O- β-D-glucopyranoside isomer	DPI
33	5.50	$C_{26}H_{28}O_{12}$	+	555.1468	−0.9	555.1466(100), 392.0859(12), 257.0423(7), 173.0207(45), 107.0102(18)	6-hydroxyhinokinin- 6-O- β-D-glucopyranoside	Standard

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Table S6. (continued)

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
34	5.51	$C_{27}H_{40}O_{14}$	-	577.1558	−0.9	369.0974(48), 325.1077(32), 297.1125(12), 189.0548(11), 182.0213(10), 175.0757(18), 161.0597(17), 136.0152(19), 121.0284(100), 108.0252(35), 83.0126(88)	Vitexin-2″-O-rhamnoside isomer	MassBank
35	5.52	$C_{20}H_{18}O_7$	+	371.1120	−1.3	371.1100(2), 233.0811(3), 215.0701(10), 157.0647(5), 151.0389(100), 129.0697(5)	6-Hydroxyhinokinin isomer	DPI
36	5.66	$C_{28}H_{36}O_{11}$	+	549.2326	−0.7	489.2114(89), 471.2004(34), 453.1906(20), 435.1799(20), 417.1688(5), 137.0596(100), 123.0802(11), 109.0647(25)	Xuetongdilactone E isomer	in-house database
37	6.26	$C_{10}H_{10}O_3$	+	179.0702	−0.6	179.0705(24), 178.1587(100), 161.0595(46), 133.0647(31), 105.0698(15)	4-methyoxycinnamic acid isomer	MassBank
38	6.31	$C_{20}H_{20}O_5$	+	341.1382	−0.6	341.1365(11), 323.1272(41), 201.0911(17), 149.0600111), 135.0439 (100)	d-Epigalbacin isomer	DPI
39	6.38	$C_{30}H_{48}O$	+	425.3774	−0.9	425.3766(99), 407.3680(20), 217.1944(29), 203.1795(31), 161.1327(22), 147.1168(31), 135.1166(42), 133.1009(43), 123.1165(55), 119.0854(50), 109.1010(100), 95.0854(93)	Cycloartenone isomer	in-house database
40	6.42	$C_{15}H_{20}O_4$	-	263.1287	−0.8	263.1284(27), 219.1382(100), 165.7939(7), 136.0591(8), 73.0282(17)	Abscisic acid isomer	MassBank
41	6.44	$C_{30}H_{48}O_2$	+	441.3721	−1.4	441.3717(100), 423.3622(28), 405.3532(10), 221.1890(5), 203.1796(20), 161.1323(11), 147.1167(17), 133.1007(18), 121.1013(21), 95.0854(40)	Kadsuracoccinic acid B isomer	in-house database
42	6.67	$C_{30}H_{48}O$	+	425.3772	−1.4	425.3789(100), 343.1303(26), 179.0788(28), 147.1165(42), 135.1168(34), 133.1006(22), 123.1164(24), 119.0862(23), 109.1012(97), 95.0856(43)	Cycloartenone isomer	in-house database
43	6.74	$C_{30}H_{48}O_2$	+	441.3723	−0.9	441.3723(100), 423.3629(21), 405.3539(8), 203.1790(15), 161.1322(12), 147.1170(13), 133.1009(25), 121.1012(17), 95.0854(39)	Kadsuracoccinic acid B isomer	in-house database
44	6.89	$C_{30}H_{48}O_2$	+	441.3723	−0.9	441.3722(100), 423.3622(26), 405.3511(11), 221.1895(9), 203.1793(19), 161.1322(13), 147.1167(16), 133.1012(22), 121.1011(25), 95.0854(37)	Kadsuracoccinic acid B isomer	in-house database
45	7.03	$C_{15}H_{24}O$	+	221.1898	−0.9	221.1897(49), 203.1792(100), 161.1322(11), 147.1167(35), 133.1010(15), 121.1011(15), 119.0854(18), 109.1011(18), 107.0854(39), 105.0698(21), 95.0854(44), 81.0698(22)	(−)-Caryophyllene oxide isomer	mzCloud
46	7.06	$C_{30}H_{48}O$	+	425.3771	−1.6	425.3763(100), 407.3664(25), 217.1949(27), 175.1481(12), 161.1323(25), 147.1167(34), 135.1167(35), 133.1010(30), 123.1167(37), 119.0854(37), 109.1011(86), 95.0854(86)	Cycloartenone isomer	in-house database

47	7.14	$C_{30}H_{46}O_2$	+	439.3565	−1.4	439.3567(39), 393.3513(5), 249.1845(20), 205.1947(27), 203.1792(100), 191.1790(72), 189.1634(41), 147.1167(28), 133.1011(40), 119.0855(41), 95.0854(56)	Heilaohu acid A isomer	in-house database
48	7.34	$C_{20}H_{16}O_7$	+	369.0967	−0.5	369.0966(8), 351.0857(100), 321.0754(29), 293.0803(19), 235.0750(19), 203.0335(94), 175.0386(39), 161.0594(40), 135.0438(64), 131.0490(58)	Coumarinlignan	DPI
49	7.63	$C_{15}H_{24}O$	+	221.1900	0.0	221.1899(66), 203.1792(100), 161.1324(17), 147.1167(91), 133.1012(23), 121.1011(23), 119.0854(39), 109.1011(36), 107.0854(36), 105.0698(40), 95.0854(38), 81.0697(22)	(−)-Caryophyllene oxide isomer	mzCloud
50	7.67	$C_{22}H_{24}O_6$	+	385.1642	−1.0	367.1532(34), 233.1170(46), 218.0938(64), 203.0703(26), 181.0856(33), 166.0625(14), 135.0439(100)	Schizandrin C	in-house database
51	7.74	$C_{20}H_{20}O_5$	+	341.1383	−0.3	341.1373(29), 323.1283(9), 161.0598(20), 149.0600(11), 135.0439(100)	d-Epigalbacin isomer	DPI
52	7.78	$C_{20}H_{16}O_7$	+	369.0966	−0.8	351.0865(10), 231.0651(35), 203.0334(15), 187.0751(72), 175.0390(13), 161.0594(13), 157.0647(62), 135.0439(49), 131.0489(22), 129.0697(100)	Coumarinlignan isomer	DPI
53	7.88	$C_{15}H_{24}O$	+	221.1900	0.0	221.1897(88), 203.1792(100), 161.1322(21), 147.1167(54), 133.1010(25), 123.1166(32), 121.1012(22), 119.0854(37), 109.1011(88), 107.0854(37), 105.0698(45), 95.0854(40), 81.0698(59)	(−)-Caryophyllene oxide isomer	mzCloud
54	7.91	$C_{20}H_{18}O_7$	+	371.1123	−0.5	371.1109(2), 233.0807(4), 215.0700(9), 157.0648(5), 151.0389(100), 129.0697(5)	6-hydroxyhinokinin	Reference [9]
55	7.95	$C_{15}H_{28}O_2$	+	263.1979	−1.1	263.1985(100), 205.1959(17), 197.9750(17), 101.9496(15)	Cryptomeridiol	in-house database
56	7.99	$C_{15}H_{24}$	+	205.1950	−0.5	205.1949(16), 149.1325(14), 135.1167(50), 123.1167(100), 121.1011(4), 109.1012(14), 107.0855(13)	Isocaryophyllene isomer	ChemSpider
57	7.99	$C_{10}H_{14}$	+	135.1167	−0.7	135.1168(66), 107.0855(100), 93.0699(99), 91.0542(28),79.0542(39)	Cymol isomer	ChemSpider
58	8.00	$C_{32}H_{44}O_7$	+	563.2974	−0.9	563.2975(100), 521.2543(5), 503.2778(46), 459.2842(11), 181.1255(9)	Heteroclitalactone M isomer	DPI
59	8.23	$C_{10}H_{16}$	+	137.1325	0.0	137.1323(27), 95.0854(80), 81.0698(100)	Sabinene isomer	MassBank
60	8.28	$C_{30}H_{38}O_6$	+	495.2733	−1.6	477.2634(78), 459.2529(39), 323.1999(50), 263.1424(19), 155.0699(28), 109.0648(100), 95.0854(15)	Kadheterilactone A isomer	in-house database
61	8.28	$C_{30}H_{48}O$	+	425.3771	−1.6	425.3774(93), 407.3668(32), 217.1950(22), 189.1640(27), 161.1323(24), 147.1165(31), 135.1167(35), 133.1010(26), 123.1167(44), 119.0852(39), 109.1011(100), 95.0854(85)	Cycloartenone isomer	in-house database

(continued on next page)

Table S6. (continued)

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
62	8.48	$C_{15}H_{26}O_2$	+	239.2004	−0.8	239.1996(67), 221.1901(93), 203.1795(80), 179.6898(49), 133.1012(65), 121.1013(48), 116.9716(100), 107.0856(71), 95.0855(49), 81.0697(73)	Oplodiol isomer	DPI
63	8.57	$C_{15}H_{24}$	+	205.1951	0.0	205.1954(16), 149.1325(14), 135.1167(51), 123.1167(100), 121.1010(8), 109.1011(15), 107.0854(19)	Isocaryophyllene isomer	ChemSpider
64	8.57	$C_{15}H_{24}O$	+	221.1900	0.0	221.1897(93), 203.1792(100), 161.1323(28), 147.1167(48), 133.1010(22), 121.1010(21), 119.0855(27), 109.1012(32), 107.0854(51), 105.0698(33), 95.0854(47), 81.0698(27)	(−)-Caryophyllene oxide isomer	mzCloud
65	8.59	$C_{22}H_{32}O_3$	+	345.2423	−0.3	345.2420(70), 327.2314(100), 309.2208(27), 203.1429(41), 185.1322(40), 159.1166(39), 133.1010(32),119.0854(41), 111.0803(44), 93.0698(43)	Micranoic acid B	DPI
66	8.60	$C_{22}H_{34}O_4$	-	361.2383	−0.3	361.2381(100), 303.1971(10), 135.0807(7), 57.0334(35)	7(S),17(S)-Dihydroxy-8(E),10(Z),13(Z),15(E),19(Z)-docosapentaenoic acid isomer	mzCloud
67	8.63	$C_{24}H_{32}O_7$	+	433.2217	−0.9	415.2109(100), 384.1926(81), 373.1638(14), 369.1692(34), 346.1405(29), 338.1508(26), 331.1168(18), 315.1226(15)	Schizandrin isomer	in-house database
68	8.72	$C_{15}H_{24}$	+	205.1950	−0.5	205.1954(20), 149.1323(26), 135.1166(60), 123.1166(100), 121.1011(24), 109.1011(24), 107.0853(28), 81.0698(39)	Isocaryophyllene isomer	ChemSpider
69	9.04	$C_{35}H_{44}O_{12}$	+	679.2715	−1.5	679.2726(100), 579.2152(13), 519.1968(44), 475.2062(23)	Xuetongdilactone D/Wuweizidilactone B	in-house database
70	9.20	$C_{30}H_{38}O_6$	+	495.2735	−1.2	495.2728(93), 477.2625(100), 459.2519(60), 441.2426(49), 323.2002(57), 159.1167(64), 143.0854(61)	Kadheterilactone A	in-house database
71	9.21	$C_{32}H_{42}O_8$	+	555.2946	−1.1	495.2702(32), 477.2621(95), 459.2524(93), 441.2430(34), 325.2159(67), 323.2011(41), 305.1887(36), 241.1946(66), 221.0944(24), 183.1167(33), 181.1009(40), 171.1167(45), 169.1013(53), 157.1011(61), 143.0857(63), 131.0855(53), 109.0285(100), 105.0699(80)	Longipedlactone M isomer	in-house database
72	9.24	$C_{35}H_{44}O_{12}$	+	679.2717	−1.2	679.2727(100), 579.2173(11), 519.1973(19), 475.2080(5)	Xuetongdilactone D/Wuweizidilactone B	in-house database
73	9.31	$C_{30}H_{38}O_7$	+	511.2687	−0.6	511.2719(100), 427.2479(54), 367.2277(37), 323.2020(31), 155.0851(30), 143.0854(37), 105.0700(34)	Kadlongilactone F	in-house database
74	9.31	$C_{32}H_{42}O_9$	+	571.2894	−1.4	511.2676(100), 427.2473(58), 369.2267(34), 324.2089(24), 323.2002(25), 281.1531(19), 263.1424(18), 235.1480(20), 221.1330(16), 197.0963(28), 183.1173(22), 157.1014(33), 143.0857(36), 105.0700(34)	Longipedlactone P	in-house database

75	9.43	$C_{15}H_{24}O_2$	+	237.1848	−0.4	237.1847(53), 219.1742(58), 201.1638(52), 161.1323(100), 159.1168(47), 133.1010(32), 121.1011(47), 119.0855(81), 109.1012(56), 105.0698(54), 95.0854(54)	10α-hydroxyamorphan-4-en-3-one	Reference [43]
76	9.56	$C_{32}H_{40}O_7$	+	537.2844	−0.6	537.4486(100), 537.2829(7), 519.2731(5), 477.2634(36), 323.1999(19), 261.1272(11), 249.1268(11), 225.0899(10), 155.0703(11), 109.0648(32)	Heteroclitalactone E isomer	DPI
77	9.56	$C_{32}H_{44}O_7$	+	563.2977	−0.4	563.2972(100), 503.2758(48), 459.2781(13), 178.7752(4), 144.0420(4)	Heteroclitalactone M isomer	DPI
78	9.70	$C_{30}H_{44}O_7$	+	517.3151	−1.7	499.3066(5), 439.2839(100), 421.2724(15), 119.0858(9), 95.0854(12)	Kadcoccilactone C	in-house database
79	9.86	$C_{30}H_{42}O_4$	+	467.3152	−0.9	467.3135(62), 449.3027(41), 431.2929(36), 407.2546(42), 385.1780(68), 247.1691(38), 233.1528(34), 159.1167(40), 145.1009(42), 133.1009(75), 119.0854(61), 107.0854(48), 95.0855(100)	Schisanlactone B isomer	DPI
80	9.95	$C_{30}H_{42}O_5$	+	483.3099	−1.2	483.3092(59), 465.2993(100), 447.2880(53), 429.2783(28), 325.2177(28), 307.2068(20), 247.1682(16), 159.1166(59), 133.1012(45), 119.0855(64), 107.0855(64), 95.0855(89)	Kadsulactone A	DPI
81	10.02	$C_{30}H_{44}O_7$	+	539.2999	3.7	479.2784(12), 461.2686(25), 325.2162(35), 241.1945(35), 155.0702(40), 109.0647(100)	Kadcoccilactone A	in-house database, ClogP
82	10.02	$C_{32}H_{42}O_7$	+	539.2999	−0.7	479.2794(12), 461.2686(25), 443.2573(9), 425.2474(6), 325.2162(35), 307.2058(9), 241.1945(35), 199.1479(11), 195.1171(11), 171.1168(14), 157.1011(21), 143.0855(13), 137.0598(15), 109.0647(100)	Heteroclitalactone L isomer	in-house database
83	10.12	$C_{32}H_{40}O_7$	+	537.2843	−0.7	477.2632(100), 303.1735(5), 261.1189(18), 249.1269(6), 225.0909(5), 109.0648(27)	Heteroclitalactone E isomer	DPI
84	10.18	$C_{32}H_{44}O_7$	+	563.2973	−1.1	563.2970(100), 503.2759(75), 459.2853(8)	Heteroclitalactone M isomer	DPI
85	10.20	$C_{30}H_{38}O_7$	+	511.2686	−0.8	511.2697(100), 427.2454(28), 367.2263(45), 169.1006(70), 157.1009(35), 145.1013(45), 105.0697(45)	kadcoccilactone N	in-house database
86	10.20	$C_{30}H_{40}O_5$	+	481.2944	−1.0	481.2979(34), 463.2833(100), 445.2734(36), 307.2053(29), 159.1169(28), 133.1012(25), 119.0855(28)	Longipedlactone B isomer	in-house database
87	10.22	$C_{30}H_{38}O_4$	+	463.2836	−1.5	463.2840(100), 445.2737(39), 427.2631(36), 323.2002(23), 305.1894(14), 277.1580(20), 269.1532(28), 221.1322(45), 183.1170(10), 157.1009(18), 119.0858(11), 95.0854(29)	Lancilactone B	in-house database
88	10.29	$C_{32}H_{44}O_7$	+	563.2972	−1.2		Heteroclitalactone M	Standard
89	10.32	$C_{23}H_{28}O_6$	+	401.1954	−1.2	401.1954(100), 370.1784(44), 355.1532(19), 337.1424(30), 323.1281(21), 318.1093(25)	Kadsuranin isomer	in-house database
90	10.33	$C_{20}H_{20}O_5$	+	341.1381	−0.9	341.1379(13), 201.0908(47), 167.0701(100), 153.0546(56), 149.0232(20), 135.0438(25)	d-Epigalbacin isomer	DPI

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Table S6. (continued)

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
91	10.40	$C_{22}H_{24}O_6$	+	385.1627	−4.9	385.1615(59), 352.1631(83), 297.1850(32), 241.1232(27), 179.4693(23), 159.0414(100), 133.0643(77), 105.0698(20)	Schizandrin C isomer	in-house database
92	10.44	$C_{32}H_{40}O_7$	+	537.2842	−0.9	537.4486(100), 477.2623(31), 459.2520(34), 323.2006(12), 263.1433(11), 207.1127(12), 193.1014(11), 155.0854(15), 143.0854(19), 119.0855(16)	Heteroclitalactone E isomer	DPI
93	10.49	$C_{30}H_{42}O_5$	+	483.3101	−0.8	465.2993(100), 447.2885(13), 429.2767(7), 325.2158(18), 307.2044(4), 247.1682(16), 159.1170(9), 133.1009(11), 119.0855(18), 107.0854(18), 95.0854(23)	Kadsuphilactone B	in-house database
94	10.57	$C_{30}H_{48}O$	+	425.3773	−1.2	425.2679(100), 407.2575(23), 285.1847(33), 183.1167(13), 171.11670(26), 157.1011(23), 145.1011(15) 133.1010(11), 119.085(21), 109.1011(8), 95.0854(21)	Cycloartenone isomer	in-house database
95	10.64	$C_{30}H_{36}O_{11}$	+	595.2140	−1.7	554.2394(48), 431.2054(100), 356.1627(58)	Kadsurarin iosmer	in-house database
96	10.72	$C_{30}H_{38}O_5$	+	479.2789	−0.6	479.2784(47), 461.2669(37), 443.2583(20), 325.2151(36), 241.1946(44), 143.0850(27), 109.0647(100)	Longipedlactone A	in-house database
97	10.72	$C_{30}H_{44}O_7$	+	539.2999	3.7	479.2786(36), 461.2682(48), 325.2157(50), 241.1947(55), 157.1010(31), 109.0647(100)	Angustific acid B	in-house database, ClogP
98	10.72	$C_{32}H_{42}O_7$	+	539.2999	−0.7	479.2786(36), 461.2682(48), 443.2572(21), 425.2440(6), 325.2157(50), 307.2041(12), 241.1947(55), 229.1220(19), 197.1320(18), 171.1165(20), 157.1010(31), 143.0854(29), 137.0597(16), 109.0647(100)	Heteroclitalactone L isomer	in-house database
99	10.75	$C_{32}H_{40}O_7$	+	537.2842	−0.9	537.4481(19), 477.2630(100), 303.1736(5), 267.1375(11), 261.1270(19), 249.1273(7), 233.0959(9), 225.0908(5), 207.0802(10), 109.0647(19)	Heteroclitalactone E	Standard
100	10.78	$C_{20}H_{24}O_5$	+	345.1695	−0.6	345.1676(13), 223.1328(17), 205.1221(19), 191.1064(16), 175.1115(28), 153.0545(51), 135.0439(100)	Kadsurindutin E	DPI, Clog P
101	10.82	$C_{30}H_{48}O$	+	425.3771	−1.6	425.3775(100), 407.3680(25), 343.1305(64), 217.1944(27), 189.1639(34), 147.1166(34), 135.1167(33), 133.1013(38), 123.1167(49), 119.0857(47), 109.1012(96), 95.0854(83)	Cycloartenone isomer	in-house database
102	10.89	$C_{30}H_{44}O_5$	+	485.3254	−1.6	467.3148(30), 431.2980(14), 327.2306(20), 221.1532(21), 173.1330(26), 159.1173(33), 145.1011(34), 133.1011(34), 119.0855(37), 105.0698(100), 95.0855(83)	Kadcotrione C	in-house database, ClogP
103	10.91	$C_{30}H_{36}O_{11}$	+	595.2137	−2.2	535.1956(51), 371.1488(53), 105.0697(100)	Kadsurarin	Standard

104	11.09	$C_{30}H_{42}O_5$	+	483.3096	−1.9	483.3077(74), 465.3026(100), 447.2913(33), 429.2750(27), 211.1479(25), 159.1170(43), 145.1012(44), 133.1015(34), 119.0856(36), 107.0855(42), 95.0854(83)	Kadsuphilactone B isomer	in-house database
105	11.14	$C_{16}H_{30}O_4$	-	285.2069	−0.7	285.2070(40), 267.1960(43), 223.2062(100), 115.9196(8)	Hexadecanedioic acid	mzCloud
106	11.30	$C_{30}H_{40}O_6$	+	497.2894	−0.8	479.2782(30), 461.2670(20), 383.2577(27), 365.2481(22), 341.2467(24), 243.1743(20), 201.1634(51), 159.1167(47), 145.1011(54), 119.0855(54), 107.0854(76), 95.0854(100)	Longipedlactone C	in-house database, ClogP
107	11.36	$C_{32}H_{46}O_8$	+	581.3077	−1.4	581.3066(100), 521.2863(66), 477.2963(27), 375.2271(12), 105.0698(10)	Xuetongdilactone A isomer	in-house database
108	11.46	$C_{30}H_{44}O_4$	+	469.3311	−0.2	469.3289(31), 451.3191(29), 433.3083(27), 423.3232(13), 249.1855(12), 235.2696(12), 173.1324(23), 159.1167(59), 145.1011(64), 133.1010(100), 119.0854(73), 95.0854(89)	Schisanlactone E isomer	DPI
109	11.46	$C_{30}H_{44}O_5$	+	485.3256	−1.2	485.3241(17), 467.3164(19), 449.3043(37), 431.2949(17), 309.2210(7), 215.1428(13), 173.1322(27), 159.1167(44), 145.1012(36), 133.1012(36), 119.0855(56), 105.0698(62), 95.0855(100)	Kadcoccitone C	in-house database, ClogP
110	11.47	$C_{32}H_{46}O_8$	+	581.3077	−1.4	581.3073(100), 521.2861(62), 503.2753(35), 477.2980(7), 459.2855(23)	Xuetongdilactone A	in-house database
111	11.56	$C_{30}H_{40}O_6$	+	497.2894	−0.8	479.2789(25), 461.2679(13), 383.2584(20), 365.2494(14), 341.2451(15), 259.1681(14), 201.1630(20), 163.1480(52), 145.1012(41), 119.0854(43), 107.0854(86), 95.0854(100)	Longipedlactone C isomer	in-house database, ClogP
112	11.59	$C_{16}H_{30}O_2$	+	255.2316	−1.2	237.2206(43), 219.2104(58), 214.2528(54), 149.1324(30), 135.1170(35), 121.1011(34), 107.0853(46), 97.1011(58), 83.0854(90), 69.0699(100), 57.0702(99)	Palmitoleic acid	mzCloud
113	11.63	$C_{30}H_{38}O_4$	+	463.2838	−1.1	463.2833(92), 445.2730(100), 427.2626(25), 417.2801(20), 323.2001(40), 277.1588(11), 263.1430(20), 221.1315(18), 213.1270(2), 157.1011(33), 145.1010(32), 119.0855(35), 95.0854(59)	Lancilactone B isomer	in-house database
114	11.63	$C_{32}H_{42}O_6$	+	523.3048	−1.1	463.2824(47), 445.2731(100), 427.2646(23), 417.2766(26), 323.2017(18), 305.1895(27), 277.1570(13), 213.1271(25), 201.1274(17), 183.0808(28), 175.0750(23), 157.1016(23), 145.1013(34), 131.0853(27), 119.0853(30), 95.0855(45)	Heteroclitalactone D	Standard
115	11.66	$C_{15}H_{24}$	+	205.1949	−1.0	205.1948(66), 149.1324(50), 135.1166(30), 123.1166(22), 121.1010(100), 109.1011(35), 107.0854(35), 81.0698(50)	Isocaryophyllene isomer	ChemSpider

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Table S6. (continued)

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
116	11.73	$C_{30}H_{42}O_4$	+	467.3153	−0.6	467.3169(100), 449.3052(71), 421.3082(12), 327.2317(56), 309.2206(23), 247.1690(14), 159.1166(57), 145.1011(47), 133.1011(36), 119.0855(55), 107.0855(41), 95.0854(63)	Schisanlactone B isomer	DPI
117	11.79	$C_{15}H_{24}$	+	205.1950	−0.5	205.1948(100), 149.1325(67), 135.1167(62), 123.1166(29), 121.1011(77), 109.1012(72), 107.0854(62), 81.0698(27)	Isocaryophyllene isomer	ChemSpider
118	11.95	$C_{32}H_{40}O_6$	+	521.2891	−1.3	461.2695(62), 443.2576(100), 425.2468(28), 415.2617(11), 377.2476(21), 245.1331(13), 221.1321(15), 213.1275(17), 207.1171(13), 193.1010(15), 184.0728(56), 169.1009(16), 157.1016(30), 143.0855(35), 131.0855(26), 105.0607(34)	Heteroclitalactone G	in-house database
119	12.03	$C_{30}H_{40}O_4$	+	465.2996	−0.6	465.2994(40), 447.2887(100), 429.2887(36), 159.1169(27), 143.0857(28), 119.1013(36), 95.0851(44)	Angustific acid A	in-house database
120	12.03	$C_{30}H_{40}O_5$	+	481.2941	−1.7	481.2981(25), 463.2833(100), 445.2728(51), 427.2654(16), 133.1006(21), 119.0854(28)	longipedlactone B isomer	in-house database
121	12.04	$C_{30}H_{38}O_4$	+	463.2837	−1.3	463.2833(92), 445.2730(100), 427.2626(25), 417.2801(20), 323.2001(40), 277.1588(11), 263.1430(20), 221.1315(18), 213.1270(2), 157.1011(33), 145.1010(32), 119.0855(35), 95.0854(59)	Lancilactone B isomer	in-house database
122	12.09	$C_{14}H_{28}O_3$	-	243.1963	−1.2	243.1977(15), 225.1891(11), 181.8507(12), 179.7054(16), 146.9602(87), 118.9652(36), 116.9271(33), 59.0127(100)	(R)-3-Hydroxy myristic acid isomer	mzCloud
123	12.12	$C_{30}H_{46}O_5$	+	487.3412	−1.2	487.3464(20), 469.3325(41), 451.3224(52), 433.3086(38), 423.3255(14), 415.1154(9), 359.2771(55), 329.2471(65), 311.2364(36), 249.1838(16), 209.1159(58), 173.1326(31), 159.1166(38), 145.1010(36), 133.1010(60), 121.1011(74), 119.0854(63), 95.0854(100)	Kadcoccilactone R isomer	in-house database
124	12.13	$C_{32}H_{44}O_7$	+	563.2972	−1.2	563.2968(34), 503.2764(75), 459.2859(9), 105.0700(6)	Heteroclitalactone M isomer	DPI
125	12.17	$C_{32}H_{46}O_8$	+	581.3076	−1.5	581.3080(100), 537.3158(16), 521.2866(15), 503.2760(13), 477.2972(28), 445.2342(39), 105.0698(14)	Xuetongdilactone A isomer	in-house database
126	12.22	$C_{18}H_{30}O_3$	+	295.2265	−1.0	277.2158(59), 179.1427(100), 135.1166(35), 121.1010(27), 107.0854(31), 93.0698(51), 81.0698(46), 71.0855(49)	9-Oxo-10(E),12(E)-octadecadienoic acid isomer	mzCloud
127	12.23	$C_{15}H_{24}$	+	205.1949	−1.0	205.1949(21), 149.1324(25), 135.1167(8), 123.1166(5), 121.1011(100), 109.1011(11), 107.0854(14), 81.0698(38)	Isocaryophyllene isomer	ChemSpider
128	12.40	$C_{18}H_{30}O_3$	+	295.2265	−1.0	277.2157(100), 151.1116(36), 107.0853(20), 93.0698(31), 81.0698(39)	9-Oxo-10(E),12(E)-octadecadienoic acid	mzCloud

129	12.50	$C_{20}H_{20}O_5$	+	341.1378	−1.8	341.1377(12), 323.1273(3), 219.1013(23), 201.0905(9), 163.0752(52), 151.0389(26), 149.0232(16), 135.0439(100)	d-Epigalbacin	Standard
130	12.50	$C_{10}H_{10}O_2$	+	163.0752	−1.2	163.0751(100), 135.0439(30), 133.0646(41), 105.0698(70), 79.0541(9)	4-Methylcinnamic acid isomer	MassBank
131	12.50	$C_{13}H_{12}O_2$	+	201.0908	−1.0	201.0907(100), 186.0672(29), 171.0801(36), 143.0854(78), 128.0619(14)	3-Phenoxybenzylalcohol isomer	MassBank
132	12.50	$C_{20}H_{18}O_4$	+	323.1277	−0.3	323.1270(26), 201.0906(27), 149.0596(100), 135.0438(57), 119.0490(17), 91.0541(17)	{4-[(2E)-3-(4-Isopropylphenyl)-2-propenoyl] phenoxy} acetate	ChemSpider
133	12.52	$C_{33}H_{44}O_7$	-	551.2987	−4.9	487.2821(6), 385.2740(15), 116.9277(6), 97.0283(100), 69.0333(20)	Octahydromorellin isomer	ChemSpider
134	12.57	$C_{18}H_{30}O_3$	+	295.2265	−1.0	277.2159(100), 151.1117(21), 107.0854(22), 93.0699(30), 81.0698(37)	9-Oxo-10(E),12(E)-octadecadienoic acid isomer	mzCloud
135	12.58	$C_{27}H_{40}O_4$	+	429.2996	−0.7	429.3031(33), 411.2873(52), 393.2780(41), 147.1165(47), 133.1012(48), 121.1012(44), 119.0855(51), 107.0854(71), 95.0855(100)	Kadnanolactone E	DPI
136	12.58	$C_{30}H_{42}O_3$	+	451.3203	−0.9	451.3221(100), 433.3098(78), 415.2974(15), 231.1741(26), 201.1273(19), 159.1168(33), 133.1011(38), 119.0854(50), 95.0854(62)	Dysolenticin B isomer	ChemSpider
137	12.58	$C_{30}H_{46}O_5$	+	487.3417	−0.2	445.9855(34), 145.1013(39), 133.1012(45), 121.1012(65), 107.0855(80), 95.0854(100)	Kadcoccilactone R isomer	in-house database
138	12.58	$C_{30}H_{44}O_4$	+	469.3308	−0.9	469.3312(20), 451.3187(52), 433.3094(39), 311.2375(11), 217.1585(18), 173.1322(13), 159.1173(19), 145.1013(39), 133.1010(37), 119.0853(44), 95.0854(100)	Schisanlactone E isomer	DPI
139	12.61	$C_{30}H_{44}O_5$	+	485.3258	−0.8	485.3255(14), 467.3150(100), 449.3054(38), 431.2980(14), 327.2306(20), 221.1532(21), 173.1330(26), 159.1173(33), 145.1011(34), 133.1011(34), 119.0855(37), 105.0698(100), 95.0855(83)	Kadcotrione A isomer	in-house database, ClogP
140	12.73	$C_{14}H_{28}O_3$	-	243.1963	−1.2	243.1963(47), 197.1903(100), 146.9600(17)	(R)-3-Hydroxy myristic acid	mzCloud
141	12.78	$C_{30}H_{42}O_4$	+	467.3151	−1.1	467.3169(100), 449.3039(48), 421.3115(7), 327.2310(23), 309.2213(10), 247.1691(10), 157.1010(38), 145.1011(36), 133.1010(30), 119.0855(40), 107.0854(28), 95.0854(50)	Schisanlactone B isomer	DPI
142	12.82	$C_{24}H_{32}O_6$	+	417.2266	−1.4	417.2266(100), 347.1489(19), 316.1302(58), 301.1068(34), 285.1115(21), 242.0930(14)	Deoxyschizandrin isomer	in-house database
143	12.85	$C_{15}H_{24}$	+	205.1949	−1.0	205.1947(16), 149.1323(20), 135.1167(8), 123.1167(5), 121.1011(100), 109.1011(9), 107.0854(14), 81.0698(40)	Isocaryophyllene isomer	ChemSpider
144	12.85	$C_{10}H_{14}$	+	135.1167	−0.7	135.1166(100), 107.0853(175), 93.0698(74), 91.0540(14),79.0541(34)	Cymol isomer	MassBank
145	12.99	$C_{30}H_{44}O_5$	+	485.3249	−2.7	467.3163(14), 449.3040(30), 431.2943(22), 329.2473(34), 311.2370(9), 235.1696(14), 173.1325(16), 159.1170(36), 145.1012(32), 133.1010(39), 119.0853(64), 105.0696(57), 95.0854(100)	Kadcotrione A	in-house database, ClogP

(continued on next page)

Table S6. (continued)

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
146	13.08	$C_{30}H_{42}O_5$	+	483.3101	−0.8	483.3121(40), 465.3000(27), 447.2888(17), 429.2783(28), 357.1467(23), 247.1690(5), 159.1166(28), 133.1011(32), 119.0854(50), 107.0853(52), 95.0854(100)	Kadsuphilactone B isomer	in-house database
147	13.26	$C_{23}H_{28}O_6$	+	401.1954	−1.2	401.1952(100), 370.1761(8), 331.1169(20), 300.0988(61), 285.0755(26), 239.2367(18), 227.0695(17)	Kadsuranin isomer	in-house database
148	13.27	$C_{30}H_{40}O_3$	+	449.3045	−1.1	449.3044(100), 431.2941(91), 229.1585(52), 215.1430(47), 159.1167(50), 145.1011(57), 133.1010(48), 119.0854(59), 95.0854(72)	24-Cholanal, 3,12-dioxo-24-phenyl- isomer	PubChem
149	13.27	$C_{30}H_{42}O_4$	+	467.3153	−0.6	467.3150(21), 449.3043(79), 421.3083(14), 327.2315(8), 309.2210(9), 247.1697(9), 229.1431(43), 215.1429(35), 159.1166(44), 145.1010(54), 133.1010(54), 119.0855(60), 107.0854(61), 95.0855(100)	Schisanlactone B	Standard
150	13.40	$C_{23}H_{28}O_6$	+	401.1955	−1.0	401.1953(100), 370.1776(6), 331.1170(18), 300.0988(51), 285.0753(21), 227.0701(19)	Kadsuranin isomer	in-house database
151	13.42	$C_{33}H_{44}O_7$	-	551.2987	−4.9	551.2996(38), 505.2885(19), 483.3109(87), 179.8263(10), 116.9275(24)	Octahydromorellin isomer	ChemSpider
152	13.48	$C_{30}H_{40}O_4$	+	465.2996	−0.6	465.3001(100), 447.2890(54), 429.2890(25), 159.1163(27), 145.1212(28), 119.0854(55), 95.0854(53)	Schisanlactone A isomer	in-house database
153	13.72	$C_{30}H_{44}O_5$	+	485.3257	−1.0	485.3232(11), 467.3153(11), 449.3039(7), 431.2926(8), 223.1496(21), 173.1320(16), 159.1165(20), 145.1011(21), 133.1009(24), 119.0855(34), 105.0698(39), 83.0490(100)	Kadnanolactone B	in-house database, ClogP
154	13.77	$C_{30}H_{42}O_4$	+	467.3152	−0.9	467.3140(54), 449.3043(51), 421.3105(11), 327.2320(29), 309.2188(15), 247.1687(26), 229.1595(13), 215.1435(18), 159.1167(40), 145.1010(53), 133.1012(44), 119.0855(62), 107.0854(47), 95.0855(100)	Schisanlactone B isomer	DPI
155	13.78	$C_{33}H_{44}O_7$	-	551.2987	−4.9	483.3103(100), 439.3203(56), 187.7213(18), 180.1498(29), 115.9193(33)	Octahydromorellin isomer	ChemSpider
156	13.96	$C_{30}H_{48}O$	+	425.3773	−1.2	407.3636(58), 385.1791(53), 343.1298(58), 239.1495(45), 147.1169(32), 135.1167(63), 121.1012(67), 123.1168(37), 119.0854(31), 109.1011(56), 95.0855(100)	Cycloartenone isomer	in-house database
157	13.97	$C_{29}H_{52}O_9$	+	544.3627	3.9	467.3159(45), 449.3039(45), 431.2936(40), 327.2314(30), 247.1692(40), 173.1323(29), 159.1161(46), 145.1010(43), 133.1010(37), 119.0855(52), 109.1011(100),95.0854(73)	2-octoxy-3-[2-(oxolan-2-ylmethoxy) ethyl] undecane-1,2,3-tricarboxylic acid isomermethoxyethoxy) methyl]-L-erythro-hex-2-enonate isomer	in-house database
158	14.02	$C_{30}H_{38}O_2$	+	431.2940	−1.2	431.2931(100), 291.2101(13), 145.1011(10), 95.0854(12)	3-(3,4-Dihydro-2H-chromen-2-yl) pregna-3,5-dien-20-one isomer	ChemSpider

159	14.02	$C_{30}H_{40}O_3$	+	449.3044	−1.3	449.3048(100), 431.2944(26), 229.1587(18), 215.1429(20), 159.1168(23), 145.1013(18), 133.1010(20), 119.0857(28), 95.0855(30)	24-Cholanal, 3,12-dioxo-24-phenyl- isomer	PubChem
160	14.02	$C_{30}H_{42}O_4$	+	467.3152	−0.9	467.3156(100), 449.3052(94), 421.3089(12), 327.2313(29), 309.2188(15), 247.1693(24), 229.1592(73), 215.1426(21), 159.1163(62), 145.1015(64), 133.1012(56), 119.0854(62), 107.0853(67), 95.0854(90)	Schisanlactone B isomer	DPI
161	14.02	$C_{32}H_{46}O_6$	+	527.3365	−0.4	467.3141(37), 451.3459(24), 449.3018(35), 431.2934(28), 327.2319(38), 309.2213(17), 247.1682(22), 229.1588(15), 215.1433(11), 201.1274(19), 185.1321(21), 171.1167(33), 159.1165(48), 157.1008(42), 145.1011(41), 133.1010(44), 119.0854(61), 95.0855(100)	Heteroclitalactone A/Polysperlactone B	in-house database
162	14.07	$C_{30}H_{44}O_3$	+	453.3361	−0.4	453.3387(42), 435.3258(100), 417.3141(7), 413.3768(27), 371.1626(68), 295.2463(24), 159.1168(62), 133.1008(43), 119.0856(53), 95.0855(56)	Kadcoccine acid G	in-house database, ClogP
163	14.07	$C_{32}H_{48}O_5$	+	535.3391	−0.6	535.3392(5), 535.3401(89), 475.3181(100), 177.0545(12), 145.0284(5), 105.0700(7)	Heteroclic acid isomer	in-house database
164	14.08	$C_{30}H_{44}O_4$	+	469.3315	0.6	469.4248(100), 451.3221(4), 433.3069(3), 135.1167(8), 121.1010(12), 119.0857(5), 95.0855(25)	Schisanlactone E isomer	DPI
165	14.31	$C_{30}H_{46}O_4$	+	471.3465	−0.8	471.3458(22), 453.3352(21), 435.3252(20), 417.3147(7), 247.1693(14), 235.1689(21), 175.1478(14), 161.1322(35), 159.1168(17), 145.1011(20), 135.1167(28), 121.1011(72), 109.1011(47), 95.0854(100)	Kadpolysperin M	in-house database, ClogP
166	14.45	$C_{30}H_{46}O_5$	+	487.3413	−1.0	487.3601(99), 469.4253(100), 451.4112(8), 423.3229(6), 163.1480(11), 149.1325(14), 135.1165(21), 121.1012(33), 119.0857(10), 109.1011(35)	Kadcoccilactone R isomer	in-house database
167	14.51	$C_{30}H_{42}O_4$	-	465.3005	−1.1	465.3014(3), 325.1844(3), 183.0114(5), 116.9275(100), 99.9246(8)	Schisanlactone B isomer	DPI
168	14.54	$C_{30}H_{46}O_4$	+	471.3466	−0.6	471.3445(40), 453.3349(36), 435.3261(21), 417.3148(7), 247.1692(6), 235.1682(14), 175.1480(13), 161.1322(51), 159.1168(24), 145.1012(22), 135.1167(38), 121.1012(59), 109.1011(47), 95.0854(100)	Nigranoic acid isomer	in-house database, ClogP
169	14.54	$C_{30}H_{48}O_5$	+	489.3569	−1.2	489.2964(100), 471.3485(16), 453.3357(24), 435.3245(15), 425.3400(18), 401.3039(22), 235.1685(14), 189.1635(13), 161.1323(38), 159.1167(15), 147.1166(33), 133.1010(31), 121.1010(39), 95.0854(81)	Kadnanosic acid A	in-house database
170	14.60	$C_{30}H_{42}O_3$	+	451.3203	−0.9	451.3197(100), 433.3095(46), 201.1275(6), 159.1167(29), 133.1011(23), 119.0855(33), 95.0854(39)	Dysolenticin B isomer	ChemSpider

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Table S6. (continued)

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
171	14.60	$C_{30}H_{46}O_5$	+	487.3415	−0.6	487.3596(36), 469.3315(8), 451.3206(25), 433.3094(28), 329.2476(7), 311.2345(6), 249.1847(13), 215.1434(10), 173.1324(19), 159.1167(28), 145.1010(29), 133.1010(38), 121.1010(50), 119.0855(53), 95.0854(100)	Kadcoccilactone R isomer	in-house database
172	14.76	$C_{30}H_{46}O_4$	+	471.3465	−0.8	471.3459(78), 453.3348(31), 435.3241(23), 417.3140(7), 247.1684(15), 235.1689(22), 173.1321(23), 161.1324(30), 159.1168(34), 145.1010(39), 135.1166(29), 121.1011(61), 109.1011(57), 95.0854(100)	Nigranoic acid isomer	in-house database, ClogP
173	14.80	$C_{30}H_{38}O_2$	+	431.2938	−1.6	431.2937(100), 291.2092(13), 197.1320(19), 145.1012(14), 95.0854(13)	3-(3,4-Dihydro-2H-chromen-2-yl) pregna-3,5-dien-20-one isomer	ChemSpider
174	14.80	$C_{30}H_{40}O_3$	+	449.3043	−1.6	449.3041(100), 431.2935(63), 229.1584(46), 215.1427(80), 159.1166(31), 145.1010(48), 133.1010(48), 119.0854(46), 95.0854(71)	24-Cholanal, 3,12-dioxo-24-phenyl- isomer	PubChem
175	14.80	$C_{30}H_{42}O_4$	+	467.3153	−0.6	467.3149(100), 449.3044(65), 421.3105(9), 327.2313(36), 309.2215(22), 247.1693(17), 229.1583(7), 159.1168(52), 145.1011(44), 133.1010(40), 119.0855(57), 107.0854(54), 95.0855(91)	Schisanlactone B isomer	DPI
176	14.82	$C_{30}H_{42}O_3$	+	451.3198	−2.0	451.3193(100), 433.3092(73), 415.2971(11), 231.1744(20), 201.1273(19), 159.1170(25), 133.1010(41), 119.0855(46), 95.0854(64)	Dysolenticin B isomer	ChemSpider
177	14.82	$C_{30}H_{44}O_4$	+	469.3306	−1.3	469.3310(21), 451.3219(50), 433.3095(35), 423.3276(9), 415.2991(10), 329.2477(12), 311.2370(7), 249.1843(25), 235.1696(12), 219.1378(13), 173.1324(23), 159.1167(35), 145.1009(33), 133.1010(40), 119.0855(60), 95.0855(100)	Schisanlactone E	Standard
178	14.82	$C_{22}H_{32}O_2$	+	329.2469	−1.8	329.2470(100), 173.1321(14), 159.1166(15), 145.1010(15), 133.1011(18), 121.1011(21), 119.0854(22), 107.0854(28), 95.0854(35)	Docosahexaenoic acid	MassBank
179	14.83	$C_{31}H_{46}O_4$	+	483.3460	−1.9	483.3465(20), 465.3355(10), 451.3201(54), 433.3102(41), 247.1693(11), 215.1427(16), 201.1634(13), 173.1322(33), 159.1166(39), 145.1011(42), 133.1010(56), 121.1011(49), 95.0854(100)	Heteroclitalactone F isomer	DPI
180	14.83	$C_{31}H_{48}O_5$	+	501.3564	−2.2	469.3290(39), 451.3199(65), 433.3094(46), 423.3237(13), 415.2982(7), 329.2474(19), 261.1847(17), 249.1848(17), 235.1688(13), 219.1381(10), 173.1316(25), 159.1164(29), 145.1012(47), 133.1008(48), 119.0855(62), 95.0854(100)	Kadnanolactone D isomer	DPI

181	14.90	$C_{20}H_{38}O_2$	+	311.2943	−0.6	293.2838(34), 184.8882(24), 149.1326(26), 135.1167(32), 116.9720(41), 107.0855(35), 97.1010(48), 83.0854(63), 71.0855(82), 57.0701(100)	Ethyloleate	mzCloud
182	14.96	$C_{23}H_{32}O_2$	-	339.2327	−0.9	339.2323(8), 163.1119(100)	2,2′-Methylenebis (4-methyl-6-tert-butylphenol)	ChemSpider
183	14.97	$C_{20}H_{40}O_3$	-	327.2903	−0.6	327.2902(100), 281.0057(7), 185.0061(50), 183.0112(43)	L-2-Hydroxyphytanate isomer	ChemSpider
184	15.07	$C_{30}H_{40}O_4$	+	465.2996	−0.6	465.2986(100), 447.2884(78), 429.2782(48), 159.1167(35), 145.1010(34), 119.0855(74), 95.0854(74)	Schisanlactone A isomer	in-house database
185	15.07	$C_{30}H_{44}O_4$	+	469.3309	−0.6	469.3298(23), 451.3201(54), 433.3094(37), 423.3244(8), 329.2472(8), 311.2357(9), 249.1853(12), 235.1683(11), 219.1382(8), 173.1324(23), 159.1167(31), 145.1009(32), 133.1010(44), 119.0854(52), 95.0854(100)	Schisanlactone E isomer	DPI
186	15.28	$C_{30}H_{40}O_5$	+	481.2930	−3.9	481.3708(100), 481.3067(68), 277.1775(45), 119.0852(15)	Longipedlactone B	in-house database
187	15.30	$C_{30}H_{44}O_4$	+	469.3311	−0.2	469.3177(70), 451.3199(47), 433.3090(41), 423.3250(8), 329.2466(13), 311.2370(7), 249.1843(25), 235.1691(15), 219.1386(6), 173.1323(19), 159.1170(34), 145.1011(38), 133.1009(51), 119.0854(55), 95.0854(100)	Schisanlactone E isomer	DPI
188	15.30	$C_{32}H_{48}O_5$	+	513.3570	−1.0	513.3538(4), 453.3353(22), 435.3250(56), 417.3148(5), 407.3320(7), 313.2520(70), 233.1532(15), 227.1785(15), 219.1742(15), 201.1636(31), 199.1481(21), 173.1323(24), 161.1322(35), 159.1161(47), 145.1010(52), 133.1010(100), 119.0854(57), 105.0698(65)	Heteroclic acid isomer	in-house database
189	15.37	$C_{18}H_{32}O_2$	-	279.2327	−1.1	279.2328(100), 179.2416(4), 90.2343(3)	Linoleic acid	MassBank
190	15.50	$C_{33}H_{48}O_6$	+	563.3336	−1.2	563.3326(99), 503.3122(100), 145.1011(7), 135.0442(10), 119.0854(9), 105.0696(8)	Heteroclitalactone B	Standard
191	15.78	$C_{22}H_{42}O_4$	-	369.3008	−0.5	369.2986(29), 351.2910(17), 307.3003(100), 115.9195(8)	Docosanedioic acid	ChemSpider
192	16.11	$C_{30}H_{44}O_3$	+	453.3358	−1.1	453.3347(23), 435.3259(42), 371.1628(13), 201.1639(31), 173.1324(23), 159.1166(31), 133.1010(39), 119.0854(40), 109.1011(100), 95.0854(85)	Neokadsuranic acid B	in-house database, ClogP
193	16.14	$C_{20}H_{40}O_3$	-	327.2903	−0.6	327.2905(9), 326.1873(65), 185.0060(100), 183.0114(97), 59.009(67)	L-2-Hydroxyphytanate isomer	ChemSpider
194	16.19	$C_{30}H_{44}O_4$	+	469.3310	−0.4	469.3296(35), 451.3199(14), 433.3080(16), 423.3269(6), 249.1852(7), 235.1688(29), 219.1375(9), 173.1322(26), 159.1165(29), 145.1009(31), 133.1009(42), 119.0854(64), 95.0854(100)	Kadsuranic acid A	DPI, Clog P
195	16.20	$C_{20}H_{24}O_5$	+	345.1697	0.0	345.1690(11), 223.1326(14), 205.1221(16), 175.1116(25), 153.0546(44), 135.0439(100)	Kadsurindutin E isomer	in-house database

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Table S6. (continued)

NO.	t_R (min)	Formula	Ion mode	Measured Mass (m/z)	Error (ppm)	MS/MS Fragments (m/z)	Compound Identification	Identification references
196	16.20	$C_{30}H_{42}O_3$	+	451.3203	−0.9	451.3198(100), 433.3096(59), 415.2992(14), 201.1271(28), 159.1167(34), 133.1011(31), 119.0854(46), 95.0854(53)	Dysolenticin B isomer	ChemSpider
197	16.27	$C_{30}H_{46}O_4$	+	471.3465	−0.8	471.3461(41), 453.3346(24), 435.3239(20), 247.1684(24), 235.1684(34), 173.1326(20), 161.1323(49), 159.1168(17), 145.1011(20), 135.1166(32), 121.1012(59), 109.1011(55), 95.0854(100)	Nigranoic acid	in-house database, ClogP
198	16.27	$C_{31}H_{48}O_4$	+	485.3618	−1.4	453.3360(24), 435.3251(24), 425.3402(16), 407.3298(7), 249.1845(19), 228.1591(51), 201.1640(11), 189.1641(16), 173.1327(16), 161.1325(29), 159.1165(25), 147.1168(28), 133.1011(50), 121.1012(58), 119.0856(51), 95.0854(100)	Kadpolysperin J isomer	in-house database
199	16.45	$C_{18}H_{34}O_2$	-	281.2484	−0.7	281.2485(100), 249.4335(3), 150.2208(3), 96.9584(3)	Oleic acid isomer	MassBank
200	16.65	$C_{20}H_{24}O_5$	+	345.1693	−1.2	345.1697(7), 223.1326(14), 205.1221(18), 175.1115(26), 153.0547(41), 135.0439(100)	Kadsurindutin E isomer	in-house database
201	16.77	$C_{31}H_{46}O_4$	+	483.3463	−1.2	483.3470(17), 465.3406(7), 451.3198(29), 433.3090(31), 263.2001(19), 249.1848(16), 233.1533(11), 215.1433(13), 201.1637(11), 173.1325(27), 159.1168(32), 145.1011(40), 133.1010(59), 121.1011(57), 95.0854(100)	Heteroclitalactone F	Standard
202	17.10	$C_{30}H_{46}O_2$	+	439.3566	−1.1	439.3593(34), 357.1466(88), 249.1848(14), 205.1947(27), 203.1792(100), 191.1791(94), 121.1011(45), 119.0855(26), 95.0854(100)	Heilaohu acid A isomer	in-house database
203	17.76	$C_{30}H_{46}O_2$	+	439.3566	−1.1	439.3572(45), 357.1466(100), 233.1896(17), 159.1170(11), 135.1168(10), 121.1010(10), 119.0852(14), 95.0853(14)	Heilaohu acid A isomer	in-house database
204	17.97	$C_{30}H_{46}O_3$	+	455.3515	−1.1	455.3510(30), 437.3405(38), 419.3296(7), 409.3465(3), 329.2464(3), 235.1689(30), 217.1592(9), 201.1636(22), 189.1633(21), 187.1476(14), 173.1320(14), 161.1322(50), 147.1127(30), 133.1010(36), 121.1010(43), 119.0854(43), 107.0854(40), 95.0854(100)	Schisandronic acid	Standard

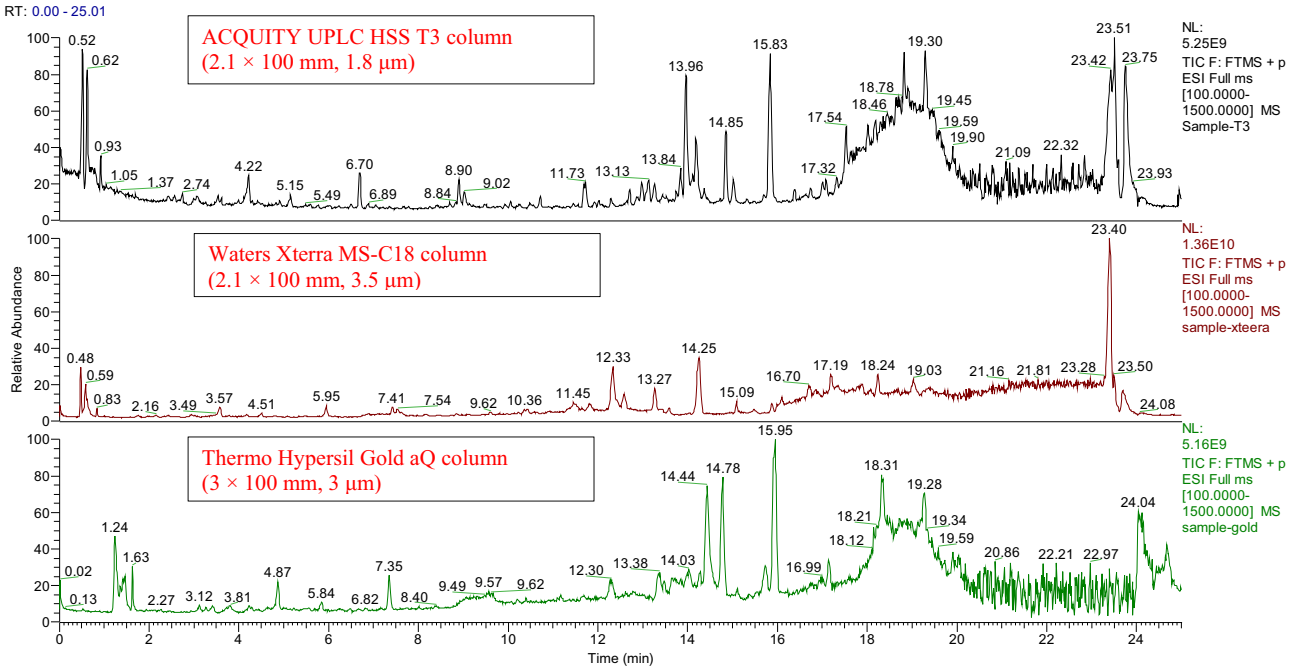

Fig. S1. The total ion chromatograms of KHS obtained by using different columns.

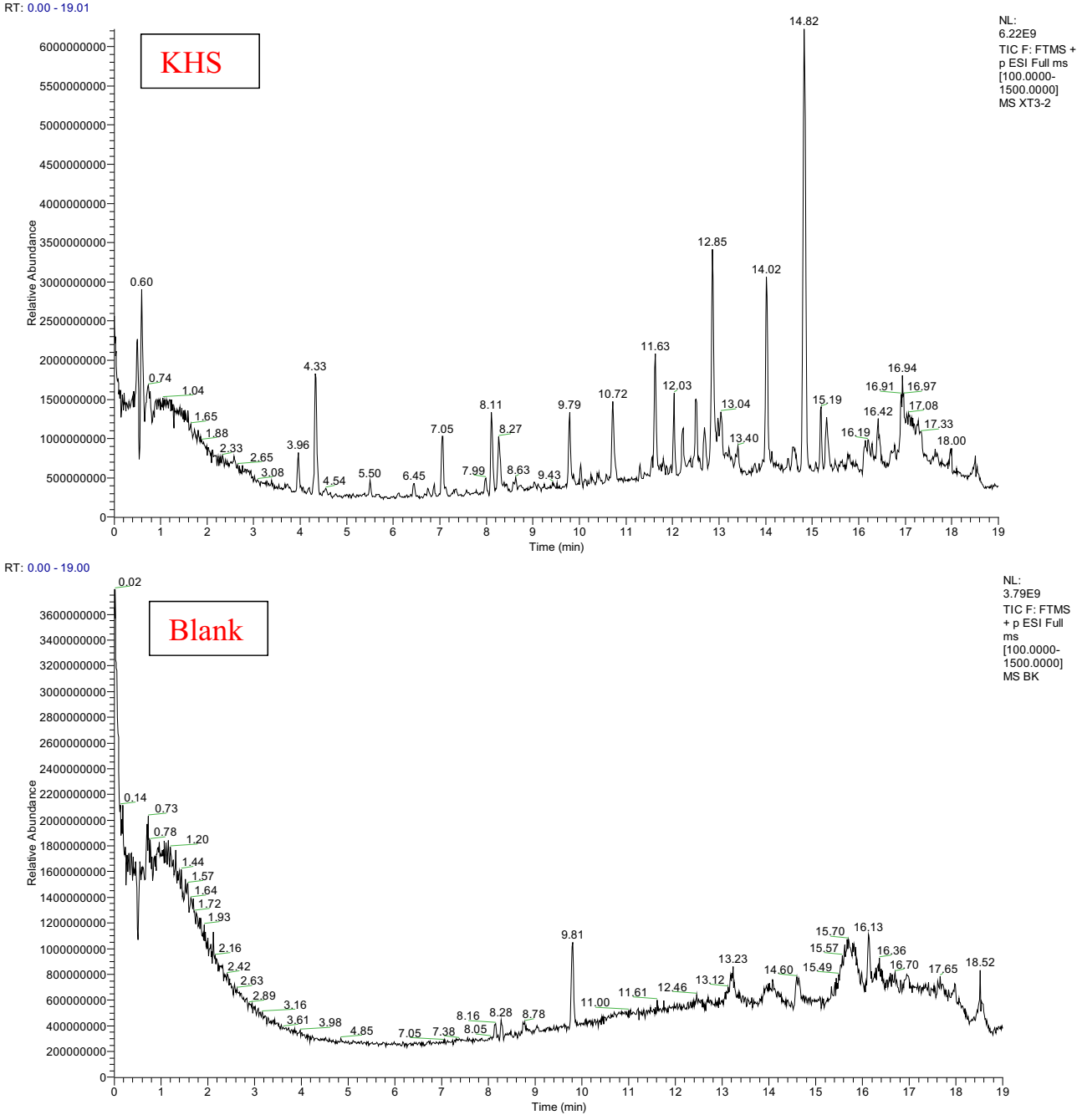

Fig. S2. Total ion chromatograms in positive ion mode of KHS extracts and blank solvent.

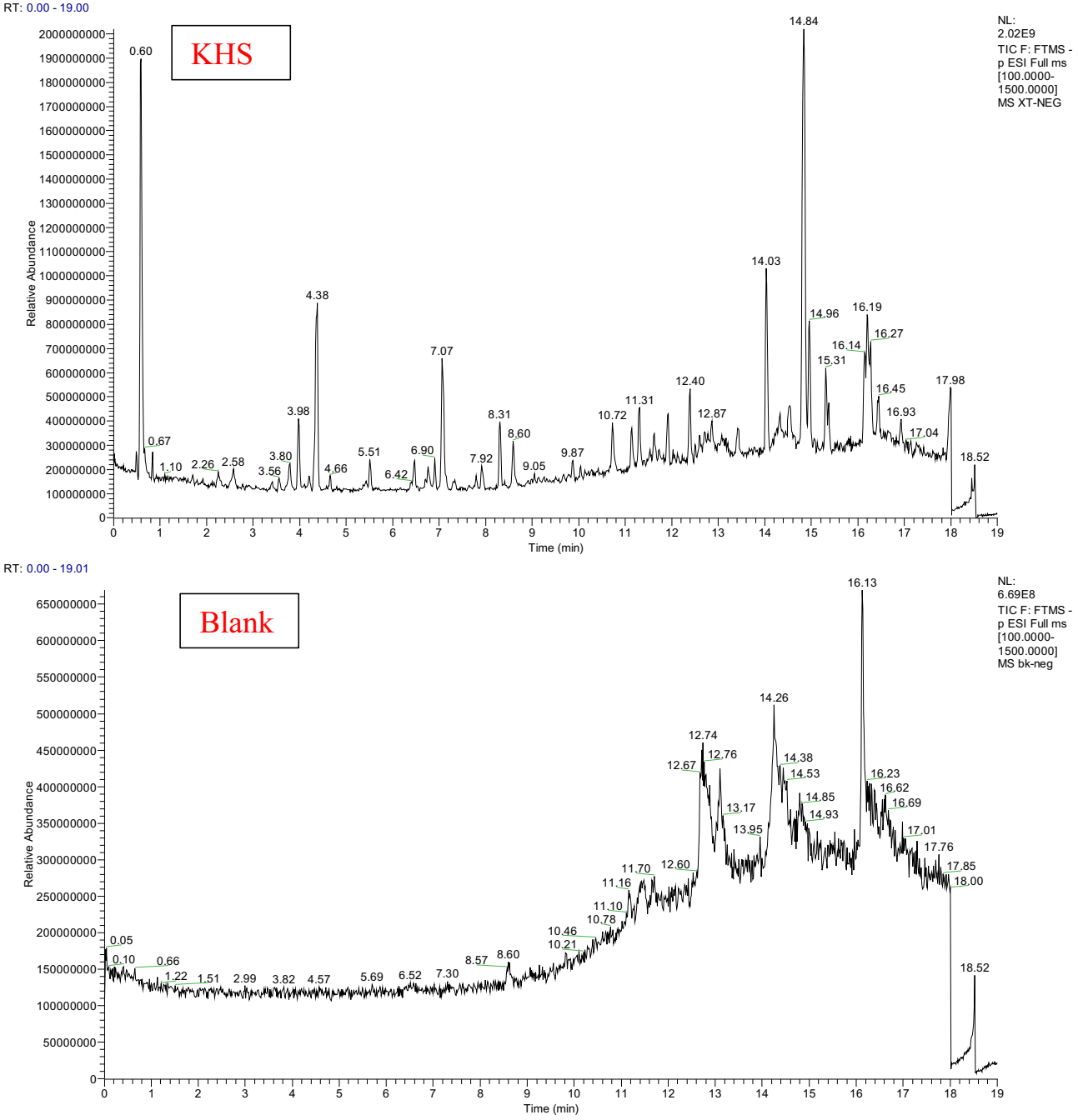

Fig. S3. Total ion chromatograms in negative ion mode of KHS extracts and blank solvent.

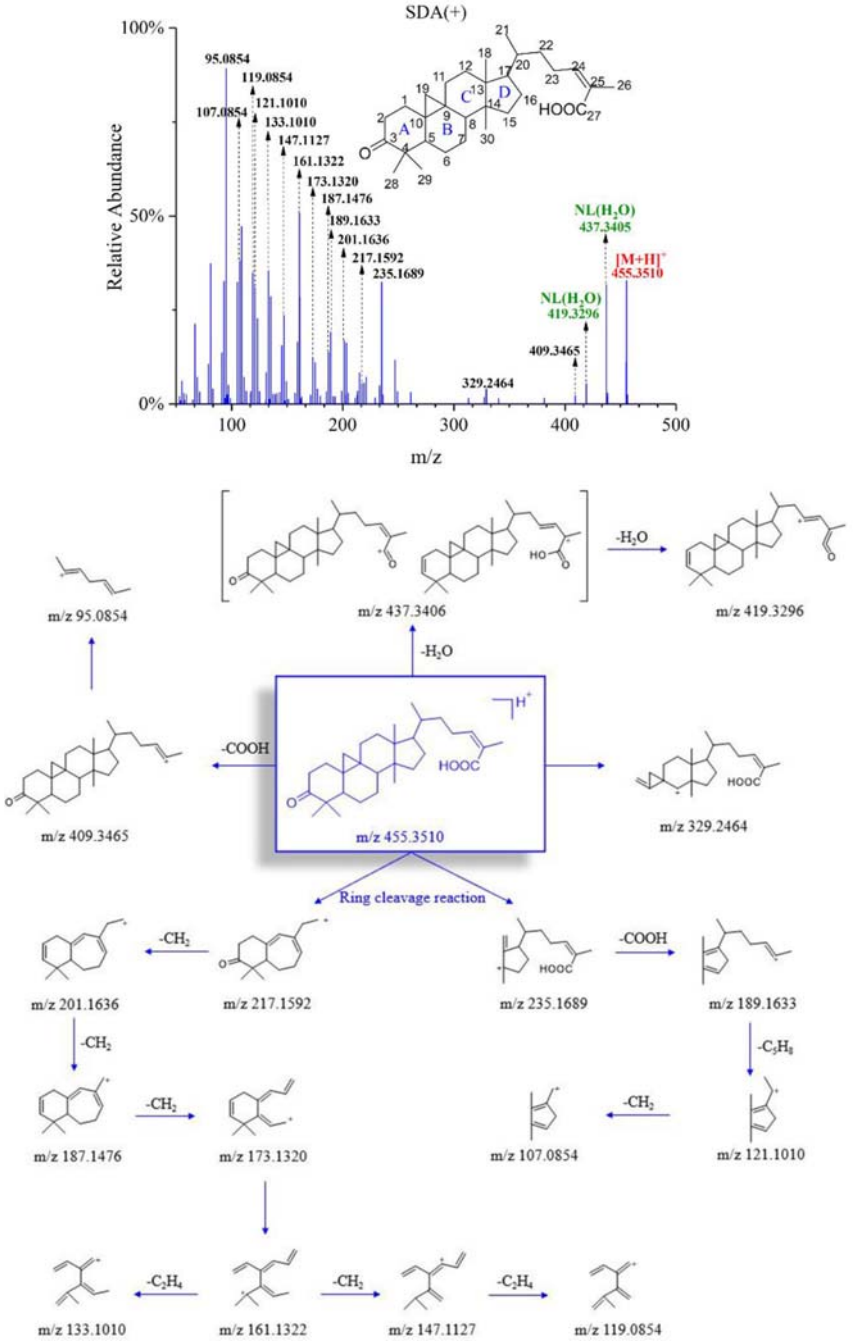

Fig. S4. The exact MS^2 spectrum and proposed fragmentation pathways of schisandronic acid (SDA) in positive ion mode.

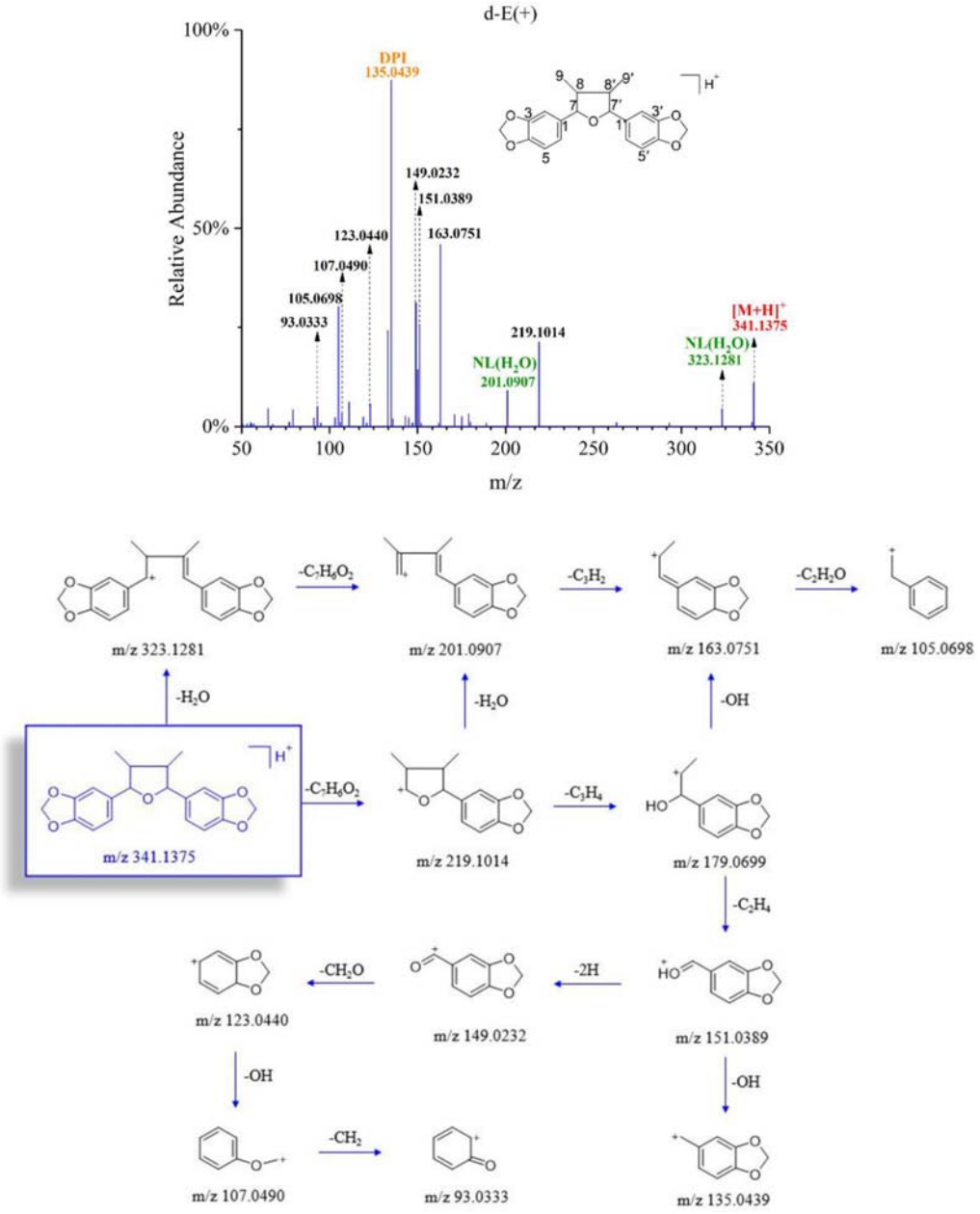

Fig. S5. The exact MS^2 spectrum and proposed fragmentation pathways of d-Epigalbacin (d-E) in positive ion mode.

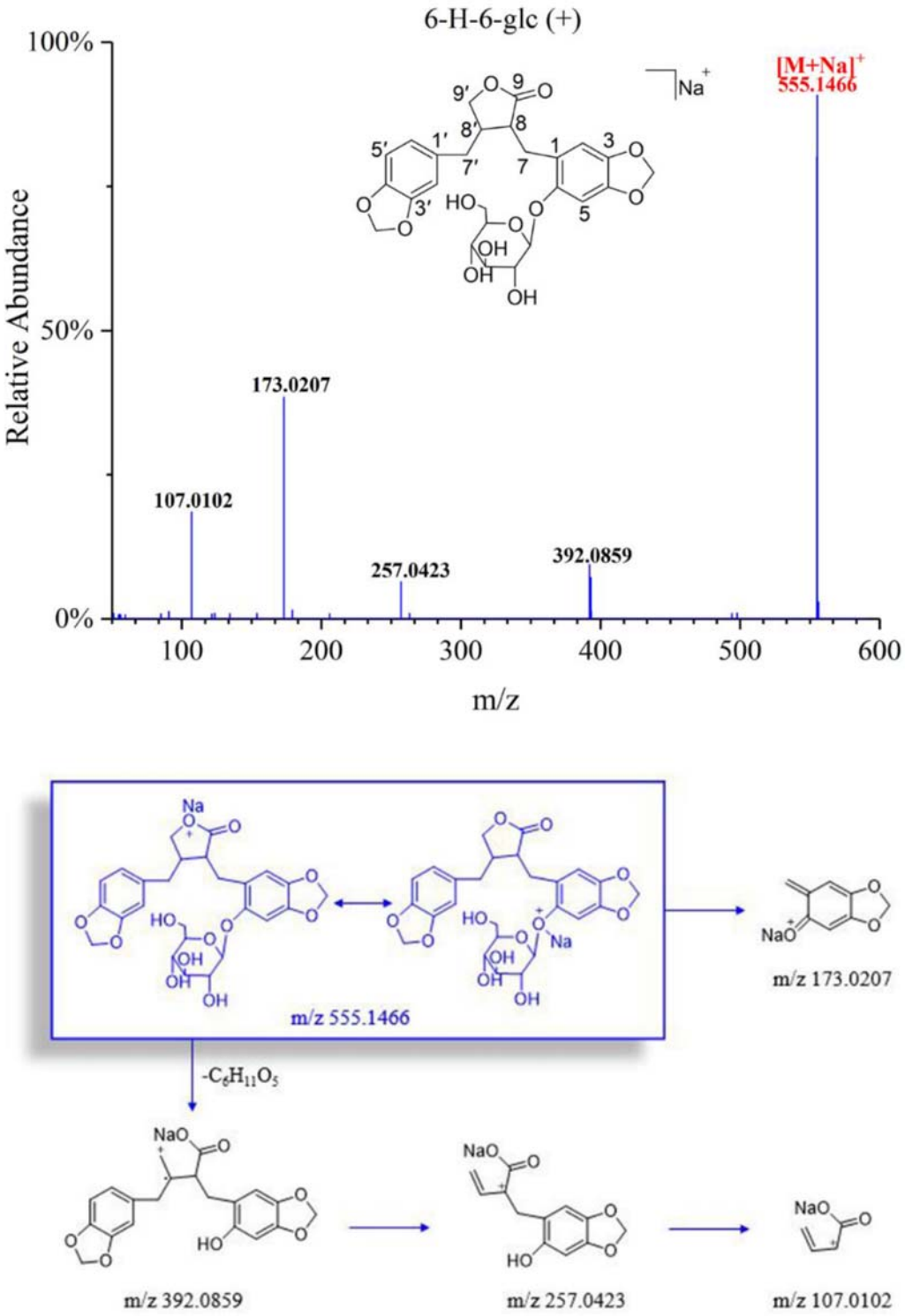

Fig. S6. The exact MS^2 spectrum and proposed fragmentation pathways of 6-hydroxyhinokinin-6-O-β-D-glucopyranoside (6-H-6-glc) in positive ion mode.

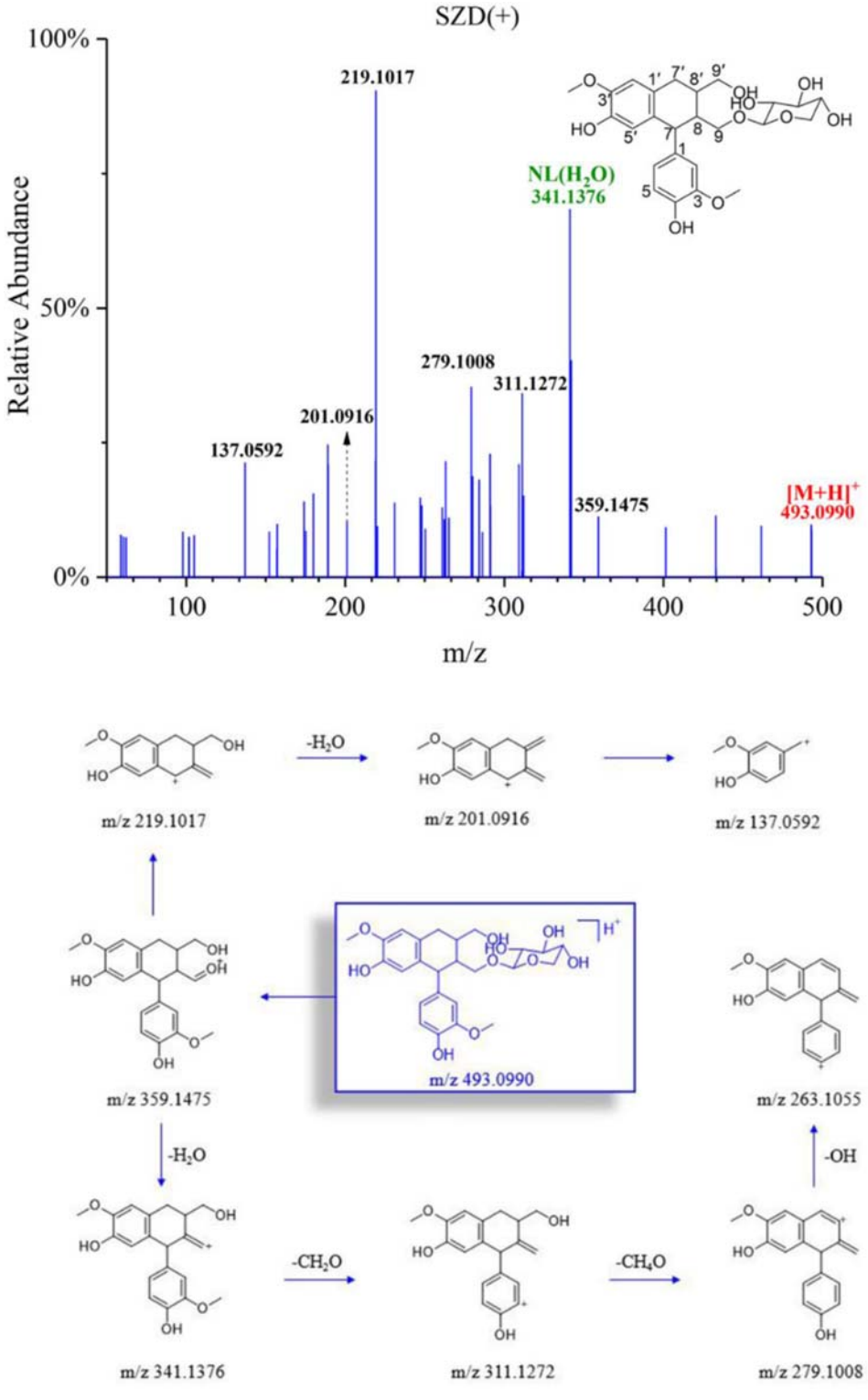

Fig. S7. The exact MS^2 spectrum and proposed fragmentation pathways of schizandriside (SZD) in positive ion mode.

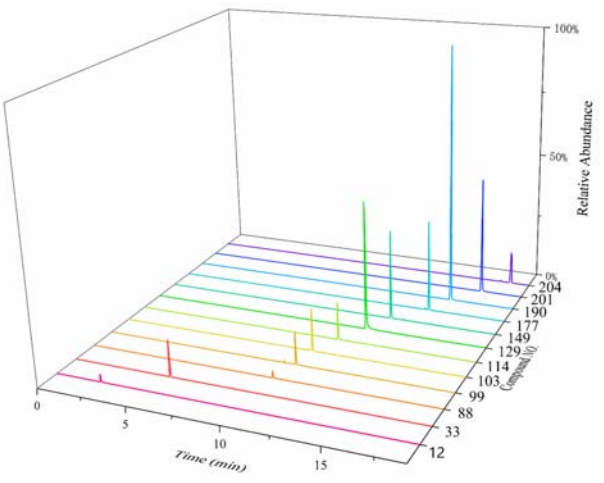

Fig. S8. The extracted ion chromatogram of mixed reference standards (12 analytes). Peak identification: ***12****, schizandriside;* ***33****, 6-Hydroxyhinokini-6-O-β-D-glucopyranoside;* ***88****, heteroclitalactone M;* ***99****, heteroclitalactone E;* ***103****, kadsurarin;* ***114****, heteroclitalactone D;* ***129****, d-Epigalbacin;* ***149****, schisanlactone B;* ***177****, schisanlactone E;* ***190****, heteroclitalactone B;* ***201****, heteroclitalactone F;* ***204****, schisandronic acid.*

Reference

[1] Liu JS, Qi YD, Lai HW, Zhang J, Jia XG, Liu HT, et al. Genus *Kadsura*, a good source with considerable characteristic chemical constituents and potential bioactivities. Phytomedicine 2014;21:1092−7.

[2] Shen FY, Liu Y, Su W, Huang JH, Peng CY, Li B, Wang W. Research on the Tujia Ethnomedicine "Seven" Drugs. J Hunan Univ Chin Med 2015;35:1−6.

[3] Xiang Y, Zhang TT, Yin CP, Zhou JW, Huang R, Gao SS, et al. Effects of the stem extracts of *Schisandra glaucescens* Diels on collagen-induced arthritis in Balb/c mice. J Ethnopharmacol 2016;194:1078−86.

[4] Yu HH, Lin Y, Zeng R, Li X, Zhang T, Tasneem S, et al. Analgesic and anti-inflammatory effects and molecular mechanisms of *Kadsura heteroclita* stems, an anti-arthritic Chinese Tujia ethnomedicinal herb. J Ethnopharmacol 2019;238:111902.

[5] Yu HH, Zeng R, Lin Y, Li X, Tasneem S, Yang Z, et al. *Kadsura heteroclita* stem suppresses the onset and progression of adjuvant-induced arthritis in rats. Phytomedicine 2019;58:152876.

[6] Wang W, Liu JZ, Han J, Xu ZR, Liu RX, Wang LP, et al. New triterpenoids from *Kadsura heteroclita* and their cytotoxic activity. Planta Med 2006;72:450−7.

[7] Wang W, Liu JZ, Liu RX, Xu ZR, Yang M, Wang WX, et al. Four new lignans from the stems of *Kadsura heteroclita*. Planta Med 2006;72:284−8.

[8] Wang W, Liu JZ, Ma XC, Yang M, Wang WX, Xu ZR, et al. Three new cyclolanostane triterpenoids from the ethanol extract of the stems of *Kadsura heteroclita*. Helv Chim Acta 2006;89:1888−93.

[9] Wang W, Ma XC, Liu P, Liu RX, Guan SH, Guo DA. Two new dibenzylbutyrolactone type Lignans from the stems of *Kadsura heterodita*. Nat Prod Commun 2006;1:109−12.

[10] Xu LJ, Peng ZG, Chen HS, Jie W, Xiao PG. Bioactive triterpenoids from *Kadsura heteroclita*. Chem Biodivers 2010;7:2289−95.

[11] Minh PTH, Lam DT, Tien NQ, Tuan NN, Hyun KS. New Schiartane-type Triterpene from *Kadsura heteroclita* and their Cytotoxic Activities. Nat Prod Commun 2014;9:373−4.

[12] Cao L, Li B, Shehla N, Gong L, Jian Y, Peng C, et al. Triterpenoids from stems of *Kadsura heteroclita*. Fitoterapia 2020;140:104441.

[13] Cao L, Shehla N, Li B, Jian YQ, Peng CY, Sheng WB, et al. Schinortriterpenoids from Tujia ethnomedicine Xuetong—The stems of *Kadsura heteroclita*. Phytochemistry 2020;169:112178.

[14] Shehla N, Li B, Cao L, Zhao JP, Jian YQ, Daniyal M, et al. Highly oxidized lanostane and cycloartanetriterpenoids from *kadsura heteroclita* roxb. craib. Front Chem 2020;7:935.

[15] Wang W, Liu J, Yang M, Sun J, Wang X, Liu R, et al. Simultaneous determination of six major constituents in the stems of *Kadsura heteroclita* by LC-DAD. Chromatographia 2006;64:297−302.

[16] Makarov A, Scigelova M. Coupling liquid chromatography to Orbitrap mass spectrometry. J Chromatogr A 2010;1217:3938−45.

[17] Ranninger C, Schmidt LE, Rurik M, Limonciel A, Jennings P, Kohlbacher O, Huber CG. Improving global feature detectabilities through scan range splitting for untargeted metabolomics by high-performance liquid chromatography-Orbitrap mass spectrometry. Anal Chim Acta 2016;930:13−22.

[18] Liu RX, Zhao ZY, Dai SJ, Che X, Liu WH. Identification and quantification of bioactive Compounds in *diaphragma juglandis* fructus by UHPLC-Q-Orbitrap HRMS and UHPLC-MS/MS. J Agric Food Chem 2019;67:3811−25.

[19] Liu RX, Su CN, Xu XM, Shang KL, Sun K, Li CH, et al. Identifying potential active components of walnut leaf that action diabetes mellitus through integration of UHPLC-Q-Orbitrap HRMS and network pharmacology analysis. J Ethnopharmacol 2020;253:112659.

[20] Liu RX, Liu QQ, Li B, Liu LP, Cheng DS, Cai X, et al. Pharmacokinetics, bioavailability, excretion, and metabolic analysis of Schisanlactone E, a bioactive ingredient from *Kadsura heteroclita* (Roxb) Craib, in rats by UHPLC-MS/MS and UHPLC-Q-Orbitrap HRMS. J Pharmaceut Biomed 2020;177:112875.

[21] Xu LL, Shang ZP, Bo T, Sun L, Guo QL, Qiao X, et al. Rapid quantitation and identification of the chemical constituents in Danhong Injection by liquid chromatography coupled with orbitrap mass spectrometry. J Chromatogr A 2019;1606:460378.

[22] Wang J, Chow W, Leung D, Chang J. Application of ultrahigh-performance liquid chromatography and electrospray ionization quadrupole orbitrap high-resolution mass spectrometry for determination of 166 pesticides in fruits and vegetables. J Agric Food Chem 2012;60:12088−104.

[23] Gómez-Pérez María Luz, Romero-González Roberto, Martínez Vidal José Luis, Frenich AG. Analysis of pesticide and veterinary drug residues in baby food by liquid chromatography coupled to Orbitrap high resolution mass spectrometry. Talanta 2015;131:1−7.

[24] Zhou S, Guo C, Shi F, Jiang W, Wang L. Application of an ultrahigh-performance liquid chromatography coupled to quadrupole-orbitrap high-resolution mass spectrometry for the rapid screening, identification and quantification of illegal adulterated glucocorticoids in herbal medicines. J Chromatogr B 2016;1038:34−42.

[25] Liu JS, Huang MF. Isolation and structures of schisanlactone E and changnanic acid. Acta Chimica Sinica 1991;41:502−6.

[26] Chen YG, Wu ZC, Lv YP, Gui SH, Halaweish F. Triterpenoids from *Schisandra henryi* with cytotoxic effect on leukemia and Hela cells *in vitro*. Archives of Pharmacal Research 2003;26:912−6.

[27] Sadhu SK, Khatun A, Phattanawasin P, Ohtsuki T, Ishibashi M. Lignan glycosides and flavonoids from Saraca asoca with antioxidant activity. J Nat Med 2007;61:480−2.

[28] Kwon JH, Kim JH, Choi SE, Park KH, Lee MW. Inhibitory effects of phenolic compounds from needles ofPinus densifloraon nitric oxide and PGE2 production. Arch Pharm Res 2010;33:2011−6.

[29] Peng ZG, Xu LJ, Ye WC, Xiao PG, Chen HS. Effective components against HIV-1 replicative enzymes isolated from plants. Acta Pharma Sin 2010;45:235−40.

[30] Kim KH, Moon E, Kim SY, Choi SU, Lee KR. Lignan constituents of Tilia amurensis and their biological evaluation on antitumor and anti-inflammatory activities. Food & Chemical Toxicology 2012;50:3680–6.
[31] Zhang LK, Chen HX, Tian JG, Chen SH. Antioxidant and anti-proliferative activities of five compounds from Schisandra chinensis fruit. Industrial Crops & Products 2013;50:690–3.
[32] Fu CQ, Yu P, Wang MY, Qiu F. Phytochemical analysis and geographic assessment of flavonoids, coumarins and sesquiterpenes in Artemisia annua L. based on HPLC-DAD quantification and LC-ESI-QTOF-MS/MS confirmation. Food Chem 2020;312:126070.
[33] Liao XY, Hu FL, Chen ZL. Identification and quantification of active components in osmanthus fragrans fruits by HPLC-ESI-MS/MS. J Agric Food Chem 2018;66:359–67.
[34] Guo S, Cui XQ, Jiang M, Bai L, Tian X, Guo TT, et al. Simultaneous characterization and quantification of 17 main compounds in Rabdosia rubescens by high performance liquid chromatography. J Food Drug Anal 2017;25:417–24.
[35] Zhou J, Yi H, Zhao ZX, Shang XY, Zhou MJ, Kang GJ, et al. Simultaneous qualitative and quantitative evaluation of Ilex kudingcha C. J. tseng by using UPLC and UHPLC-qTOF-MS/MS. J Pharm Biomed Anal 2018;155:15–26.
[36] Chan C, Xie XJ, Wan SW, Zhou GL, Yuen AC-y, Mok DK-w, et al. Qualitative and quantitative analysis of sesquiterpene lactones in *Centipeda minima* by UPLC-Orbitrap-MS & UPLC-QQQ-MS. J Pharmaceut Biomed 2019;174:360–6.
[37] Zhu LX, Wang X, Li SC, Qi ER, Meng J, Lam KYC, et al. Qualitative and quantitative characterization of carbohydrate profiles in three different parts of *Poria cocos*. J Pharmaceut Biomed 2020;179:113009.
[38] Grund B, Marvin L, Rochat B. Quantitative performance of a quadrupole-orbitrap-MS in targeted LC–MS determinations of small molecules. J Pharmaceut Biomed 2016;124:48–56.
[39] Duan SN, Qi W, Zhang SW, Huang KK, Yuan D. Simultaneous quantification combined with multivariate statistical analysis of multiple chemical markers of Wu Ji Bai Feng Pill by UHPLC-MS/MS. J Food Drug Anal 2019;27:275–83.
[40] Zhang G, Chen SS, Zhou W, Meng J, Deng K, Zhou HN, et al. Rapid qualitative and quantitative analyses of eighteen phenolic compounds from *Lycium ruthenicum* Murray by UPLC-Q-Orbitrap MS and their antioxidant activity. Food Chem 2018;269:150–6.
[41] Cortese M, Gigliobianco MR, Peregrina DV, Sagratini G, Martino PD. Quantification of phenolic compounds in different types of crafts beers, worts, starting and spent ingredients by liquid chromatography-tandem mass spectrometry. Journal of Chromatography A 2020;1612:460622.
[42] Gai QY, Jiao J, Wang X, Fu YJ, Lu Y, Liu J, et al. Simultaneous quantification of eleven bioactive phenolic compounds in pigeon pea natural resources and *in vitro* cultures by ultra-high performance liquid chromatography coupled with triple quadrupole mass spectrometry (UPLC-QqQ-MS/MS). Food Chem 2021;335:127602.

Further reading

[43] He K, Zeng L, Shi G, Zhao GX, Kozlowski J, Mclaughlin J. Bioactive compounds from Taiwania cryptomerioides. J Nat Prod 1997;60:38–40.