SUPPORTING INFORMATION

Deep-clustering based mass spectral data visualization strategy for the anti-renal fibrotic lead compound identification from natural products

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Experimental Section

Chemicals and materials

Methanol and acetonitrile of LC-MS grade were purchased from Merck (Damstadt, Germany). Ultrapure water (RSJ water purification technology co.) was prepared using Unique-R2 purification system under a resistivity of 18.25 MΩ/cm. Other reagent solutions were analytical grade.

The 16 reference standards including geniposidic acid (1), vanillic acid (2), caffeic acid (3), asperuloside (4), ferulic acid (5), plantamajoside (6), acetoside (7), calceolarioside B (8), plantainoside D (9), homoplantaginin (10), isoacetoside (11), 2′-acetylacteoside (12), baicalin (13), apigenin (14), kaempferol (15), and oleanolic acid (16) were purchased from Chengdu Desit Company (Chengdu, China) (detailed structures are shown in **Figure S1**. The 132 reference standards (purity above 98%, Desit, Chengdu, China) for method validation were listed in the supplementary documents **Table S1**. TGF-β, Antibodies to Fibronectin (ab2413), α-SMA (14395), Collagen I (14695-1-AP) were purchased from Abcam.

The salt we used during processing was cooking salt bought from the supermarket (food grade salt, Tangshan Yinhai Salt CO. LTD, China), with the content of sodium chloride was above 98.5g/100 g.

The seeds of *Plantago adsiatica* L. (Plantaginis Semen, PS) were purchased from Zhejiang University of Chinese Medicine Traditional Chinese Medicine Sliced Medicine Co., Ltd. (Hangzhou, China). The plant materials were authenticated by Prof. Luping Qin (School of Pharmaceutical Sciences, Zhejiang Chinese Medical University). The voucher specimens of the PS and the salt processed Plantaginis Semen

(SPS) were deposited in the School of Pharmacy, Zhejiang Chinese Medical University (Nos. 20210910 and 20210910S, respectively).

Supplementary Figures

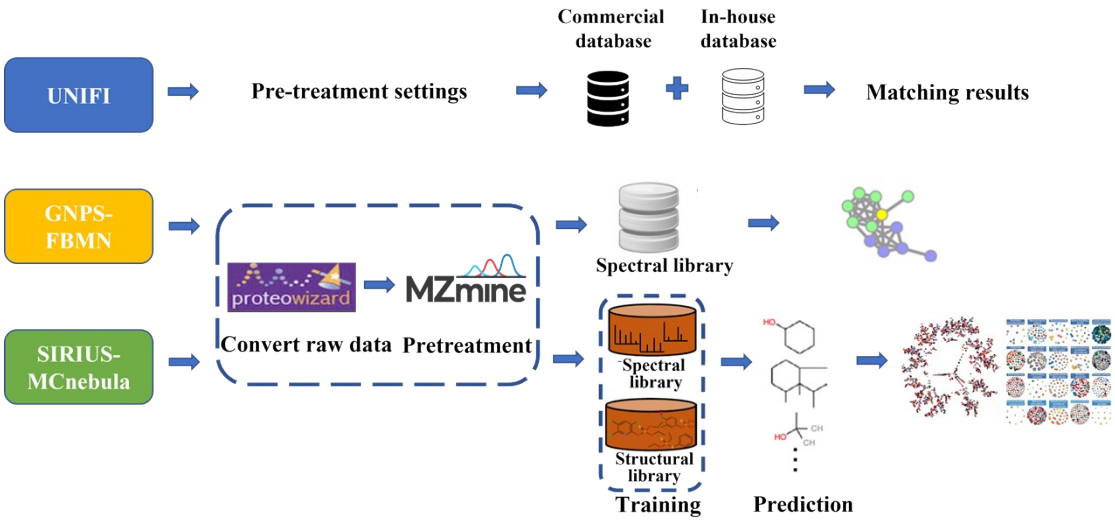

Figure S1. The flow chart of the three computational annotation workflows.

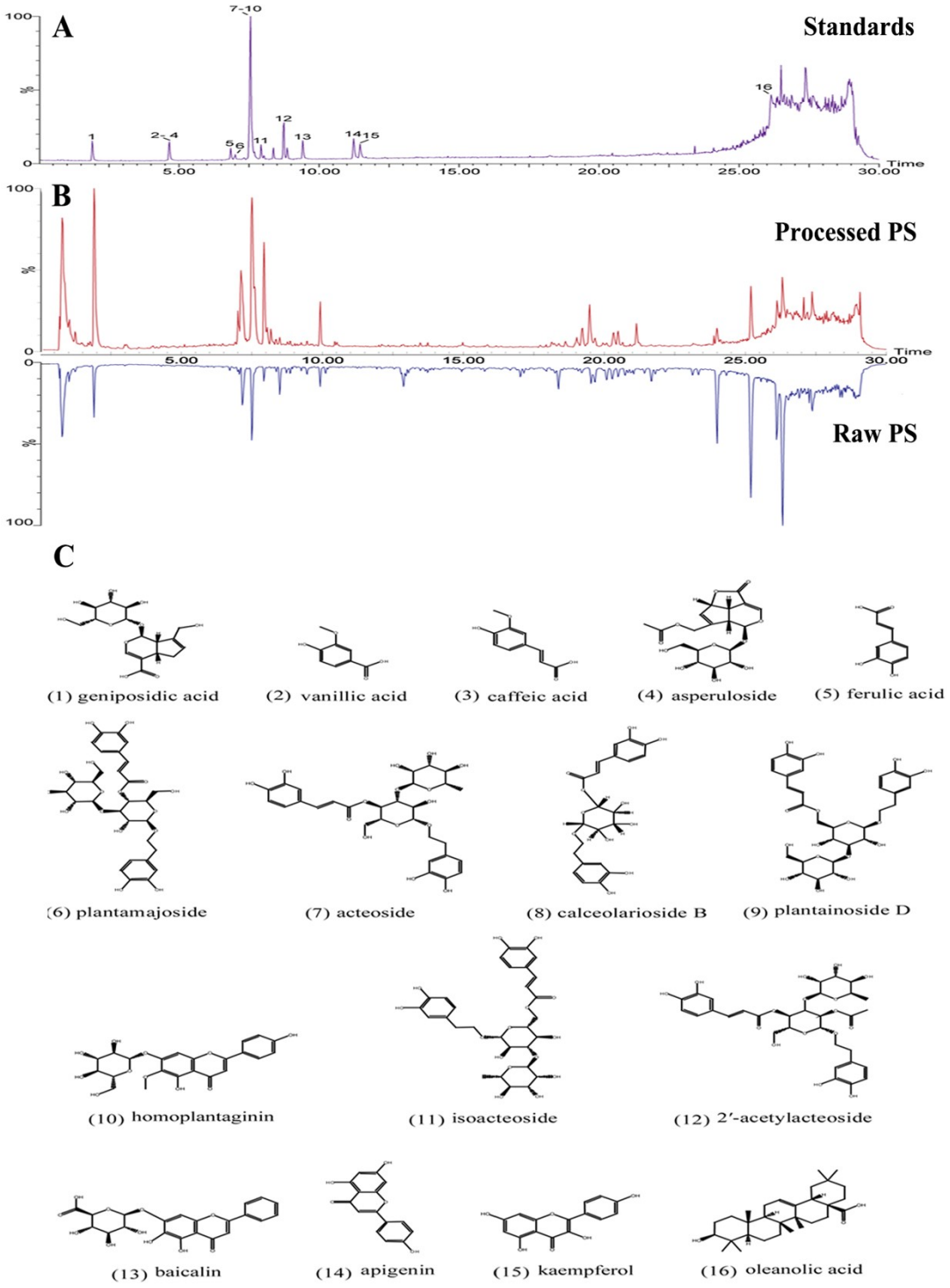

Figure S2. Typical TIC chromatograms of Plantaginis Semen (PS) in the negative ion mode. (A) The TIC chromatograms of the reference standards. (B) The typical TIC plots of the raw and processed PS. (C) The chemical structures of the 16 differentiate reference standards.

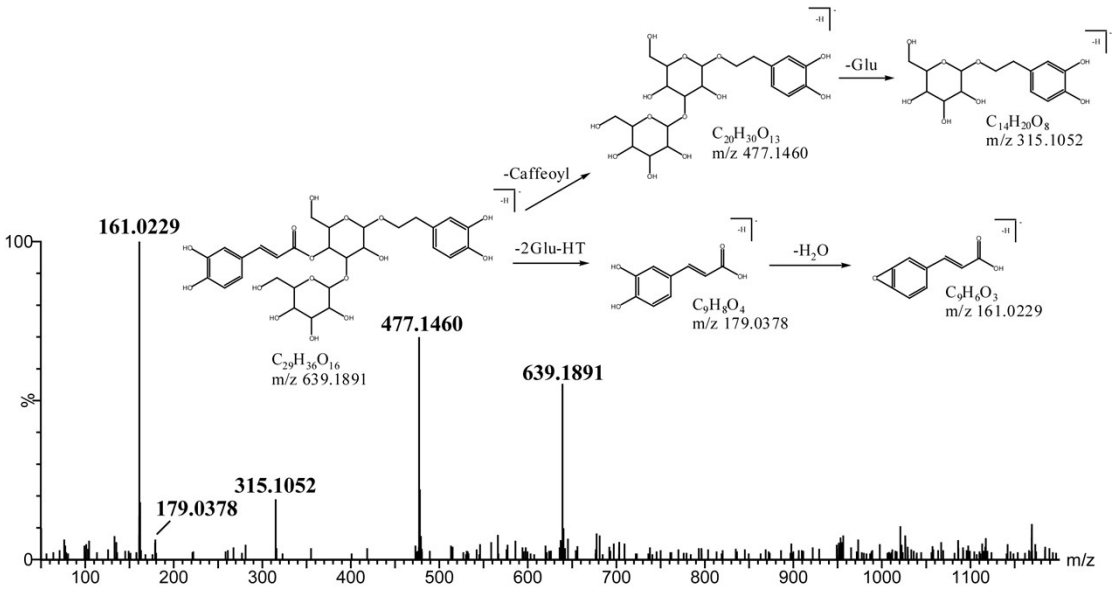

Figure S3. The proposed MS/MS fragmentation of Plantamajoside.

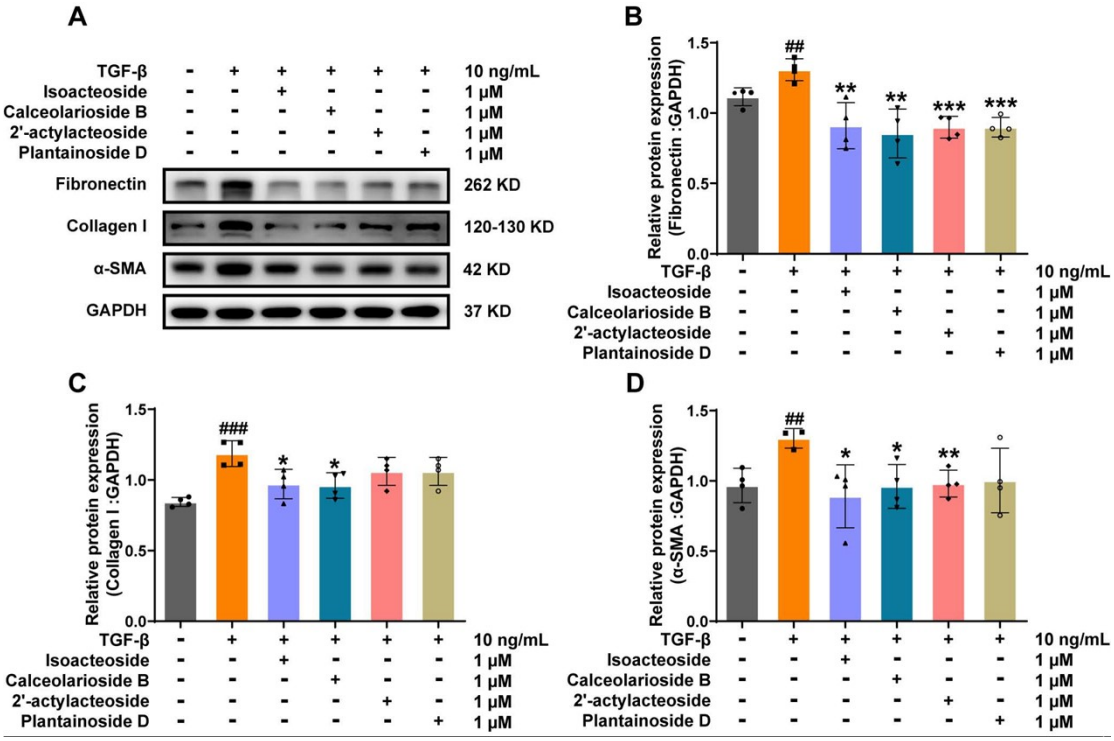

Figure S4. Western blot analyses of renal fibrotic proteins in TGF-β (10 ng mL^{-1}) induced NRK-52E cells with the treatment of the four potential lead compounds (1 μM) screened from PS extracts after processing. (A) Protein level of fibronectin, collagen I, α-SMA in NRK-52E cells treated with isoacteoside, calceolarioside B, 2'-actylacteoside, and plantainoside D at 1 μM. (B-D) Quantitative analyses of fibronectin, collagen I, α-SMA levels in NRK-52E cells treated with isoacteoside, calceolarioside B, 2'-actylacteoside, and plantainoside D at 1 μM. $^{\#\#}P<0.01$, $^{\#\#\#}P<0.001$ versus control; $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ versus TGF-β induced fibrotic model.

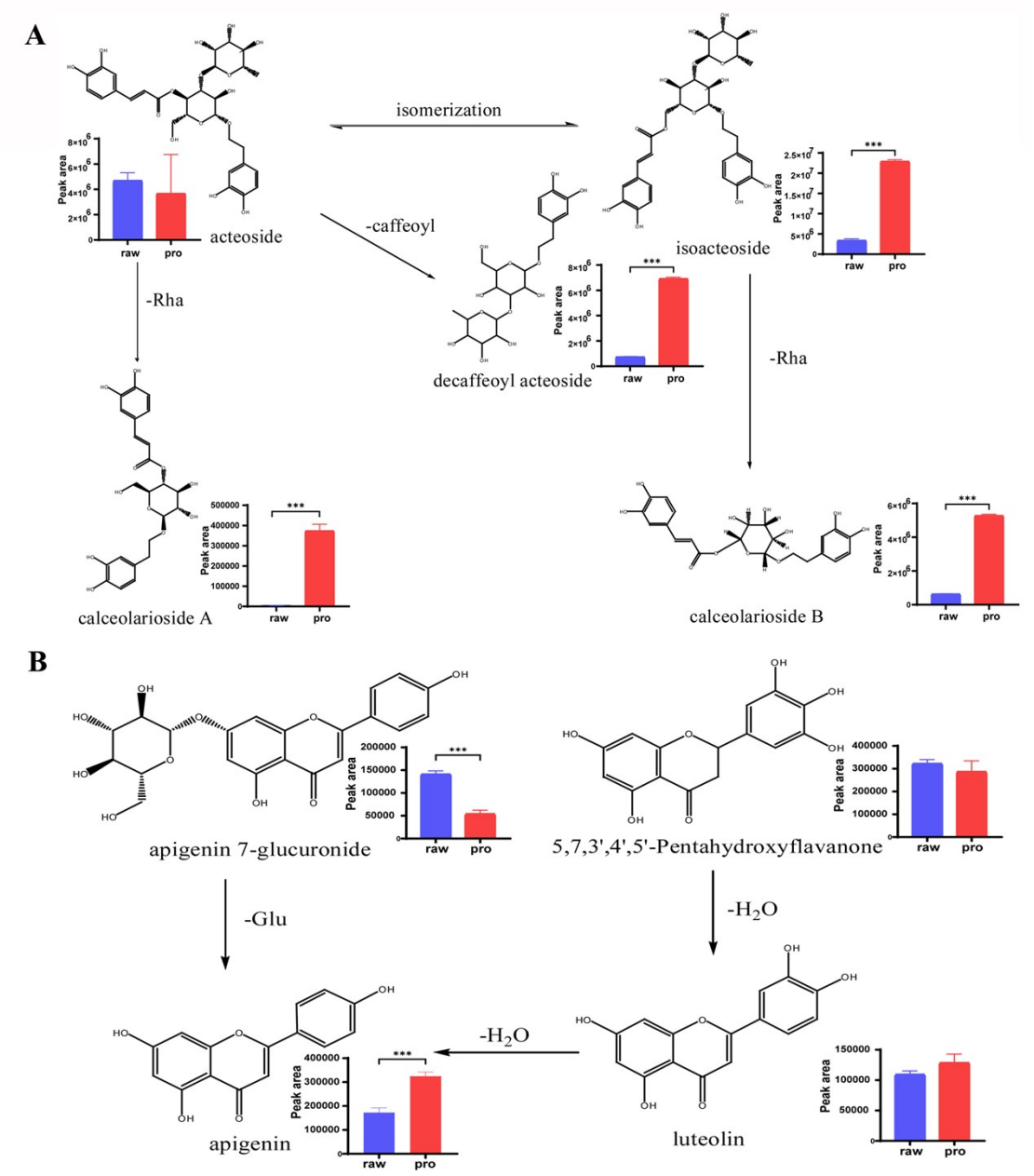

Figure S5. Possible chemical transformation of (A) phenyl ethanol glycosides and (B) flavonoid in PS after the traditional processing procedure. (Blue and red bars indicated relative contents in raw and processed PS extract, respectively ($^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$).

Supplementary Table

Table S1. *In silico* mass spectra annotation results by UNIFI, GNPS-FBMN, SIRIUS-MCnebula workflow based on chemical reference standard pool (n=132). We use XlogP as the polarity indicator of each compound and roughly estimated their retention time distribution. Each group contained about 10 references, with isomers separated into different groups, and compounds within groups distributed separately by estimated retention time.

Group	No.	Compound name	CAS	XlogP	Retention Time (min)	Formula	Predicted Mass(m/z)	Detected		
								UNIFI	GNPS-FBMN	SIRIUS-MCnebula
1	1	Geniposidic acid	27741-01-1	-2.7	1.90	$C_{16}H_{22}O_{10}$	374.1213	×	○	○
	2	Plantainoside D	147331-98-4	-1	4.05	$C_{29}H_{36}O_{16}$	640.2003	×	×	○
	3	Plantamajoside	104777-68-6	-1	4.44	$C_{29}H_{36}O_{16}$	640.2003	×	×	○
	4	Isoacteoside	61303-13-7	-0.5	4.35	$C_{29}H_{36}O_{15}$	624.2054	×	○	○
	5	Acteoside	61276-17-3	-0.5	4.61	$C_{29}H_{36}O_{15}$	624.2054	×	×	○
	6	Baicalin	21967-41-9	1.1	5.67	$C_{21}H_{18}O_{11}$	446.0849	×	×	○
	7	Vanillin	121-33-5	1.2	4.09	$C_8H_8O_3$	152.0473	×	×	○
	8	Vanillic acid	121-34-6	1.4	3.29	$C_8H_8O_4$	168.0423	×	×	○
	9	Ferulic acid	1135-24-6	1.5	4.42	$C_{10}H_{10}O_4$	194.0579	×	×	○
	10	Baicalein	491-67-8	1.7	7	$C_{15}H_{10}O_5$	270.0528	×	○	○
	11	Kaempferol	520-18-3	1.9	7.19	$C_{15}H_{10}O_6$	286.0477	×	○	○

	12	Asperuloside	14259-45-1	-2.4	3.09	$C_{18}H_{22}O_{11}$	414.1162	○	×	○
2	1	Quercetin 3-O-rutinoside	949926-49-2	-1.3	4.09	$C_{27}H_{30}O_{16}$	610.1534	×	○	○
	2	Crocin II	55750-84-0	-0.3	5.43	$C_{38}H_{54}O_{19}$	814.3259	×	×	×
	3	Gallic acid	149-91-7	0.7	1.49	$C_7H_6O_5$	170.0215	○	×	○
	4	Quercitrin	522-12-3	0.9	4.80	$C_{21}H_{20}O_{11}$	448.1006	×	×	○
	5	Quercetin	117-39-5	1.5	6.24	$C_{15}H_{10}O_7$	302.0427	×	○	○
	6	Isorhamnetin	480-19-3	1.9	7.34	$C_{16}H_{12}O_7$	316.0583	×	×	×
	7	Emodin	518-82-1	2.7	10.92	$C_{15}H_{10}O_5$	270.0528	○	×	○
	8	Isoliquiritigenin	961-29-5	3.2	7.85	$C_{15}H_{12}O_4$	256.0736	○	○	○
3	1	Pinoresinol diglucoside	63902-38-5	-1.3	3.47	$C_{32}H_{42}O_{16}$	682.2473	×	○	○
	2	Saikosaponin C	20736-08-7	-0.2	7.66	$C_{48}H_{78}O_{17}$	926.5239	×	○	○
	3	Astragalin	480-10-4	0.7	4.73	$C_{21}H_{20}O_{11}$	448.1006	×	○	○
	4	Astragaloside A	83207-58-3	1.3	7.91	$C_{41}H_{68}O_{14}$	784.4609	○	×	○
	5	Isoferulic acid	537-73-5	1.5	4.63	$C_{10}H_{10}O_4$	194.0579	×	×	×
	6	Saikosaponin G	99365-19-2	2.8	9.22	$C_{42}H_{68}O_{13}$	780.4660	×	○	○
	7	demethoxycurcumin	22608-11-3	3.3	9.74	$C_{20}H_{18}O_5$	338.1154	×	○	○
	8	Medioresil	40957-99-1	2.3	7.15	$C_{21}H_{24}O_7$	388.1522	×	×	○
	9	Betulinic acid	472-15-1	8.2	15.40	$C_{30}H_{48}O_3$	456.3603	×	×	×

4	1	Aucubin	479-98-1	-3	1.49	$C_{15}H_{22}O_9$	346.1264	×	×	○
	2	Esculentoside H	66656-92-6	-1	5.63	$C_{48}H_{76}O_{21}$	988.4879	○	×	×
	3	Chlorogenic acid	327-97-9	-0.4	2.81	$C_{16}H_{18}O_9$	354.0951	○	○	○
	4	vitexin	3681-93-4	0.2	4.18	$C_{21}H_{20}O_{10}$	432.1056	×	○	○
	5	(+)-pinoresinol-β-D-glucoside	69251-96-3	0.5	4.72	$C_{26}H_{32}O_{11}$	520.1945	×	×	○
	6	Baicalein 6-O-glucoside	28279-72-3	0.9	4.92	$C_{21}H_{20}O_{10}$	432.1057	×	○	○
	7	Wogonoside	51059-44-0	1.4	6.64	$C_{22}H_{20}O_{11}$	460.1006	×	○	○
	8	Taxifolin	480-18-2	1.5	4.55	$C_{15}H_{12}O_7$	304.0583	×	○	○
	9	Saikosaponin F	62687-63-2	2.1	7.75	$C_{48}H_{80}O_{17}$	928.5396	○	×	○
	10	Saikosaponin B4	58558-09-1	2.5	8.35	$C_{43}H_{72}O_{14}$	812.4922	×	○	○
5	1	L-cysteine	52-90-4	-2.5	0.82	$C_3H_7NO_2S$	121.0198	○	×	×
	2	Albiflorin	39011-90-0	-1	3.64	$C_{23}H_{28}O_{11}$	480.1632	○	○	○
	3	Galloylpaeoniflorin	122965-41-7	-0.4	4.53	$C_{30}H_{32}O_{15}$	632.1741	○	×	○
	4	Isovitexin	29702-25-8	0.2	4.19	$C_{21}H_{20}O_{10}$	432.1056	×	○	○
	5	Benzoylalbiflorin	184103-78-4	0.7	7.06	$C_{30}H_{32}O_{12}$	584.1894	×	×	○
	6	3,4-Dihydroxybenzoic acid	99-50-3	1.1	2.26	$C_7H_6O_4$	154.0266	○	×	○
	7	(α)-methoxysaikosap	104109-37-7	1.5	7.10	$C_{49}H_{82}O_{18}$	958.5501	×	×	×

		onin F								
	8	Saikosaponin I	103629-71-6	1.8	7.64	$C_{48}H_{78}O_{17}$	926.5239	×	○	○
	9	Saikosaponin B2	58316-41-9	2.5	8.87	$C_{42}H_{68}O_{13}$	780.4660	×	○	○
	10	Evodiamine	518-17-2	3.1	9.72	$C_{19}H_{17}N_3O$	303.1372	○	○	○
	1	Gardenia yellow	94238-00-3	-2.5	7.04	$C_{44}H_{64}O_{24}$	976.3788	○	×	×
	2	Vitexin-2-O-rhamnoside	64820-99-1	-0.9	4.08	$C_{27}H_{30}O_{14}$	578.1636	×	○	○
	3	Neochlorogenic acid	906-33-2	-0.4	2.32	$C_{16}H_{18}O_9$	354.0951	○	×	×
	4	Catechin	88191-48-4	0.4	2.91	$C_{15}H_{14}O_6$	290.0790	×	○	○
	5	Esculentoside A	65497-07-6	0.8	7.45	$C_{42}H_{66}O_{16}$	826.4351	○	×	○
6	6	Doxorubicin hydrochloride	25316-40-9	1.3	5.60	$C_{27}H_{29}NO_{11}$	543.1741	×	×	○
	7	trans-4-Hydroxycinnamic acid	501-98-4	1.5	4.13	$C_9H_8O_3$	164.0473	×	×	○
	8	Apigenin	520-36-5	1.7	7.05	$C_{15}H_{10}O_5$	270.0528	×	○	○
	9	Procyanidin B1	20315-25-7	2.4	2.53	$C_{30}H_{26}O_{12}$	578.1424	×	○	○
	10	Rutaecarpine	20575-76-2	3	10.00	$C_{18}H_{13}N_3O$	287.1059	×	×	×
	1	Lactiflorin	88623-95-4	-0.5	5.57	$C_{23}H_{26}O_{10}$	462.1526	×	×	○
	2	Kaempferitrin	482-38-2	-0.1	4.23	$C_{27}H_{30}O_{14}$	578.1636	×	○	○
	3	Emodin-8-glucoside	38840-23-2	0.9	6.51	$C_{21}H_{20}O_{10}$	432.1056	×	○	○

	4	p-Hydroxybenzaldehyde	123-08-0	1.4	3.69	$C_7H_6O_2$	122.0368	×	×	○
	5	Saikosaponin H	91990-63-5	1.6	7.93	$C_{48}H_{78}O_{17}$	926.5239	×	○	○
	6	(-)-Epipinoresinol	10061-38-8	2.3	1.71	$C_{20}H_{22}O_6$	358.1416	×	×	×
	7	Saikosaponin B3	58316-42-0	2.5	8.22	$C_{43}H_{72}O_{14}$	812.4922	×	×	○
	8	Ursolic Acid	77-52-1	7.3	15.89	$C_{30}H_{48}O_3$	456.3603	×	×	○
	1	Liriodendrin	96038-87-8	-1.4	3.74	$C_{34}H_{46}O_{18}$	742.2684	×	○	×
	2	kaempferol-3-rutinoside	17650-84-9	-0.9	4.51	$C_{27}H_{30}O_{15}$	594.1585	×	○	○
	3	Cryptochlorogenic acid	905-99-7	-0.4	2.94	$C_{16}H_{18}O_9$	354.0951	×	○	○
	4	epicatechin	35323-91-2	0.4	3.36	$C_{15}H_{14}O_6$	290.0790	○	○	○
8	5	4-Hydroxybenzoic acid	99-96-7	1.6	2.95	$C_7H_6O_3$	138.0317	○	×	×
	6	Pinoresinol	4263-88-1	2.3	7.16	$C_{20}H_{22}O_6$	358.1416	×	×	×
	7	Saikosaponin D	20874-52-6	2.5	10.48	$C_{42}H_{68}O_{13}$	780.4660	×	○	○
	8	Curcumin	458-37-7	3.2	9.98	$C_{21}H_{20}O_6$	368.1260	×	○	○
	9	Saikogenin D	5573-16-0	5.8	13.25	$C_{30}H_{48}O_4$	472.3553	×	×	×
	1	Oxypaeoniflora	39011-91-1	-1.4	2.71	$C_{23}H_{28}O_{12}$	496.1581	○	×	○
	2	Salvianic acid A	76822-21-4	-0.2	1.98	$C_9H_{10}O_5$	198.0528	×	×	○
	3	Isoquercitrin	21637-25-2	0.4	4.30	$C_{21}H_{20}O_{12}$	464.0955	○	○	○

	4	Polydatin	65914-17-2	1.7	4.25	$C_{20}H_{22}O_8$	390.1315	×	○	○
	5	procyanidin B2	29106-49-8	2.4	2.47	$C_{30}H_{26}O_{12}$	578.1424	×	○	○
	6	Curcumol	4871-97-0	2.8	12.31	$C_{15}H_{24}O_2$	236.1776	×	×	×
	7	Germacrone	6902-91-6	3.5	13.45	$C_{15}H_{22}O$	218.1671	×	×	×
	8	Resveratrol	501-36-0	3.1	5.66	$C_{14}H_{12}O_3$	228.0786	×	○	○
	9	Phytolaccagenin	1802-12-6	4.5	9.21	$C_{31}H_{48}O_7$	532.3400	○	○	×
	1	Genipin 1-gentiobioside	29307-60-6	-4.5	0.79	$C_{23}H_{34}O_{15}$	550.1898	×	×	×
	2	Deacetylasperulosidic acid methyl ester	52613-28-2	-3.5	2.08	$C_{17}H_{24}O_{11}$	404.1319	×	×	○
	3	(+)-medioresinol Di-o-beta-d-glucopyranoside	88142-63-6	-1.4	3.61	$C_{33}H_{44}O_{17}$	712.2579	×	×	○
	4	Liquiritin	551-15-5	0.4	4.33	$C_{21}H_{22}O_9$	418.1264	○	○	○
	5	Saikosaponin A	20736-09-8	2.5	8.89	$C_{42}H_{68}O_{13}$	780.4660	×	○	○
	6	Bisdemethoxycurcumin	33171-05-0	3.3	9.55	$C_{19}H_{16}O_4$	308.1049	×	○	○
	1	Ascorbic acid	50-81-7	-1.6	0.87	$C_6H_8O_6$	176.0321	○	×	○
	2	L-Malic acid	97-67-6	-1.3	0.88	$C_4H_6O_5$	134.0215	×	×	○
	3	Esculin	531-75-9	-0.6	2.45	$C_{15}H_{16}O_9$	340.0794	○	×	○
	4	Hyperoside	482-36-0	0.4	4.25	$C_{21}H_{20}O_{12}$	464.0955	×	○	○

	5	Dihydromyricetin	27200-12-0	1.1	3.59	$C_{15}H_{12}O_8$	320.0532	×	×	○
	6	Luteolin	286.2363	1.4	5.25	$C_{15}H_{10}O_6$	286.0477	×	○	○
	7	Umbelliferone	93-35-6	1.6	4.37	$C_9H_6O_3$	162.0317	○	×	○
	8	Fisetin	528-48-3	2	6.20	$C_{15}H_{10}O_6$	286.0477	×	○	×
	9	Naringenin	480-41-1	2.4	7.09	$C_{15}H_{12}O_5$	272.0685	×	○	○
12	1	D-(-)-Quinic acid	77-95-2	-2.4	0.83	$C_7H_{12}O_6$	192.0634	○	○	○
	2	D-(-)-Isoascorbic acid	89-65-6	-1.6	0.72	$C_6H_8O_6$	176.0321	×	×	×
	3	Kaempferol 3-o-glucorhamnoside	482-39-3	-0.4	4.54	$C_{27}H_{30}O_{15}$	594.1585	×	×	×
	4	Guaijaverin	22255-13-6	0.4	4.63	$C_{20}H_{18}O_{11}$	434.0849	×	○	○
	5	Xanthotoxol	2009-24-7	1.6	5.56	$C_9H_6O_2$	202.02661	○	×	○
	6	Daidzein	486-66-8	2.5	5.92	$C_{15}H_{10}O_4$	254.0579	×	○	○
13	1	Troxerutin	7085-55-4	-2.4	4.22	$C_{33}H_{42}O_{19}$	742.2320	×	×	○
	2	Quercetin 3-O-sophoroside	18609-17-1	-1.2	3.58	$C_{27}H_{30}O_{17}$	626.1483	×	○	×
	3	Myricetrin	17912-87-7	0.5	4.19	$C_{21}H_{20}O_{12}$	464.0955	○	×	×
	4	Daphnetin	486-35-1	1.2	3.55	$C_9H_6O_4$	178.0266	×	○	○
	5	Scopoletin	92-61-5	1.5	4.36	$C_{10}H_8O_4$	192.0423	×	×	○
	6	Icariin	489-32-7	1.7	6.39	$C_{33}H_{40}O_{15}$	676.2367	○	○	○
	7	Kaempferide	491-54-3	2.2	9.48	$C_{16}H_{12}O_6$	300.0634	×	○	○

	8	Auraptene	495-02-3	5.3	11.87	$C_{19}H_{22}O_3$	298.1569	○	×	×
14	1	Hesperidin	520-26-3	-1.1	4.58	$C_{28}H_{34}O_{15}$	610.1898	×	×	×
	2	Myricetin 3-O-galactoside	15648-86-9	0	3.71	$C_{21}H_{20}O_{13}$	480.0904	○	×	○
	3	Quercetin-3-O-glucuronide	22688-79-5	0.6	4.34	$C_{21}H_{18}O_{13}$	478.0747	○	○	○
	4	Myricetin	529-44-2	1.2	5.23	$C_{15}H_{10}O_8$	318.0376	○	○	○
	5	Herbacetin	527-95-7	2.2	5.94	$C_{15}H_{10}O_7$	302.0427	×	○	○
	6	5,5'-Dithiobis(2-nitrobenzoic acid)	69-78-3	2.7	8.04	$C_{14}H_8N_2O_8S_2$	395.9722	×	×	○
	7	Bergamotine	7380-40-7	5.6	16.99	$C_{21}H_{22}O_4$	338.1518	×	×	×
15	1	L(+)-Tartaric acid	87-69-4	-1.9	0.87	$C_4H_6O_6$	150.0164	×	×	○
	2	Narcissoside	604-80-8	-1	4.58	$C_{28}H_{32}O_{16}$	624.1690	×	○	○
	3	Adipic acid	124-04-9	0.1	2.32	$C_6H_{10}O_4$	146.0579	×	×	○
	4	isorhamnetin-3-O-glucoside	5041-82-7	0.7	4.82	$C_{22}H_{22}O_{12}$	478.1111	×	○	○
	5	3，5-Dinitrosalicylic acid	609-99-4	1.3	6.05	$C_7H_4N_2O_7$	228.0019	×	×	○
	6	（-）-Epicatechin	490-46-0	1.5	4.95	$C_{22}H_{18}O_{10}$	442.0900	×	×	×
	7	Genistein	446-72-0	2.7	7.04	$C_{15}H_{10}O_5$	270.0528	×	○	○
	1	Quercetin 3-	7431-83-6	-1.8	3.68	$C_{27}H_{30}O_{17}$	626.1483	×	○	○

	gentiobioside								
2	Avicularin	572-30-5	1	4.70	$C_{20}H_{18}O_{11}$	434.0849	×	○	○
3	Bergaptol	486-60-2	2	6.26	$C_{11}H_6O_4$	202.0266	○	×	○
4	Galangin	548-83-4	2.3	9.46	$C_{15}H_{10}O_5$	270.0528	×	○	○

Table S2. Comparison of the three computational annotation workflows on annotation rate and validation rate.

UNIFI	**MS**	**GNPS-FBMN**	**MS**	**SIRIUS-MCnebula**	**MS**
		Number of nodes	2445		
Number of observed features	27110	Number of edges	2617	Number of features	2363
		Number of connected notes	890		
Features with matched library annotations[a]	3462	Number of annotated nodes (≥ 0.7 similarity)	117	Number of annotated features	873
Annotation rate (%)[b]	12.77	Annotation rate (%)	4.79	Annotation rate (%)	36.94
Reference standard hit	35	Reference standard hit	64	Reference standard hit	102
Validation rate (%)[c]	26.52	Validation rate (%)	48.48	Validation rate (%)	77.27

a: The commercial database of UNIFI.

b: Annotation rate (%) = Number of annotated features/Number of features × 100%

c: Validation rate (%) = Number of compounds validated by the standards /Total reference standard pool (n=132) × 100%.

Table S3. Tentatively identified components of raw and processed PS extracts.

No.	RT(min)	Formula	Tentatively Identification	Ion mode	Measured Mass(m/z)	Predicted Mass(m/z)	Error (ppm)	Fragment ions(m/z)	Content variation[b]	Ref.
1	0.79	$C_{18}H_{32}O_{16}$	melitose	$[M+Na]^+$	527.1582	527.1588	1.14	365.1053 347.0946 527.1579 203.0522	↑***	
2	0.82	$C_{12}H_{22}O_{11}$	trehaose	$[M+Na]^+$	365.1052	365.1060	2.14	203.0523 265.1045 185.0415	↑***	
3	1.05	$C_6H_{10}O_8$	Allarate	$[M-H]^-$	209.0292	209.0297	2.58	85.0284 209.0292 133.0134 191.0196	↓***	
4	1.60	$C_{13}H_{16}O_{10}$	1-O-galloyl-β-D-glucose	$[M-H]^-$	331.0670	331.0665	1.45	169.0132 125.0234 331.0677 168.0054	↑***	
5	1.86	$C_{16}H_{24}O_{11}$	caryoptosidic acid	$[M-H]^-$	391.1238	391.1240	0.61	391.1238 165.0549 183.0652 139.0389	↑***	
6	2.18	$C_8H_8O_4$	pacitron	$[M+H]^+$	169.0490	169.0501	6.39	93.0340 151.0393 125.0604 110.0358	↑**	
7	2.43	$C_{10}H_{10}O_4$	2-[(4,6-dimethylpyrimidin-2-yl) amino] pentanoic acid	$[M+H]^+$	195.0646	195.0657	5.79	121.0652 149.0597 177.0536 91.0545	↑**	
8	2.43	$C_{10}H_8O_3$	[(1R,2R,5R,6S)-2,6-dihydroxy-5-[(2S,3S,4R,5R,6S)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxycyclohex-3-en-1-yl] (E)-3-(3,4-dihydroxyphenyl) prop-2-enoate	$[M+H]^+$	177.0542	177.0552	5.48	149.0596 177.0544 121.0643 131.0494 105.0701	↑***	
9	2.74	$C_8H_8O_4$	5-methoxysalicylate	$[M-H]^-$	167.0345	167.0344	0.42	152.0108 108.0202 123.0478 153.0139	↑***	

10	2.74	$C_{28}H_{36}O_{18}$	[4-[(2S,3R,4S,5R,6R)-3,5-Dihydroxy-6-(hydroxymethyl)-4-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxyoxan-2-yl] oxy-3,5-dimethoxyphenyl] methyl 3,4,5-trihydroxybenzoate	$[M-H]^-$	659.1827	659.1823	0.55	167.0338 152.0103 123.0442 108.0206	↑***	
11 [ab]	3.01	$C_{16}H_{22}O_{10}$	geniposidic acid	$[M-H]^-$	373.1137	373.1135	0.58	123.0442 149.0599 373.1136 211.0608	↑**	[1]
12	3.02	$C_{25}H_{42}O_2$	5-(n-Nonadecenyl) resorcinol	$[M-H]^-$	373.3119	373.3107	3.32	123.0442 747.2328 149.0599 373.1136	↑**	
13 [b]	3.22	$C_{22}H_{32}O_{15}$	desacetylhookerioside	$[M-H]^-$	535.1667	535.1663	0.72	123.0448 149.0615 535.1652 211.0639	↑***	[2]
14 [b]	3.37	$C_{15}H_{22}O_{10}$	catalpol	$[M-H]^-$	361.1141	361.1135	1.87	315.1088 135.0465 373.1175	↑***	[3]
15	3.43	$C_{14}H_{20}O_8$	2-(3,4-dihydroxyphenyl)-ethyl-O-β-D-glucopyranoside	$[M-H]^-$	315.1083	315.1080	0.98	135.0436 315.1129 101.0235 89.0244 113.0227	↑***	
16	3.82	$C_{16}H_{24}O_{10}$	mussaenosidic Acid	$[M-H]^-$	375.1287	375.1291	1.12	125.0595 151.0753 213.0765 101.0238 112.0242	↑***	
17	4.21	$C_{16}H_{24}O_{10}$	loganate	$[M-H]^-$	375.1297	375.1291	1.55	151.0757 169.0879 125.0596 169.0579 107.0515	↑***	
18 [b]	4.35	$C_{20}H_{30}O_{12}$	decaffeoyl acteoside	$[M-H]^-$	461.1657	461.1659	0.43	461.1656 135.0442 113.0235 315.1077	↑***	[4]
19 [b]	4.81	$C_{16}H_{22}O_{10}$	gardoside	$[M-H]^-$	373.1145	373.1135	2.76	149.0632 123.0443 167.0708 193.0450	↑**	[2]
20	5.20	$C_9H_{10}O_3$	mesotol	$[M-H]^-$	165.0549	165.0552	1.64	165.0570 137.0250 119.0507	↑***	
21	5.32	$C_8H_8O_4$	vanillate	$[M+H]^+$	169.0486	169.0501	8.75	151.0388 125.0604 110.0270 65.0377	↑*	

22	5.61	$C_{15}H_{20}O_9$	2-(beta-D-glucopyranosyloxy)-4-hydroxybenzenepropionic acid	$[M-H]^-$	343.1044	343.1029	4.34	181.0499 137.0609 135.0452 121.0216	↑	
23 [b]	5.97	$C_{18}H_{24}O_{11}$	alpinoside	$[M-H]^-$	415.1248	415.1240	1.72	161.0237 415.1281 123.0438 149.0603	↑***	2
24 [ab]	6.09	$C_8H_8O_3$	vanillin	$[M-H]^-$	151.0396	151.0395	0.76	151.0383 108.0239 138.0108 109.0291	↑***	5
25 [ab]	6.13	$C_8H_8O_4$	vanillic acid	$[M-H]^-$	167.0341	167.0344	2.01	152.0107 108.0210 123.0451 187.0381	↑**	5
26 [ab]	6.18	$C_{10}H_{10}O_4$	ferulic acid	$[M-H]^-$	193.0500	193.0501	0.41	193.0511 150.0323 108.0214 123.0458	↑***	6
27 [ab]	6.20	$C_{18}H_{22}O_{11}$	asperuloside	$[M-H]^-$	413.1090	413.1084	1.48	147.0441 119.0491 413.1089 191.0351	↑	3
28 [ab]	6.26	$C_9H_8O_4$	caffeic acid	$[M-H]^-$	179.0343	179.0344	0.73	135.0439 179.0382 134.0386 138.0478	↑***	1
29 [b]	6.70	$C_{16}H_{20}O_9$	gentiopicroside	$[M-H]^-$	355.1032	355.1029	0.82	175.0389 134.0361 193.0500 160.0159 235.0607	↓**	1
30	6.94	$C_{21}H_{22}O_{11}$	helicioside A	$[M-H]^-$	449.1097	449.1084	2.92	259.0616 269.0451 125.0235 287.0556	↓***	
31	6.95	$C_{10}H_{10}O_3$	3-Formyl-4-hydroxyphenylpropanal	$[M-H]^-$	177.0553	177.0552	0.73	177.0536 134.0365 162.0326 159.0457	↑***	
32	7.30	$C_{31}H_{40}O_{17}$	[(2S,3R,4S,5R,6S)-4,5-dihydroxy-6-[[(1S,2S,4S,5S,6R,10S)-2-(hydroxymethyl)-10-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxy-3,9-dioxatricyclo [4.4.0.02,4] dec-7-en-5-yl] oxy]-2-methyloxan-3-yl] (Z)-3-(4-hydroxy-3-methoxyphenyl) prop-2-enoate	$[M-H]^-$	683.2191	683.2187	0.56	123.0441 149.0595 165.0551 483.2098 267.0654	↑***	
33 [b]	7.99	$C_{23}H_{26}O_{11}$	calceolarioside A	$[M-H]^-$	477.1403	477.1397	1.36	161.0238 477.1407 133.0290 179.0344	↑***	7

34	8.02	$C_{15}H_{16}O_8$	skimmin	$[M+H]^+$	325.0917	325.0923	1.97	163.0388 145.0284 135.0442 117.0337	↑*	
35	8.03	$C_{15}H_{16}O_7$	(1R,5R,6R)-3,5,6-trihydroxycyclohex-3-en-1-yl (2E)-3-(3,4-dihydroxyphenyl) prop-2-enoate	$[M+H]^+$	309.0962	309.0974	3.98	163.0386 145.0281 135.0446 117.0340	↑*	
36	8.03	$C_9H_6O_3$	(E)-3-(6-Hydroxycyclohexa-1,3,5-trien-1-yl) prop-2-enoic acid	$[M+H]^+$	163.0390	163.0395	3.19	135.0442 117.0339 163.0388 89.0392	↑**	
37	8.03	$C_8H_6O_2$	4-Ethynylbenzene-1,2-diol	$[M+H]^+$	135.0439	135.0446	5.18	135.0442 89.0387 117.0335 107.0469	↑**	
38 [ab]	8.07	$C_{29}H_{36}O_{16}$	plantamajoside	$[M-H]^-$	639.1917	639.1925	1.27	161.0238 639.1923 477.1604 315.1081	↑***	[1]
39	8.20	$C_{10}H_{10}O_3$	2,4-diacetylphenol	$[M-H]^-$	177.0550	177.0552	0.96	177.0543 135.0440 133.0282 162.0312	↑***	
40	8.29	$C_{25}H_{30}O_{12}$	albidoside	$[M-H]^-$	521.1662	521.1659	0.58	175.0395 160.0154 193.0489 134.0375	↓	
41 [b]	8.31	$C_{21}H_{22}O_{12}$	plantagoside	$[M-H]^-$	465.1031	465.1033	0.43	151.0388 313.0932 303.0492 465.1030	↓	[1]
42	8.45	$C_{35}H_{46}O_{20}$	lamiuside A	$[M-H]^-$	785.2514	785.2504	1.25	161.0232 623.2169 133.0275 461.1690	↑***	
43	8.46	$C_{21}H_{26}O_{12}$	2,6-dihydroxy-5-{[3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxy} cyclohex-3-en-1-yl 3-(3,4-dihydroxyphenyl) prop-2-enoate	$[M+H]^+$	471.1498	471.1503	0.96	163.0385 145.0284 135.0442 117.0326	↑***	
44 [ab]	8.47	$C_{29}H_{36}O_{15}$	acteoside	$[M-H]^-$	623.1972	623.1976	0.65	161.0234 461.1657 623.1887 133.0285	↓	[1]
45 [b]	8.48	$C_{23}H_{26}O_{11}$	plantainoside B	$[M-H]^-$	477.1403	477.1397	1.25	161.0235 477.1403 133.0287 179.0345	↑***	[7]
46 [ab]	8.73	$C_{23}H_{26}O_{11}$	calceolarioside B	$[M-H]^-$	477.1400	477.1397	0.56	161.0234 623.1975 477.1386 315.1070	↑***	[7]
47 [ab]	8.74	$C_{29}H_{36}O_{16}$	plantainoside D	$[M-H]^-$	639.1921	639.1925	0.67	161.0235 477.1801 639.1910 315.1088	↑***	[7]
48 [ab]	8.74	$C_{29}H_{36}O_{15}$	isoacteoside	$[M-H]^-$	623.1969	623.1976	1.20	161.0238 623.1985 461.1662 315.1074	↑***	[1]

49	8.84	$C_{21}H_{22}O_{11}$	2-hydroxy-2,3-dihydro-genistein	$[M-H]^-$	449.1094	449.1084	2.25	287.0558 449.1109 166.9982 327.1256	↑**	
50 [b]	8.85	$C_{29}H_{36}O_{16}$	suspensaside	$[M-H]^-$	639.1926	639.1925	0.64	161.0237 639.1922 477.1607 135.0441	↑	[1]
51	8.97	$C_{25}H_{28}O_{12}$	(1S,4aR,6S,7aS)-1-[(2R,3S,4R,5R,6S)-4,5-dihydroxy-6-(hydroxymethyl)-3-[(E)-3-(4-hydroxyphenyl) prop-2-enoyl] oxyoxan-2-yl] oxy-6-hydroxy-7-methylidene-4a,5,6,7a-tetrahydro-1H-cyclopenta[c]pyran-4-carboxylic acid	$[M-H]^-$	519.1509	519.1503	1.25	145.0283 149.0595 163.0393 123.0447 205.0499	↑**	
52 [b]	9.00	$C_{20}H_{30}O_{12}$	verbasoside	$[M-H]^-$	461.1665	461.1659	1.20	113.0238 481.1888 135.0421 315.1027	↑***	[1]
53	9.18	$C_{33}H_{28}O_8$	8-[(5,7-Dihydroxy-6-methyl-4-oxo-2-phenyl-2,3-dihydrochromen-8-yl) methyl]-5,7-dihydroxy-6-methyl-2-phenyl-2,3-dihydrochromen-4-one	$[M-H]^-$	551.1693	551.1706	2.34	151.0395 303.0511 125.0241 177.0184	↑	
54	9.19	$C_{15}H_{12}O_6$	steppogenin	$[M+H]^+$	289.0697	289.0712	5.22	153.0177 163.0381 145.0275 289.0696	↓*	
55	9.20	$C_{26}H_{30}O_{13}$	lippianoside B	$[M-H]^-$	549.1606	549.1608	0.40	175.0391 123.0443 149.0597 193.0496 235.0603	↑***	
56 [ab]	9.27	$C_{21}H_{18}O_{12}$	homoplantaginin	$[M-H]^-$	461.1082	461.0720	78.41	283.0237 461.1012 163.0008 297.0421	↑	[8]
57	9.29	$C_{29}H_{36}O_{14}$	2-(3,4-dihydroxyphenyl) ethyl 3-O-alpha-L-rhamnopyranosyl-4-O-[(Z)-3-(4-hydroxyphenyl) propenoyl]-beta-D-glucopyranoside	$[M-H]^-$	607.2023	607.2027	0.63	161.0235 145.0286 577.1564 133.0284	↑***	
58 [b]	9.31	$C_{27}H_{30}O_{14}$	rhoifolin	$[M-H]^-$	577.1556	577.1557	0.31	269.0447 577.1551 413.0824 288.0373	↑***	[9]
59 [b]	9.53	$C_{21}H_{20}O_{10}$	cosmosiin	$[M-H]^-$	431.0983	431.0978	1.23	268.0388 431.0964 629.1978 151.0029	↑***	[8]
60 [b]	9.53	$C_{30}H_{38}O_{15}$	leucosceptoside A	$[M-H]^-$	637.2132	637.2133	0.12	175.0386 637.2107	↑***	[1]

								461.1656 315.1124		
61	9.68	$C_{21}H_{24}O_9$	2-[5-[2-(3,5-dihydroxyphenyl) ethenyl]-2-methoxyphenoxy]-6-(hydroxymethyl) oxane-3,4,5-triol	$[M-H]^-$	419.1345	419.1342	0.69	165.0547 150.0312 208.0378 223.0600	↓**	
62 [b]	9.72	$C_{15}H_{12}O_7$	5,7,3',4',5'-Pentahydroxyflavanone	$[M-H]^-$	303.0505	303.0505	0.10	151.0388 107.0088 125.0270 177.0104	↓	[5]
63 [b]	9.75	$C_{22}H_{22}O_{11}$	luteolin 7-O-β-D-glucoside	$[M-H]^-$	461.1096	461.1084	2.57	283.0237 461.1078 163.0027 297.0396	↑*	[10]
64	9.78	$C_{20}H_{18}O_6$	2,4-Bis[(2,4-dihydroxyphenyl) methyl] benzene-1,3-diol	$[M-H]^-$	353.1032	353.1025	1.95	323.0546 279.0666 338.0817 251.0694	↑**	
65 [b]	9.88	$C_{21}H_{22}O_{11}$	miscanthoside	$[M-H]^-$	449.1079	449.1084	1.13	151.0027 287.0554 135.0444 125.0233	↑	[1]
66 [b]	10.19	$C_{30}H_{38}O_{15}$	plantainoside C	$[M-H]^-$	637.2130	637.2133	0.39	175.0289 461.1710 315.1104 161.0229	↑***	[7]
67	10.25	$C_8H_8O_2$	vinylcatechol	$[M-H]^-$	135.0448	135.0446	1.48	135.0435 134.0384 117.0328	↑***	
68	10.31	$C_{30}H_{34}O_{17}$	7-[(6-O-Acetyl-2-O-beta-D-allopyranosyl-beta-D-glucopyranosyl) oxy]-5-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4H-1-benzopyran-4-one	$[M-H]^-$	665.1725	665.1718	1.10	269.0446 619.1687 577.1589 268.0363	↓*	
69	10.55	$C_{23}H_{22}O_{11}$	3-(4-Hydroxyphenyl)-5-(6-O-acetyl-beta-D-glucopyranosyloxy)-7-hydroxy-4H-1-benzopyran-4-one	$[M-H]^-$	473.1098	473.1084	2.98	268.0375 269.0450 473.1105 239.0359	↓**	
70 [b]	10.71	$C_{21}H_{18}O_{11}$	apigenin 7-glucuronide	$[M-H]^-$	445.0776	445.0771	1.15	269.0452 241.0489 197.0628 225.0568	↓***	[9]
71 [ab]	10.60	$C_{31}H_{38}O_{16}$	2′-acetylacteoside	$[M-H]^-$	665.2073	665.2082	1.2928	161.0234 133.0285 665.2136 135.0446	↑**	[11]

72	10.63	$C_{23}H_{24}O_{12}$	coccinoside A	$[M-H]^-$	491.1204	491.1190	2.95	151.0030 135.0436 287.0571 165.0579	↑	
73	10.95	$C_{20}H_{36}O_{12}$	ebracteatoside C	$[M-H]^-$	467.2125	467.2128	0.75	467.2129 289.1653 161.0445 101.0234	↑***	
74	11.05	$C_{21}H_{24}O_{11}$	roccellin	$[M+Na]^+$	475.1228	475.1216	2.46	271.0597 153.0168	↑***	
75	11.29	$C_{22}H_{26}O_8$	rayalinol	$[M-H]^-$	417.1560	417.1549	2.54	323.0577 338.0810 341.1049 267.0653	↑*	
76	11.32	$C_{20}H_{20}O_7$	averantin	$[M-H]^-$	371.1133	371.1131	0.59	267.0646 323.0553 279.0665 353.1005	↑**	
77	11.53	$C_{15}H_{12}O_6$	eriodictiol	$[M-H]^-$	287.0552	287.0556	1.25	135.0443 151.0027 489.2312 287.0582	↑**	
78	11.60	$C_{29}H_{32}O_{15}$	7-[(6-O-Acetyl-2-O-alpha-L-rhamnopyranosyl-beta-D-glucopyranosyl) oxy]-4',5-dihydroxyflavone	$[M-H]^-$	619.1664	619.1663	0.16	269.0446 268.0366 619.1662 577.1678	↑***	
79 [ab]	11.62	$C_{15}H_{10}O_6$	luteolin	$[M-H]^-$	285.0399	285.0399	0.10	285.0406 135.0448 107.0130 151.0033	↑	[1]
80	11.74	$C_{23}H_{22}O_{11}$	6-o-acetylgenistin	$[M-H]^-$	473.1087	473.1084	0.66	268.0370 473.1089 240.0434 239.0349	↑***	
81	12.18	$C_{40}H_{54}O_{17}$	[(3R,6S)-6-[(3R,6S)-6-[[(6S,7R)-4,10-dihydroxy-7-[(1S,3S,4R)-3-hydroxy-1-methoxy-2-oxo-4-propanoyloxypentyl]-6-methoxy-3-methyl-5-oxo-7,8-dihydro-6H-anthracen-2-yl] oxy]-3-hydroxy-2-methyloxan-4-yl] oxy-3-hydroxy-2-methyloxan-4-yl] propanoate	$[M-H]^-$	805.3298	805.3282	1.89	651.2434 805.3303 490.2004 773.3055	↓**	
82	12.28	$C_{31}H_{30}O_{14}$	(2R)-2beta-(3,4-Dihydroxyphenyl)-5-hydroxy-7-[6-O-[3-(3-methoxy-4-hydroxyphenyl) acryloyl]-beta-D-glucopyranosyloxy]-3,4-dihydro-2H-1-benzopyran-4-one	$[M-H]^-$	625.1573	625.1557	2.51	151.0030 135.0439 287.0556 337.0917	↑	

83 [b]	12.86	$C_{15}H_{10}O_5$	baicalein	$[M-H]^-$	269.0449	269.0450	0.42	269.0459 151.0038 117.0385 201.0516	↑***	[12]
84 [ab]	12.87	$C_{15}H_{10}O_5$	apigenin	$[M-H]^-$	269.0447	269.0450	1.20	269.0454 117.0349 151.0044 225.0579	↑***	[13]
85	12.92	$C_{32}H_{54}O_{16}$	[(2R,3S,4R,5R,6R)-6-[Acetyloxy-[(2S,3S,4R,5R)-4-acetyloxy-2-hydroxy-5-(hydroxymethyl)-3-(5-methylheptanoyloxy) oxolan-2-yl] methoxy]-4,5-dihydroxy-2-(hydroxymethyl) oxan-3-yl] 5-methylheptanoate	$[M-H]^-$	693.3338	693.3334	0.63	311.2586 355.2484 693.3333 337.2389	↓*	
86	14.76	$C_{30}H_{48}O_6$	brahmic acid	$[M-H]^-$	503.3363	503.3373	1.91	503.3370 401.3070 485.3274 459.3509	↓	
87	24.78	$C_{30}H_{46}O_2$	(6aR,6bR,12aR,14bS)-2,2,6a,6b,9,9,12a-heptamethyl-10-oxo-3,4,5,6,6a,7,8,8a,11,12,13,14b-dodecahydro-1H-picene-4a-carbaldehyde	$[M+H]^+$	439.3573	439.3576	0.71	203.1787 189.1632 119.0857 149.1326	↓*	
88	24.92	$C_{18}H_{30}O_2$	crepenynate	$[M-H]^-$	277.2168	277.2168	0.14	277.2169 259.2067 275.2018 233.2277	↓*	
89 [ab]	25.06	$C_{30}H_{48}O_3$	ursolic acid	$[M-H]^-$	455.3527	455.3525	0.40	455.3525 407.3335 409.3466	↓***	[14]

[a] Comparison with reference standards.

[b] "↑" indicates the increased levels of the compound contents after processing; "↓" indicates the decrease levels of the compound contents after processing; *, $P<0.05$; **, $P<0.01$; ***, $P<0.001$.

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