

Supporting Information

Non-targeted metabolite profiling and specific targeted discrimination
strategy for quality evaluation of Cortex Phellodendri from different
varieties

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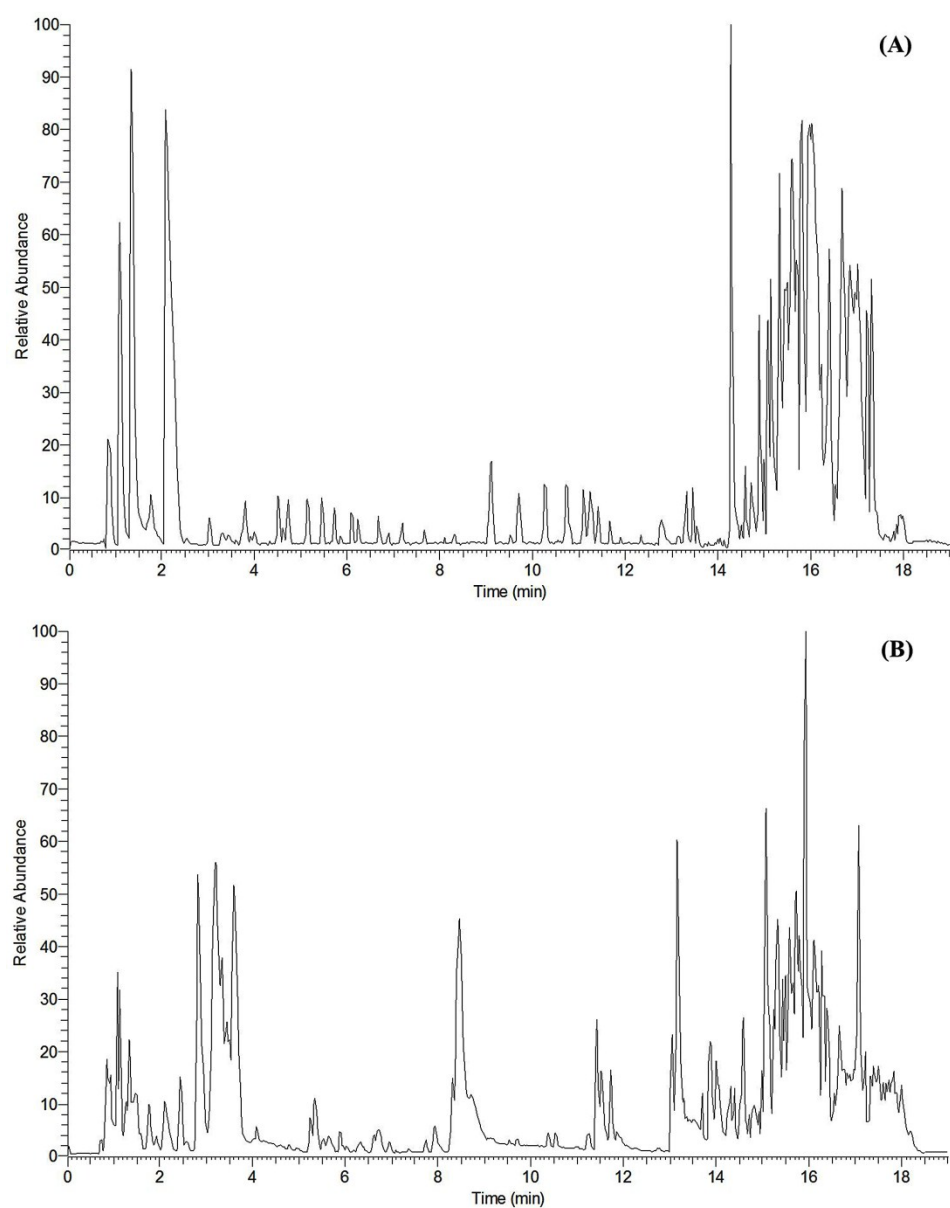


Fig.S1 The UHPLC-Q-Orbitrap MS total ion chromatograms of *HB*-containing plasma after oral administration of *HB* in negative ion mode and positive mode in positive (A) and negative ion mode (B)

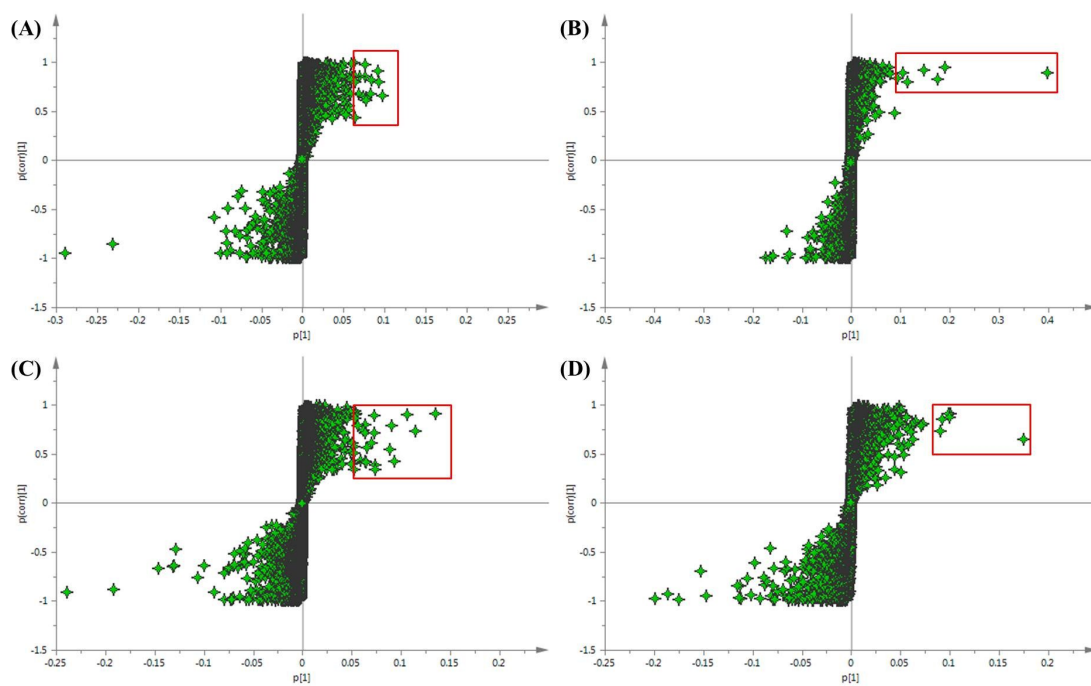


Fig.S2 S-plot of OPLS-DA model between blank plasma samples and *HB*-containing plasma samples in positive ion mode (A) and negative ion mode (B); S-plot of OPLS-DA model between blank plasma samples and *GHB*-containing plasma samples in positive ion mode (C) and negative ion mode (D)

Table S1. Identification of prototype constituents of *HB* and *GHB* in rat plasma by UHPLC-Q-Orbitrap MS

No.	t_R (min)	Formula	Determined mass/Da [M+H] ⁺ /[M-H] ⁻ /[M] ⁺ (m/z)	Error/p pm	MS/MS		Identification
					ESI ⁺	ESI ⁻	
P1	1.07	C ₁₁ H ₁₈ NO	180.1377	-6.106	121.0647[M-C ₃ H ₁₀ N] ⁺		N-Candicine
P2	1.14	C ₁₃ H ₁₆ O ₁₀	331.0673	0.602		313.0570[M-H-H ₂ O] ⁻ 168.0057[M-H-GLc] ⁻ 125.0232[M-C ₇ H ₄ O ₅ -2H ₂ O] ⁻	b-Glucogallin
P3	3.61	C ₂₀ H ₂₄ NO ₄	342.1700	-1.461	297.1103[M-OCH ₃ -CH ₃] ⁺ 192.1020[M-C ₉ H ₁₁ O ₂] ⁺ 177.0744[M-C ₉ H ₁₁ O ₂ -CH ₃] ⁺		Phellodendrine
P4	3.87	C ₁₉ H ₂₄ NO ₃	314.1759	0.955	297.1910[M-OH] ⁺ 269.1610[M-(CH ₃) ₂ NH] ⁺ 177.1124[M-(CH ₃) ₂ NH] ⁺		Oblongine
P5	4.38	C ₂₀ H ₂₄ NO ₄	342.1703	-0.585	297.0685[M-(CH ₃) ₂ NH] ⁺ 192.0322[M-(CH ₃) ₂ NH-CH ₃ OH-CO-C ₂ H ₄] ⁺		Magnoflorine
P6	4.80	C ₁₇ H ₂₀ O ₉	367.0969	8.635		191.0554[M-H-C ₁₀ H ₈ O ₃] ⁻ 173.0446[M-H-C ₁₀ H ₁₁ O ₄] ⁻ 134.0360[M-H-CH ₃ -C ₈ H ₁₀ O ₇] ⁻ 111.0440[M-H-C ₁₀ H ₉ O ₄ -CO ₂ -OH] ⁻	3-O-feruloylquinic acid
P7	5.49	C ₁₉ H ₂₄ NO ₃	314.1752	-1.273	299.1514[M-CH ₃] ⁺ 269.1175[M-N(CH ₃) ₂] ⁺ 237.0911[M-N(CH ₃) ₂ CH ₂ -OH] ⁺ 192.1023[M-CH ₃ -C ₇ H ₈ O] ⁺ 143.0494[M-C ₉ H ₁₈ NO ₂] ⁺ 107.0497[M-C ₁₂ H ₁₈ NO ₂] ⁺		Lotusine

P8	6.03	C ₂₀ H ₁₇ NO ₅	352.1183	1.139	336.1231[M+H-CH ₄] ⁺ 322.0488[M+H-2CH ₃] ⁺ 308.0910[M+H-CH ₄ O-CH ₃] ⁺ 276.1267[M+H-CH ₂ O ₂ -2CH ₃] ⁺	Oxyberberine
P9	6.55	C ₂₁ H ₂₆ NO ₄	356.1843	-5.334	311.1267[M-C ₂ H ₇ N] ⁺ 296.1034[M-4CH ₃] ⁺ 279.1007[M-C ₂ H ₇ N-OCH ₃] ⁺ 192.1013[M-C ₁₀ H ₁₃ O ₂] ⁺ 165.0904[M-C ₁₀ H ₁₃ O ₂ -2CH ₃] ⁺	Menisperine
P10	6.81	C ₂₀ H ₂₆ NO ₃	328.1911	-0.609	283.1754[M-N(CH ₃) ₂] ⁺ 269.1384[M-N(CH ₃) ₂ CH ₂] ⁺ 254.0479[M-N(CH ₃) ₂ CH ₂ -CH ₃] ⁺ 206.0851[M-CH ₃ -C ₇ H ₆ O] ⁺	Armepavine
P11	7.59	C ₁₉ H ₁₆ NO ₄	322.1207	-6.209	307.0835[M-CH ₃] ⁺ 292.1150[M-2CH ₃] ⁺	Berberrubine
P12	7.62	C ₂₁ H ₂₆ NO ₄	356.1841	-5.896	192.1012[M-C ₉ H ₁₁ O ₂] ⁺ 177.0744[M-C ₉ H ₁₁ O ₂ -CH ₃] ⁺	Tetrahydropalmatine
P13	10.81	C ₂₀ H ₁₈ NO ₄	336.1230	-1.785	321.0995[M-CH ₃] ⁺ 320.0917[M-CH ₄] ⁺ 307.1204[M-2CH ₃] ⁺ 306.0763[M-CH ₄ -CH ₃] ⁺ 292.0967[M-CH ₄ -CO] ⁺	Berberine
P14	13.59	C ₁₈ H ₃₄ O ₅	329.2325	2.422	311.2219[M-H-HO] ⁻ 293.2109[M-H-2HO] ⁻ 229.1437[M-H-HO-C ₆ H ₁₀ O] ⁻ 211.1328[M-H-CO ₂ -(CH ₂) ₄ CH ₃] ⁻ 171.1013[M-H-OH-(CH ₂) ₈ CH ₃ OH] ⁻	Sanleng acid

P15	14.39	C ₂₁ H ₂₂ NO ₄	352.1544	-1.42	336.1233[M-CH ₃] ⁺ 320.1275[M-CH ₃ -CH ₄] ⁺ 308.1278[M-CH ₃ -CO] ⁺	Palmatine
P16	15.11	C ₂₀ H ₂₀ NO ₄	338.1388	-1.183	323.1149[M-CH ₃] ⁺ 308.1252[M-2CH ₃] ⁺ 307.1202[M-CH ₃ -CH ₄] ⁺	Columbamine
P17	16.40	C ₂₀ H ₂₀ NO ₄	338.1386	-1.774	323.1146[M-CH ₃] ⁺ 322.1071[M-CH ₄] ⁺ 308.1247[M-2CH ₃] ⁺ 307.1201[M-2CH ₃ -H] ⁺ 294.1118[M-CH ₄ -CO] ⁺ 280.1332[M-2CH ₃ -CO] ⁺	Jatrorrhizine

Table S2 Identification of metabolites of *HB* and *GHB* in rat plasma by UHPLC-Q-Orbitrap MS

No.	t_R (min)	Formula	Determined mass/Da [M+H] ⁺ /[M-H] ⁻ /[M] ⁺ (m/z)	Error/p pm	MS/MS		Identification
					ESI ⁺	ESI ⁻	
M1	1.35	C ₂₄ H ₂₈ NO ₉	474.1764	0	298.1439[M-GluA] ⁺ 283.1191[M-GluA-CH ₃] ⁺ 268.1323[M-GluA-CH ₃ -CH ₃] ⁺		Hydroxymethyl armepavine-O- glucuronide
M2	1.47	C ₂₆ H ₃₂ NO ₁₀	518.2007	-3.667	342.1688[M-GluA] ⁺ 192.1012[M-GluA-C ₉ H ₁₁ O ₂] ⁺ 177.0762[M-GluA-C ₉ H ₁₁ O ₂ -CH ₃] ⁺		Phellodendrine-O- glucuronide
M3	1.88	C ₂₄ H ₂₈ NO ₉	474.1746	-3.796	298.1439[M-GluA] ⁺ 283.1191[M-GluA-CH ₃] ⁺		Hydroxymethyl armepavine-O- glucuronide
M4	2.56	C ₂₆ H ₃₂ NO ₁₀	518.2026	0	342.1700[M-GluA] ⁺ 192.1020[M-GluA-C ₉ H ₁₁ O ₂] ⁺ 177.0782[M-GluA-C ₉ H ₁₁ O ₂ -CH ₃] ⁺		Magnoflorine-O- glucuronide
M5*	2.76	C ₁₇ H ₂₀ O ₁₂ S	447.0618	3.348		367.1035[M-SO ₃ -H] ⁻ 193.0498[M-SO ₃ -H-C ₇ H ₁₁ O ₆] ⁻ 191.0554[M-SO ₃ -H-C ₁₀ H ₉ O ₄] ⁻ 175.0232[M-SO ₃ -H-C ₇ H ₁₁ O ₆ -H ₂ O] ⁻ 173.0447[M-SO ₃ -H-C ₁₀ H ₉ O ₄ -H ₂ O] ⁻	Sulfated 3-O- feruloylquinic acid
M6*	2.96	C ₁₇ H ₂₀ O ₁₂ S	447.0613	2.232		367.1040[M-SO ₃ -H] ⁻ 193.0499[M-SO ₃ -H-C ₇ H ₁₁ O ₆] ⁻ 191.0554[M-SO ₃ -H-C ₁₀ H ₉ O ₄] ⁻ 175.0495[M-SO ₃ -H-C ₇ H ₁₁ O ₆ -H ₂ O] ⁻ 173.0447[M-SO ₃ -H-C ₁₀ H ₉ O ₄ -H ₂ O] ⁻	Sulfated 5-O- feruloylquinic acid

M7	3.49	C ₃₁ H ₃₄ NO ₁₆	676.1898	2.958	500.1556[M-GluA] ⁺ 324.1231[M-2GluA] ⁺ 309.1003[M-2GluA-CH ₃] ⁺ 308.0921[M-2GluA-CH ₄] ⁺	2, 3-di -O-glucuronide demethyleneberberin e
M8	3.74	C ₁₇ H ₂₂ NO ₉	384.1141	-4.009	208.0969[M-GluA] ⁺	Armepavine metabolites
M9	4.64	C ₂₅ H ₂₄ NO ₁₁	514.1737	7.547	338.1388[M-GluA] ⁺ 323.1147[M-GluA-CH ₃] ⁺ 308.0923[M-GluA-2CH ₃] ⁺	Jatrorrhizine-3-O-β- D-glucuronide
M10	5.59	C ₂₅ H ₂₆ NO ₁₀	500.1556	-0.200	324.1231[M-GluA] ⁺ 309.0992[M-GluA-CH ₃] ⁺ 294.0734[M-GluA-CH ₃] ⁺ 280.0978[M-GluA-CH ₄ -CO ₂] ⁺	Demethyleneberberin e-O-glucuronide
M11	5.71	C ₂₆ H ₂₈ NO ₁₀	514.1716	0.583	338.1318[M-GluA] ⁺ 323.1151[M-GluA-CH ₃] ⁺ 322.1088[M-GluA-CH ₄] ⁺	Columbamine-2-O-β- D-glucuronide
M12	6.41	C ₂₅ H ₂₄ NO ₁₀	498.1375	-5.019	322.1061[M-GluA] ⁺ 307.0812[M-GluA-CH ₃] ⁺	Berberrubine-9-O-β- D-glucuronide
M13	6.93	C ₁₈ H ₁₄ NO ₆	340.1535	4.117	322.0711[M-H ₂ O] ⁺ 307.0475[M-H ₂ O-CH ₃] ⁺ 279.0536[M-H ₂ O-CH ₃ -CO] ⁺	Hydroxyldemethylen eberberine
M14	7.85	C ₂₆ H ₂₆ NO ₁₃ S	592.1170	7.600	416.0801[M-GluA] ⁺ 336.1233[M-GluA-SO ₃] ⁺ 321.1005[M-GluA-SO ₃ -CH ₃] ⁺ 306.0764[M-GluA-SO ₃ -2CH ₃] ⁺ 278.0815[M-GluA-SO ₃ -2CH ₃ -CO] ⁺	Berberine-O-sulfate- O-glucuronide

M15	8.30	C ₁₉ H ₁₈ NO ₄	324.0773	5.245	308.1785[M-CH ₄] ⁺ 293.0962[M-CH ₄ -CH ₃] ⁺ 266.0475[M-CH ₄ -CH ₃ -CO] ⁺	Demethyleneberberine
M16	8.71	C ₂₀ H ₂₀ NO ₆	370.1288	-0.811	352.1179[M-H ₂ O] ⁺ 337.0941[M-H ₂ O-CH ₃] ⁺ 308.0917[M-H ₂ O-CH ₃ -CO] ⁺ 293.1202[M-H ₂ O-2CH ₃ -CO] ⁺	Dihydroxyjatrorrhizine/Dihydroxycolumbamine
M17	9.11	C ₁₉ H ₁₆ NO ₆	354.0972	-1.694	336.0866[M-H ₂ O] ⁺ 321.0631[M-H ₂ O-CH ₃] ⁺ 306.0399[M-H ₂ O-2CH ₃] ⁺ 292.0605[M-H ₂ O-CH ₃ -CO-CH ₄] ⁺	Hydroxycolumbamine
M18	9.26	C ₁₉ H ₁₆ NO ₆	354.0975	-0.847	336.0866[M-H ₂ O] ⁺ 321.0631[M-H ₂ O-CH ₃] ⁺ 292.0602[M-H ₂ O-CH ₃ -CO-CH ₄] ⁺	Hydroxyjatrorrhizine
M19*	9.38	C ₁₉ H ₁₈ NO ₇ S	404.0830	6.434	324.1426[M-SO ₃] ⁺ 309.0901[M-SO ₃ -CH ₃] ⁺ 308.1193[M-SO ₃ -CH ₄] ⁺ 294.0871[M-SO ₃ -2CH ₃] ⁺ 280.0632[M-SO ₃ -2CH ₃ -CH ₂] ⁺	Demethyleneberberine-2-O-sulfate
M20	10.49	C ₂₀ H ₂₀ NO ₇ S	418.1138	6.697	338.1389[M-SO ₃] ⁺ 323.0374[M-SO ₃ -CH ₃] ⁺ 322.0476[M-SO ₃ -CH ₄] ⁺ 294.0794[M-SO ₃ -CH ₄ -CO] ⁺	Jatrorrhizine-3-O-sulfate

M21	10.57	C ₂₀ H ₂₀ NO ₇ S	418.1138	6.697	338.1389[M-SO ₃] ⁺ 323.0377[M-SO ₃ -CH ₃] ⁺ 322.0482[M-SO ₃ -CH ₄] ⁺	Columbamine-2-O-sulfate
M22	13.10	C ₂₁ H ₂₂ NO ₅	368.1130	-7.606	350.1024[M-CH ₃] ⁺ 336.0851[M-CH ₄ O] ⁺ 322.1076[M-CH ₄ O-CH ₂] ⁺ 307.0841[M-CH ₄ O-CH ₂ -CH ₃] ⁺ 292.0600[M-CH ₄ O-CH ₂ -2CH ₃] ⁺	Hydroxylpalmatine

* found for the first time in this herb after intragastric administration in rats