

Supplementary table 1. Composition of Pien Tze Huang by online PLE-UHPLC-IT-TOF-MS method.

Component	NO	Retention n	m/z	Formula	Putative identity
<i>Notoginseng radix et rhizoma (36)</i>	1	5.52	549.1841	C ₂₂ H ₃₂ O ₁₃	notoginsenic acid β-sophoroside [#]
	2	5.87	861.4828	C ₄₂ H ₇₂ O ₁₅	notoginsenoside SP1 [#]
	3	6.68	592.2883	C ₅₃ H ₉₀ O ₂₃	yesanchinoside-H
	4	6.89	1007.5416	C ₄₈ H ₈₂ O ₁₉	notoginsenoside R3/notoginsenoside R6/20-O-glucoginsenoside Rf
	5	7.17	879.5001	C ₄₂ H ₇₄ O ₁₆	notoginsenoside J/isomer [#]
	6	7.24	1007.5425	C ₄₈ H ₈₂ O ₁₉	notoginsenoside R3/notoginsenoside R6/20-O-glucoginsenoside Rf
	7	7.31	879.5001	C ₄₂ H ₇₄ O ₁₆	notoginsenoside J/isomer [#]
	8	7.48	977.5323	C ₄₈ H ₈₂ O ₂₀	notoginsenoside ST-5
	9	7.52	931.5273	C ₄₇ H ₈₀ O ₁₈	notoginsenoside R1*
	10	7.57	931.5273	C ₄₇ H ₈₀ O ₁₈	notoginsenoside R1 isomer
	11	7.68	991.5496	C ₄₈ H ₈₂ O ₁₈	notoginsenoside K/isomer
	12	7.76	845.4865	C ₄₂ H ₇₂ O ₁₄	ginsenoside Rg1 [#]
	13	7.85-	845.495	C ₄₂ H ₇₂ O ₁₄	ginsenoside Rf*
	14	8.50	815.4782	C ₄₁ H ₇₀ O ₁₃	notoginsenoside R2/pseudoginsenoside RT3/isomer
	15	8.55	1239.6423	C ₅₉ H ₁₀₀ O ₂₇	notoginsenoside Ra3/ginsenoside R4/notoginsenoside Fa
	16	8.71	1239.6360	C ₅₉ H ₁₀₀ O ₂₇	ginsenoside Ra3/notoginsenoside R4/notoginsenoside Fa [#]
	17	8.78	1239.6407	C ₅₉ H ₁₀₀ O ₂₇	ginsenoside Ra3/notoginsenoside R4/notoginsenoside Fa [#]
	18	11.47	947.5239	C ₄₆ H ₇₈ O ₁₇	chikusetsusaponin L5
	19	13.01	1107.5913	C ₅₄ H ₉₂ O ₂₃	ginsenoside Rb1 [#]
	20	13.4	1107.5999	C ₅₄ H ₉₂ O ₂₃	yesanchinoside-E [#]
	21	13.75	815.4796	C ₄₁ H ₇₀ O ₁₃	notoginsenoside R2/pseudoginsenoside RT3/isomer
	22	15.06	815.4758	C ₄₁ H ₇₀ O ₁₃	notoginsenoside R2/pseudoginsenoside RT3/isomer
	23	19.31	991.5481	C ₄₈ H ₈₂ O ₁₈	gypeniside VIII
	24	19.89-	991.5483	C ₄₈ H ₈₂ O ₁₈	ginsenoside Rd*
	25	20.03-	945.5457	C ₄₈ H ₈₂ O ₁₈	ginsenoside Re*
	26	20.47	683.4354	C ₃₆ H ₆₂ O ₉	ginsenoside Rh1/isomer [#]
	27	21.57	945.5458	C ₄₈ H ₈₂ O ₁₈	notoginsenoside K/isomer
	28	22.95	683.4376	C ₃₆ H ₆₂ O ₉	ginsenoside Rh1/isomer [#]
	29	26.05	915.5297	C ₄₇ H ₈₀ O ₁₇	gypeniside IX

	30	27.16	815.4796	C ₄₁ H ₇₀ O ₁₃	notoginsenoside R2/pseudoginsenoside RT3/isomer
	31	30.95-	829.4933	C ₄₂ H ₇₂ O ₁₃	ginsenoside Rg2*
	32	31.67	829.4918	C ₄₂ H ₇₂ O ₁₃	ginsenoside Rg3 isomer
	33	33.96-	829.4933	C ₄₂ H ₇₂ O ₁₃	ginsenoside F2*
	34	36.57	665.4277	C ₃₇ H ₆₂ O ₁₀	notoginsenoside T2/isomer
	35	39.23	829.4974	C ₄₂ H ₇₂ O ₁₃	ginsenoside Rg3*
	36	43.57	667.4365	C ₃₆ H ₆₂ O ₈	ginsenoside Rh2*
	37	8.06	530.2765	C ₂₆ H ₄₅ NO ₈ S	tauro-3 α , 7 α , 12 α , 23R-tetrahydroxy-5 β -cholenoic acid/isomer
	38	8.11	530.2776	C ₂₆ H ₄₅ NO ₈ S	tauro-3 α , 7 α , 12 α , 23R-tetrahydroxy-5 β -cholenoic acid/isomer
	39	8.39	530.2762	C ₂₆ H ₄₅ NO ₈ S	tauro-3 α , 7 α , 12 α , 23R-tetrahydroxy-5 β -cholenoic acid/isomer
	40	8.48	512.2667	C ₂₆ H ₄₃ NO ₇ S	tauro- Δ 8-3 β , 7 α , 12 α -trihydroxy-5 β -cholenoic acid/isomer
	41	8.6	530.2766	C ₂₆ H ₄₅ NO ₈ S	tauro-3 α , 7 α , 12 α , 23R-tetrahydroxy-5 β -cholenoic acid/isomer
	42	8.64	512.2674	C ₂₆ H ₄₃ NO ₇ S	tauro- Δ 8-3 β , 7 α , 12 α -trihydroxy-5 β -cholenoic acid/isomer
<i>Snake Bile (15)</i>	43	8.99-	423.2731	C ₂₄ H ₄₀ O ₆	3 α , 6 β , 7 α , 12 α -tetrahydroxy bile acid/isomer
	44	9.09	530.2767	C ₂₆ H ₄₅ NO ₈ S	tauro-3 α , 7 α , 12 α , 23R-tetrahydroxy-5 β -cholenoic acid/isomer
	45	9.27	512.2666	C ₂₆ H ₄₃ NO ₇ S	tauro-3 α , 7 α -dihydroxy-12-oxo-5 β -cholenoic acid/isomer
	46	12.52	512.2686	C ₂₆ H ₄₃ NO ₇ S	tauro-3 α , 7 α -dihydroxy-12-oxo-5 β -cholenoic acid/isomer
	47	15.55	530.2770	C ₂₆ H ₄₅ NO ₈ S	tauro-3 α , 7 α , 12 α , 23R-tetrahydroxy-5 β -cholenoic acid/isomer
	48	16.13-	423.274	C ₂₄ H ₄₀ O ₆	3 α , 6 β , 7 α , 12 α -tetrahydroxy bile acid/isomer
	49	17.79-	423.2737	C ₂₄ H ₄₀ O	3 α , 6 β , 7 α , 12 α -tetrahydroxy bile

					acid/isomer
	50	18.58-	423.2731	C ₂₄ H ₄₀ O ₆	3 α , 6 β , 7 α , 12 α -tetrahydroxy bile acid/isomer
	51	25.82-	487.2368	C ₂₄ H ₄₀ O ₈ S	cholic acid-sulfate
<i>Bovis Calculus</i> (9)	52	24.42	498.2879	C ₂₆ H ₄₅ NO ₆ S	taurodeoxycholic acid [#]
	53	29.5	448.3042	C ₂₆ H ₄₃ NO ₅	glycochenodeoxycholic acid
	54	37.39-	465.3209	C ₂₇ H ₄₆ O ₆	tetrahydroxycholestan-26-oic acid [#]
	55	38.65-	391.2815	C ₂₄ H ₄₀ O ₄	ursodeoxycholic acid*
	56	40.56-	391.2838	C ₂₄ H ₄₀ O ₄	hyodeoxycholic acid*
	57	40.76-	389.2681	C ₂₄ H ₃₈ O ₄	ketodeoxycholic acid [#]
	58	41.52-	391.2838	C ₂₄ H ₄₀ O ₄	chenodeoxycholic acid*
	59	42.50-	391.2838	C ₂₄ H ₄₀ O ₄	deoxycholic acid [#]
	60	44.24-	421.2950	C ₂₅ H ₄₂ O ₅	methyl cholate
Common ingredients of <i>Bovis Calculus</i> and <i>Snake Bile</i> (11)	61	9.58	514.2820	C ₂₆ H ₄₅ NO ₇ S	taurocholic acid/tauro-3 α , 7 α , 12 α -trihydroxy-5 α -cholenoic acid/isomer
	62	10	514.2827	C ₂₆ H ₄₅ NO ₇ S	taurocholic acid/tauro-3 α , 7 α , 12 α -trihydroxy-5 α -cholenoic acid/isomer
	63	10.42	514.2846	C ₂₆ H ₄₅ NO ₇ S	taurocholic acid/tauro-3 α , 7 α , 12 α -trihydroxy-5 α -cholenoic acid/isomer
	64	10.84	514.2825	C ₂₆ H ₄₅ NO ₇ S	taurocholic acid/tauro-3 α , 7 α , 12 α -trihydroxy-5 α -cholenoic acid/isomer
	65	17.11	405.2623	C ₂₄ H ₃₈ O ₅	3 α , 12 α -dihydroxy-7-oxo-5 β -cholic acid/isomer
	66	18.98-	464.3001	C ₂₆ H ₄₃ NO ₆	glycocholic acid*
	67	22.34	405.2607	C ₂₄ H ₃₈ O ₅	3 α , 12 α -dihydroxy-7-oxo-5 β -cholic acid/isomer
	68	23.48	498.2881	C ₂₆ H ₄₅ NO ₆ S	taurochenodeoxycholic acid*
	69	25.56	405.2633	C ₂₄ H ₃₈ O ₅	3 α , 12 α -dihydroxy-7-oxo-5 β -cholic acid/isomer
	70	26.79-	407.2785	C ₂₄ H ₄₀ O ₅	cholic acid*
	71	32.56	448.3054	C ₂₆ H ₄₃ NO ₅	glycodeoxycholic acid [#]
72	44.62-	299.2565	C ₁₈ H ₃₆ O ₃	unknown	
73	45.29-	795.5396	C ₄₃ H ₇₆ N ₂ O	unknown	

References

- Li, W., Jiang, Z., Li, H., Tu, P., Song, Q., Yu, J., Song, Y., 2021. [Chemome profiling of Pien-Tze-Huang by online pressurized liquid extraction-ultra-high performance liquid chromatography-ion trap-time-of-flight mass spectrometry]. *Se Pu*. 39, 478-487.
- Huang, Z., Zhou, X., Zhang, X., Huang, L., Sun, Y., Cheng, Z., Xu, W., Li, C.G., Zheng, Y., Huang, M., 2021. Pien-Tze-Huang, a Chinese patent formula, attenuates NLRP3 inflammasome-related neuroinflammation by enhancing autophagy via the AMPK/mTOR/ULK1 signaling pathway. *Biomed Pharmacother*. 141, 111814.
- Xu, W., Zhang, Y., Zhou, C., Tai, Y., Zhang, X., Liu, J., Sha, M., Huang, M., Zhu, Y., Peng, J., Lu, J.J., 2017. Simultaneous quantification six active compounds in rat plasma by UPLC-MS/MS and its application to a pharmacokinetic study of Pien-Tze-Huang. *J Chromatogr B Analyt Technol Biomed Life Sci*. 1061-1062, 314-321.

Supplementary table 2. Scoring system of Ishak's modified HAI.

Score	Periportal or periseptal interface hepatitis (piecemeal necrosis)	Confluent necrosis	Focal (spotty) lytic necrosis, apoptosis and focal inflammation	Portal inflammation
0	Absent	Absent	Absent	None
1	Mild (focal, few portal areas)	Focal confluent necrosis	One focus or less per 10×objective	Mild, some or all portal areas
2	Mild/moderate (focal, most portal areas)	Zone 3 necrosis in some areas	Two to four foci per 10×objective	Moderate, some or all portal areas
3	Moderate (continuous around 60% of tracts or septa)	Zone 3 necrosis in most areas	Five to ten foci per 10×objective	Moderate/marked, all portal areas
4	Severe (continuous around >50% of tracts or septa)	Zone 3 necrosis+occasional portal-central (P-C) bridging	More than ten foci per 10×objective	Marked, all portal areas
5		Zone 3 necrosis+multiple P-C bridging		
6		Panacinar or multiacinar necrosis		

References

- Ishak, K., Baptista, A., Bianchi, L., Callea, F., De Groote, J., Gudat, F., Denk, H., Desmet, V., Korb, G., MacSween, R.N., 1995. Histological grading and staging of chronic hepatitis. *J Hepatol.* 22, 696-699.