Supplemental Data to Drug metabolism and Disposition

Low cerebral exposure cannot hinder the neuroprotective effects of panax notoginsenosides

Haofeng Li, Jingcheng Xiao, Xinuo Li, Huimin Chen, Dian Kang, Yuhao Shao, Boyu Shen, Zhangpei Zhu, Xiaoxi Yin, Lin Xie, Guangji Wang, Yan Liang

Key Lab of Drug Metabolism & Pharmacokinetics, State Key Laboratory of Natural Medicines, China Pharmaceutical University, Tongjiaxiang 24, Nanjing 210009, China

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Table S1 Primer sequences used for RT-PCR of rat GABAA and GABAB receptor subunits.

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Figure S1 Sequence number of intestinal flora in control, I/R, I/R + PNE, PGF, PGF + I/R and PGF + I/R + PNE rats at each level of classification (Kingdom, Phylum, Class, Order, Family, Genus and Species).

Figure S2 Relative abundance of the dominant bacterial in the rat intestinal microflora. (A) Relative abundance of the dominant bacterial at phylum level. (B) Relative abundance of the dominant bacterial at class level. (C) Relative abundance of the dominant bacterial at order level.

Supplemental Table 1 Primer sequences used for RT-PCR of rat GABAA and GABAB receptor subunits

Target	Primer	Sequence 5'–3'	Annealing (◦C)
GAPDH	GA-F	ATTGTCAGCAATGCATCCTG	60
	GA-R	ATGGACTGTGGTCATGAGCC	
GABA-$A_{\alpha 2}$	$A_{\alpha 2}$-F	ACAAGAAGCCAGAGAACAAGCCAG	60
	$A_{\alpha 2}$-R	GAGGTCTACTGGTAAGCTCTACCA	
GABA-$A_{\beta 2}$	$A_{\beta 2}$-F	TGAGATGGCCACATCAGAAGC	60
	$A_{\beta 2}$-R	TCATGGGAGGCTGGAGTTTAGTTC	
GABA-A_{y2}	A_{y2}-F	TGTGAGCAACCGGAAACCAAGCAA	60
	A_{y2}-R	CGTGTGATTCAGCGAATAAGACCC	
GABA-B_{R1b}	GABA-B_{R1b}-F	CGCTGCCTCTTCTGCTGGTG	60
	GABA-B_{R1b}-R	GTCACACTTGCTGTCGTGGT	
GABA-B_{R2}	GABA-B_{R2}-F	CGGAGGTGAGCGTGCGTCTG	60
	GABA-B_{R2}-R	CGGAGGTGAGCGTGCGTCTG	

GAPDH was used as reference gene.

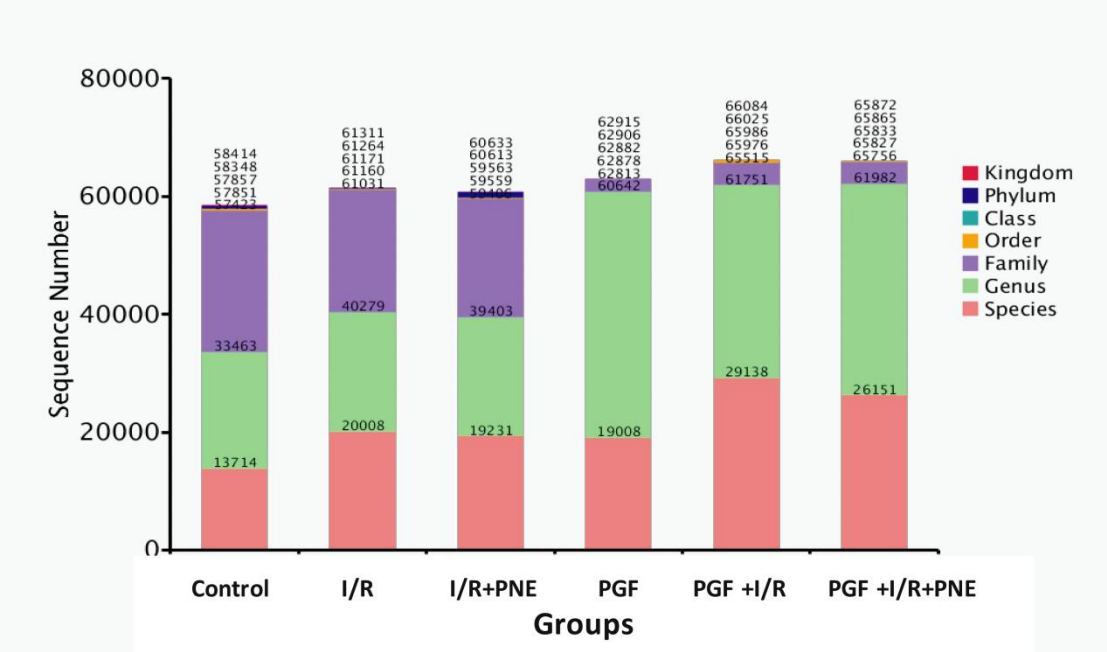
Supplemental Table 2 Optimized MRM parameters (collision energy (CE), Q1 Pre Bias and Q3 Pre Bias) of notoginsenoside Re, Rb1, Rg1, Rb2, Rd, R1 and internal standard.

Analytes	Precursor (*m/z*)	Product (*m/z*)	CE (eV)	Q1 Pre bias (V)	Q3 Pre bias (V)
Re	981.5	945.2	40	24	38
Rb1	1143.7	945.6	53	34	26
Rb2	1113.4	783.4	50	32	40
Rg1	835.6	637.6	31	24	24
R1	967.5	637.3	49	34	24
Rd	981.5	945.2	40	24	38
Digoxin	815.5	799.4	30	24	38

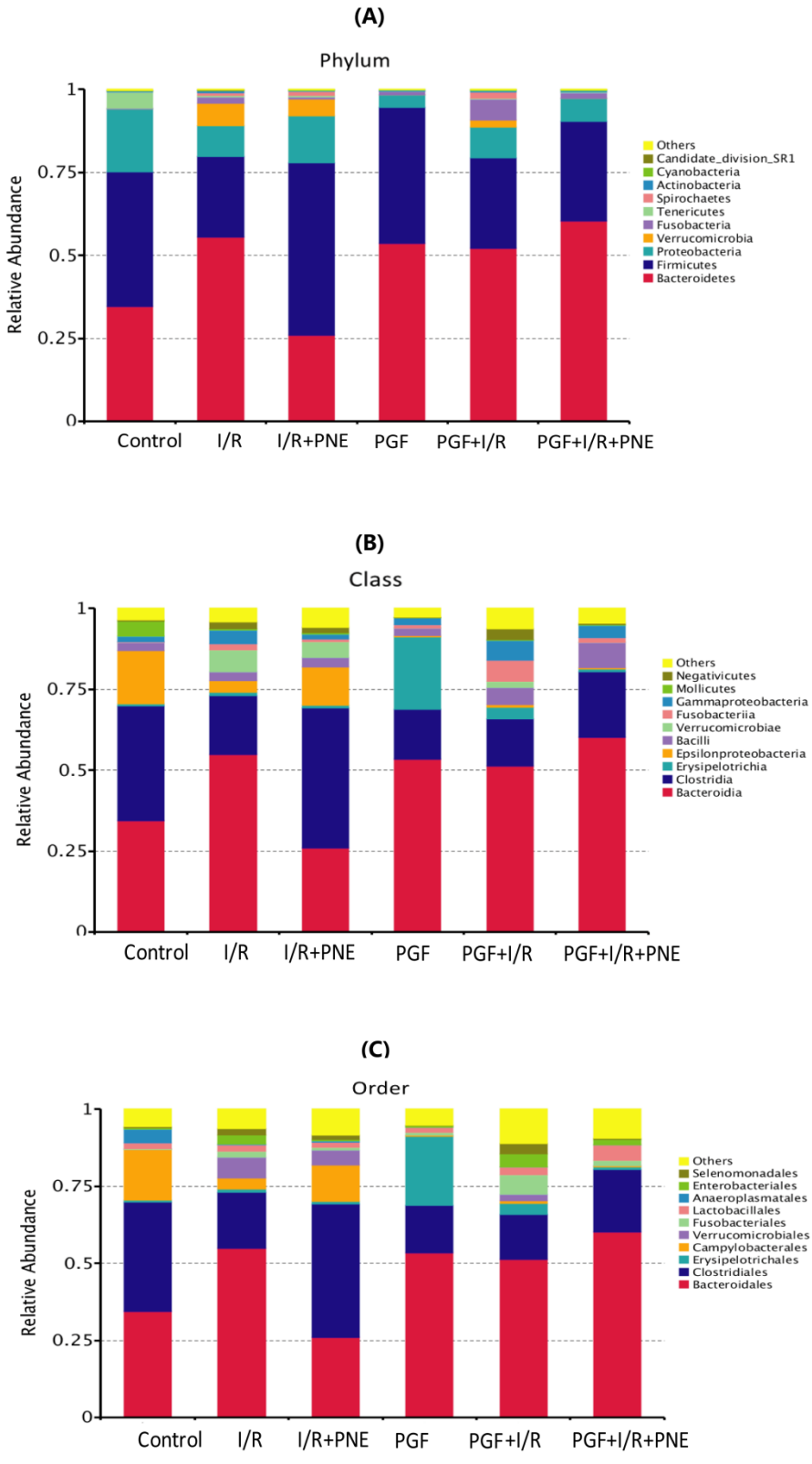
Digoxin was used as internal standard

Supplemental Table 3 The concentration ratios of brain to plasma in conventional and I/R rats.

Notoginsenoside	30 min		2 h		10 h	
	Normal	I/R	Normal	I/R	Normal	I/R
R1	0.2978±0.2355	0.4158 ±0.6880	0.4104±0.2030	0.1755±0.1957	0.4466±0.2281	0.1497±0.1320
Rd		0.0000±0.0000	0.4322±0.4473	0.9833±0.1546		N.A
Re			0.4574±0.4349	0.9533±0.5451		N.A
Rg1	0.0858±0.1282	0.0045 ±0.0015	0.5427±0.4711	0.5929±0.1929	0.0000±0.0000	N.A
Rb1	0.2924±0.2118	0.0642 ±0.0594	0.1251±0.1311	0.0604±0.0207	0.0144±0.0087	0.0000±0.0000
Rb2	0.0000±0.0000	0.0000±0.0000	0.1590±0.1384	0.1316±0.1167	0.0000±0.0000	0.0349±0.0140



Supplemental Figure 1 Sequence number of intestinal flora in control, I/R, I/R + PNE, PGF, PGF + I/R and PGF + I/R + PNE rats at each level of classification (Kingdom, Phylum, Class, Order, Family, Genus and Species).



Supplemental Figure 2 Relative abundance of the dominant bacterial in the rat intestinal microflora. (A) Relative abundance of the dominant bacterial at phylum level. (B) Relative abundance of the dominant bacterial at class level. (C) Relative abundance of the dominant bacterial at order level.