

SUPPORTING INFORMATION

**Metabolomics reveals PPAR α activation protects against
lithocholic acid-induced liver injury†**

Qi Zhao,^{‡a,b} Rui Yang,^{‡a,b} Fang Liu,^a Jing Wang,^a Dan-Dan Hu,^{a,c} Xiu-Wei Yang^d, Fei Li^{*a}

^aState Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, China

^bUniversity of Chinese Academy of Sciences, Beijing 100049, China

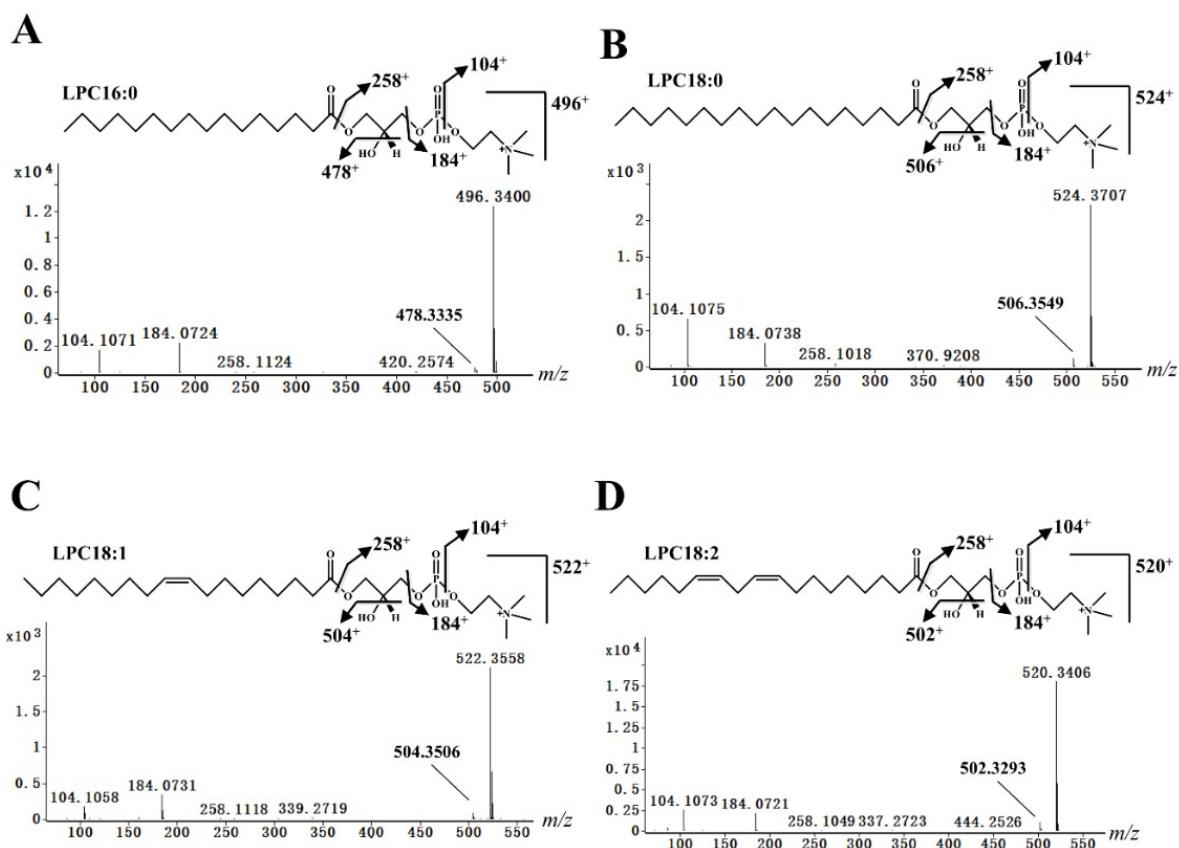
^cSchool of Pharmaceutical Science and Yunnan Key Laboratory of Pharmacology of Natural Products, Kunming Medical University, Kunming 650500, China

^dSchool of Pharmaceutical Sciences, Peking University Health Science Center, Peking University, Beijing 100191, China

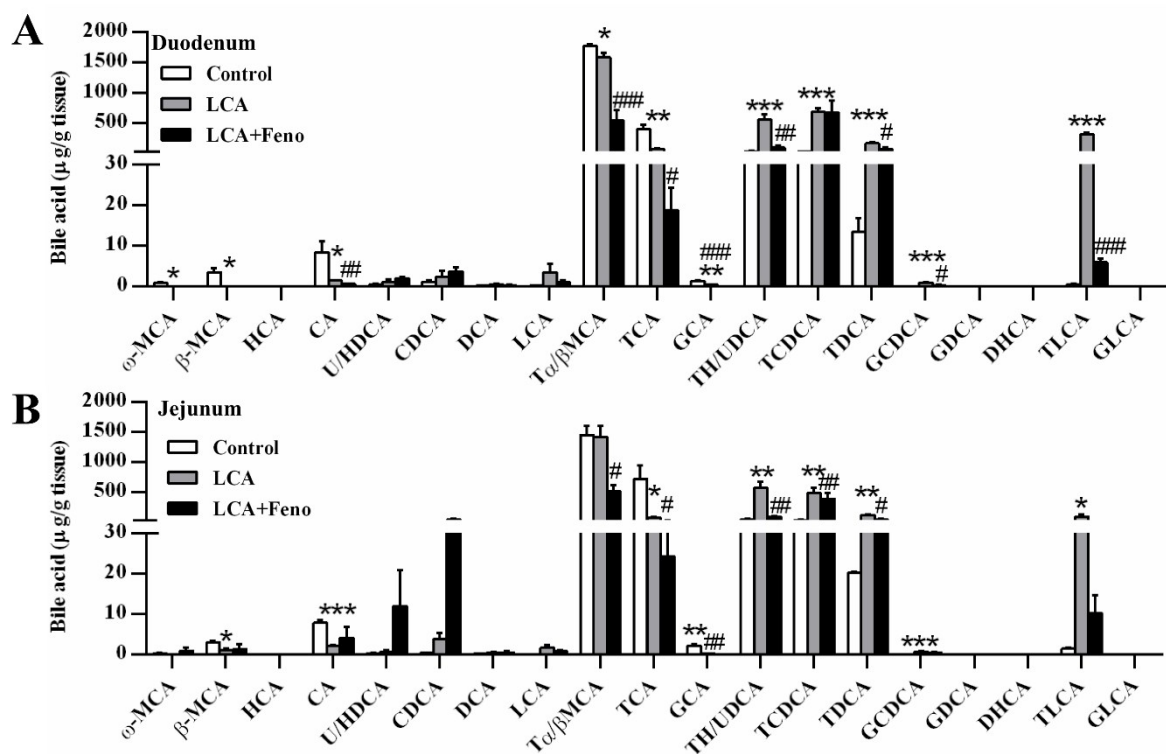
† Electronic supplementary information (ESI) available.

‡ These authors contributed equally

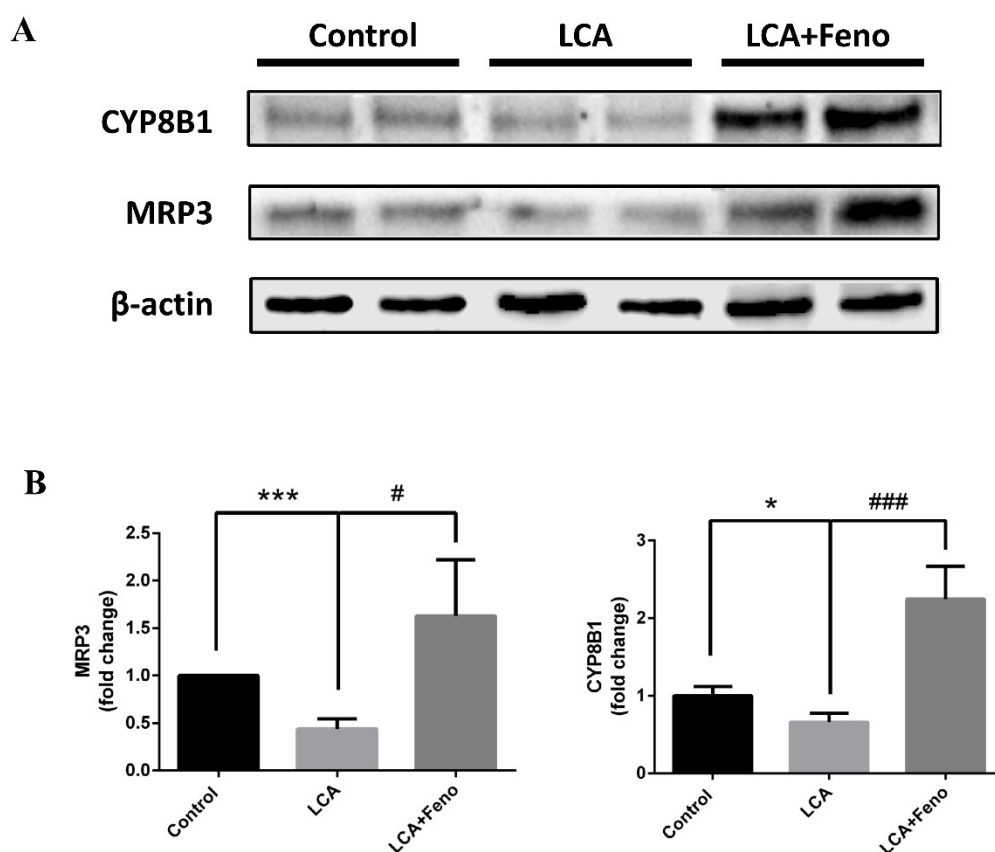
*Corresponding author: Fei Li, Ph.D., Kunming Institute of Botany, Chinese Academy of Sciences, Kunming 650201, China. Tel: +86-871-65216953, Email: lifeib@mail.kib.ac.cn



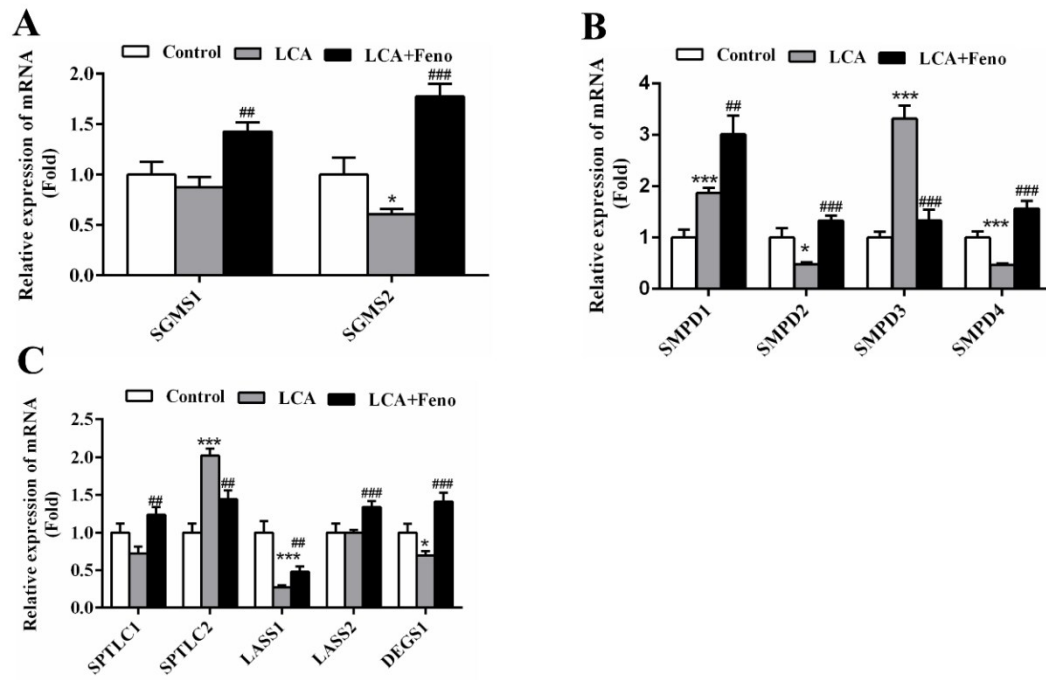
Supplementary Fig. S1. Tandem MS of LPC16:0 (A), LPC18:0 (B), LPC18:1 (C), and LPC18:2 (D). MS² fragmentation was conducted with collision energy at 10 eV.



Supplementary Fig. S2. Fenofibrate recovered the disturbed bile acid levels in duodenum (A) and jejunum (B) caused by LCA. All data were represented as mean $\pm$ SEM (n=5). * P <0.05, ** P <0.01, and *** P <0.001 *verse* control; # P <0.05, ## P <0.01, and ### P <0.001 *verse* LCA.



Supplementary Fig. S3. Fenofibrate increased hepatic protein expression of MRP3 and CYP8B1. (A) Western blot was used to measure MRP3 and CYP8B1. (B) Specific band intensity was quantified, normalized to β -actin, and expressed as the mean $\pm$ SEM (n=3). * P <0.05 and *** P <0.001 *verse* control; # P <0.05 and ### P <0.001 *verse* LCA.



Supplementary Fig. S4. Fenofibrate recovered the disturbed SM-CM homeostasis. (B) QPCR analysis of SM synthesis-related genes. (B) QPCR analysis of SM metabolism-related genes. (C) QPCR analysis the CM synthesis-related genes. Values represented fold change after normalization to control. All data were represented as mean $\pm$ SEM (n=5). * P <0.05 and *** P <0.001 *verse* control; ## P <0.01 and ### P <0.001 *verse* LCA.

Supplementary Table S1. Primer sequences for qRT-PCR.

Abbreviation	Gene	Sequence
<i>Acox1</i>	Acyl-CoA oxidase 1	CCGCCACCTTCAATCCAGAG CAAGTTCTCGATTTCTCGACGG
<i>Aim2</i>	Absent in melanoma 2	GGAACAATTGTGAATGGGCT TTGTCTCCTTCCTCGCACTT
<i>Bsep</i>	Bile salt export pump (Abcb11)	CCAGAACATGACAAACGGAA AAGGACAGCCACACCAACTC
<i>Casp1</i>	Caspase 1	TACCTGGCAGGAATTCTGGA AGTCCTGGAAATGTGCCATC
<i>Cat</i>	Catalase	CGACCAGGGCATCAAAAACCTT AACGTCCAGGACGGGTAATTG
<i>Ccl2</i>	Chemokine (C-C motif) ligand 2	AGGTCCTGTCATGCTTCTG GGGATCATCTTGCTGGTGAA
<i>Cd14</i>	CD14 antigen	CTCTGTCTTAAAGCGGCTTAC GTTGCGGAGGTTCAAGATGTT
<i>CHKa</i>	Choline kinase α	AAAGTGCTCTTGCGGCTCTA GACCTCTCTGCAAGAATGGC
<i>CHKb</i>	Choline kinase β	GCAGAGGTTTCAGAAGGGTGA CCCCAGAAAAAGTGAGATGC
<i>CHPT1</i>	Choline phosphotransferase 1	CATCAACCTGGTCACCACAC CCCAGGGCACATAAAAGGTA
<i>Col1a1</i>	Collagen, type I, alpha 1	ACATGTTTCAGCTTTGTGGACC TAGGCCATTGTGTATGCAGC
<i>Cpt 1b</i>	Carnitine palmitoyltransferase 1	CCTCTCATGGTGAACAGCAA GGTCCAGTTTACGGCGATAC
<i>Cpt 2</i>	Carnitine palmitoyltransferase 2	CAGCACAGCATCGTACCCA TCCAATGCCGTTCTCAAAAT
<i>Cybb</i>	Cytochrome b-245, beta polypeptide	GAAAACTCCTTGGGTCAGCACT ATTTCGACACACTGGCAGCA
<i>Cyp7a1</i>	Cholesterol 7 α -hydroxylase	GGGAATGCCATTTACTTGGA GTCCGATATTCAAGGATGC
<i>Cyp8b1</i>	Sterol 12 α -hydroxylase	TCCTCAGGGTGGTACAGGAG GATAGGGGAAGAGAGCCACC
<i>Ddit3</i>	DNA-damage inducible transcript 3	CAGCGACAGAGCCAGAATAA GACCAGGTTCTGCTTTTAGG
<i>DEGS1</i>	Degenerative spermatocyte homolog 1	AATGGGTCTACACGGACCAG TGGTCAGGTTTCATCAAGGAC
<i>ENPP2</i>	Ectonucleotide pyrophosphatase/phosphodiesterase 2	TCGAGGGCGAGAGAAGTTTA AAAAGAATGTCCCGGCTCTC
<i>Gpx1</i>	Glutathione peroxidase 1	TGGACTGGTGGTGCTCG CGTCACTGGGTGTTGGC
<i>LASS1</i>	LAG1 homolog ceramide synthase 1	CTGTACATTGTGGCTTTCGC GGCTGTCTGAGCTTCCAGAG
<i>LASS2</i>	LAG1 homolog ceramide synthase 2	AAGTGGGAAACGGAGTAGCG ACAGGCAGCCATAGTCGTTT
<i>IL-1</i>	Interleukin-1	CCCTGCAGCTGGAGAGTGTGGA TGTGCTCTGCTTGTGAGGTGCTG
<i>IL-6</i>	Interleukin-6	TGATGCACTTGCAAAAACA ACCAGAGGAAATTTCAATAGGC
<i>LPCAT1</i>	Lysophosphatidylcholine acyltransferase 1	CACGAGCTGCGACTGAGC ATGAAAGCAGCGAACAGGAG
<i>LPCAT2</i>	Lysophosphatidylcholine acyltransferase 2	ACCTGTTTCCGATGTCCTGA CCAGGCCGATCACATACTCT
<i>LPCAT3</i>	Lysophosphatidylcholine acyltransferase 3	AGCCTTAACAAGTTGGCGAC ATGCCGGTAAAACAGAGCC
<i>LPCAT4</i>	Lysophosphatidylcholine acyltransferase 4	GAGTTACACCTCTCCGGCCT GGCCAGAGGAGAAAGAGGAC
<i>LYPLA1</i>	Lysophospholipase A1	CCTTCACGGATTGGGAGATA GGGGCATGTGGACAGATGTA

Supplementary Table S1. (Continued)

Abbreviation	Gene	Sequence
<i>Mrp2</i>	Multidrug resistance protein (Abcc2)	TCCAGGACCAAGAGATTGTC TCTGTGAGTGCAAGAGACAGGT
<i>Mrp3</i>	Multidrug resistance protein (Abcc3)	CTGGGTCCCCTGCATCTAC GCCGTCTTGAGCCTGGATAAC
<i>Mrp4</i>	Multidrug resistance protein (Abcc4)	AGCTTCAACGGTACTGGGATA TCGTCCGGGTCATACTTCTC
<i>Myd88</i>	Myeloid differentiation primary response gene 88	TCATGTTCTCCATACCCTTGGT AAACTGCGAGTGGGGTCAG
<i>Ncf1</i>	Neutrophil cytosolic factor 1	GCCCAAAGATGGCAAGAATAAC TAGTCAGCAATGGCCCGATAG
<i>Nlrp3</i>	NLR family pyrin domain containing 3	GCTCCAACCATTTCTTGACC AAGTAAGGCCGGAATTACAC
<i>Nlrp4</i>	NLR family pyrin domain containing 4	ATCGTCATCACCGTGTGGAG GCCAGACTCGCCTTCAATCA
<i>Ntcp</i>	Sodium taurocholate cotransporting polypeptide	AGGGGGACATGAACCTCAG TCCGTCGTAGATTCTTTGC
<i>Oatp1</i>	Organic anion transporting protein 1	ACTCCATAATGCCCTTGG TAATCGGGCCAACAATCTTC
<i>Oatp4</i>	Organic anion transporting protein 4	ACCAAACCTCAGCATCCAAGC TAGCTGAATGAGAGGGCTGC
<i>Ostβ</i>	Organic solute transporter β	GTATTTTCGTGCAGAAGATGCCG TTTCTGTTTGCAGGATGCTC
<i>PCYT1a</i>	Phosphate cytidylyltransferase 1 α	AGCCCTATGTCAGGGTGACT GGCATGACCAGAGTGAAACA
<i>PCYT1b</i>	Phosphate cytidylyltransferase 1 β	ATAGAGCACACATGCCACACA GGCAACGGTCAGTTTTTCAT
<i>Pla2g6</i>	Phospholipase A ₂ g6	GTGCCTGTAACCTGTGTAGATGTC CTCTGAGTCTAGTGTGAGATGGA
<i>Pla2g7</i>	Phospholipase A ₂ g7	ATTTCTTGGAACACCCAGTATTGT GAACATTCTATTGCTCTTTGCTGA
<i>Pla2g12b</i>	Phospholipase A ₂ g12b	ATCAAGGTACCAGGAAGTATGGAC TCATAGCTCTTCTTCTCCTCCTC
<i>PLD1</i>	Phospholipase D1	CTGCATCCTCAAACGGAAG GCTTGCTGTACTCGCTGTTG
<i>PLD2</i>	Phospholipase D2	CAGCTACATCAGCATGACAGC CTGCCACAGCAGCAAAGTAA
<i>Ppara</i>	Peroxisome proliferator-activated receptor α	CCCAAGGGAGGAATAGCTTCT CTCTGCCGATGCGGTTCCTCA
<i>Pycard</i>	PYD and CARD domain containing	GAAGCTGCTGACAGTGAAC GCCACAGCTCCAGACTCTTC
<i>SGMS1</i>	SM synthase 1	GAACACGCGGAGAAGCTAGT AACATTCTGTTCCGCTCATT
<i>SGMS2</i>	SM synthase 2	CTGTGCGGAGACTTCTCTT CACCAGAAGTGACGAGGTGA
<i>SMPD1</i>	Sphingomyelin phosphodiesterase 1	GTTACCAGCTGATGCCCTTC AGCAGGATCTGTGGAGTTG
<i>SMPD2</i>	Sphingomyelin phosphodiesterase 2	CTCCAGCCATGAAGTCAAC TTCAGAAAGTCTCCAAGCG
<i>SMPD3</i>	Sphingomyelin phosphodiesterase 3	CCTGACCAGTGCCATTCTTT AGAAACCCGGTCCTCGTACT
<i>SMPD4</i>	Sphingomyelin phosphodiesterase 4	GGTTTTTGTGGAAATGTGGC GCTGGAGACAGTGAGTCGGT
<i>Sod1</i>	Superoxide dismutase 1, soluble	AAGCGGTGAACAGTTGTGTT AGCCTTGTGTAATTGCTCCCTACT
<i>Spp1</i>	Secreted phosphoprotein 1	CTCCTTGCGCCACAGAATG TTGGAAGAGTTTCTTGCTTAAAGTCA
<i>SPTLC1</i>	Serine palmitoyltransferase long chain base subunit 1	CGAGGGTTCTATGGCACATT GGTGGAAGAAGCCATACGAGT
<i>SPTLC2</i>	Serine palmitoyltransferase long chain base subunit 2	TCACCTCCATGAAGTGCATC CAGGCGTCTCTGAAATACC
<i>TGF-β</i>	Transforming growth factor beta	GGAGAGCCCTGGATACCAAC CAACCCAGTCTCTCCTAAA

Supplementary Table S1. (Continued)

Abbreviation	Gene	Sequence
<i>Tnf</i>	Tumour necrosis factor	CCACCACGCTCTTCTGTCTAC
		AGGGTCTGGGCCATAGAACT
<i>Trl2</i>	Toll-like receptor 2	CATCACCGGTCAGAAAACAA
		ACCAAGATCCAGAAGAGCCA
<i>Trl4</i>	Toll-like receptor 4	TGTTCTTCTCCTGCCTGACA
		TGTCATCAGGGACTTTGCTG