Table S1 Primer sequences used in RT-PCR in cell experiments

Target	**Primer sequence (5'-3')** **Forward and reverse**
β-actin	CCACACCTTCTACAATGAGC GGTCTCAAACATGATCTGG
Nrf2	TTCAGCAGCATCCTCTCCACAG GCATGCTGTTGCTGATACTGG
HO-1	CAGGCAGAGAATGCTGAG GCTTCACATAGCGCTGCA
NQO1	TGGCTAGGTATCATTCAACTC CCTTAGGGCAGGTAGATTCAG
TNFα	CAGCCTCTTCTCCTTCCTGA TGAGGTACAGACCCTCTGAT
IL-6	CTTTTGGAGTTTGAGGTATACCTAG GCTGCGCAGAATGAGATGAGTTGTC
Bcl-2	GACTTCGCCGAGATGTCCAG GAACTCAAAGAAGGCCACAATC
Bax	CGAACTGGACAGTAACATGGAG CAGTTTGCTGGCAAAGTAGAAA
Caspase-3	GGAAGCGAATCAATGGACTCTGG GCATCGACATCTGTACCAGACC

Table S2 Primer sequences used in RT-PCR in mouse experiments

Target gene	**Primer sequence (5'-3')** **Forward and reverse**
β-actin	TCAGCAAGCAGGAGTACGATG AACGCAGCTCAGTAACAGTCC
Nrf2	AAAGCACAGCCAGCACATTC GGGATTCACGCATAGGAGCA
HO-1	ACCGCCTTCCTGCTCAACATTG CTCTGACGAAGTGACGCCATCTG
IL-10	CCCATTCCTCGTCACGATCTC TCAGACTGGTTTGGGATAGGTTT
TNFα	ATGAGCACAGAAAGCATGATC TACAGGCTTGTCACTCGAATT
IL-1β	TTCATCTTTGAAGAAGAGCCCAT TCGGAGCCTGTAGTGCAGTT
IL-6	TGGAAATGAGAAAAGAGTTGTG C CCAGTTTGGTAGCATCCATCA

Fig. S1

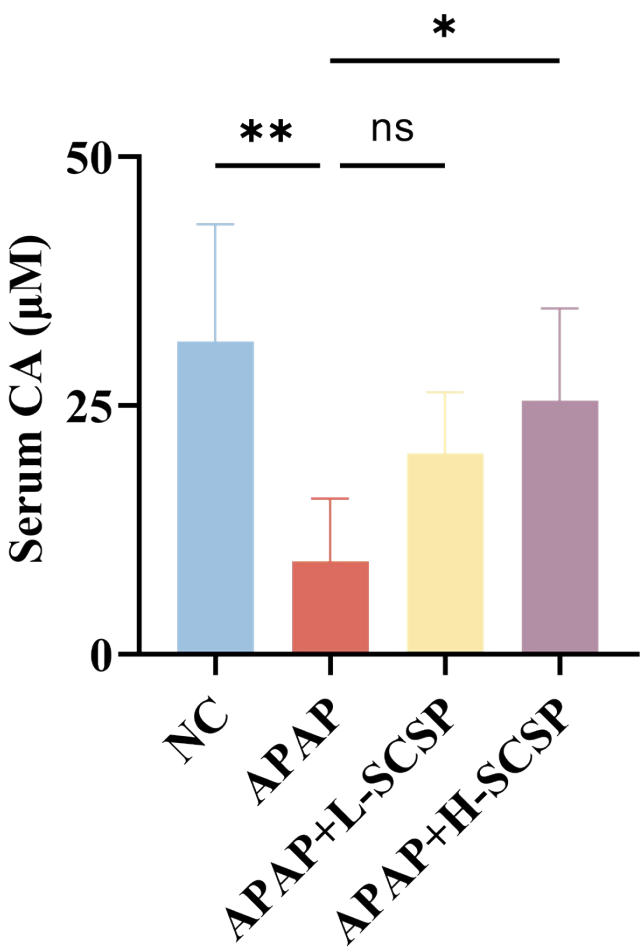

Fig. S1 SCSP mitigated APAP-induced reduction in serum CA levels.

Fig. S2

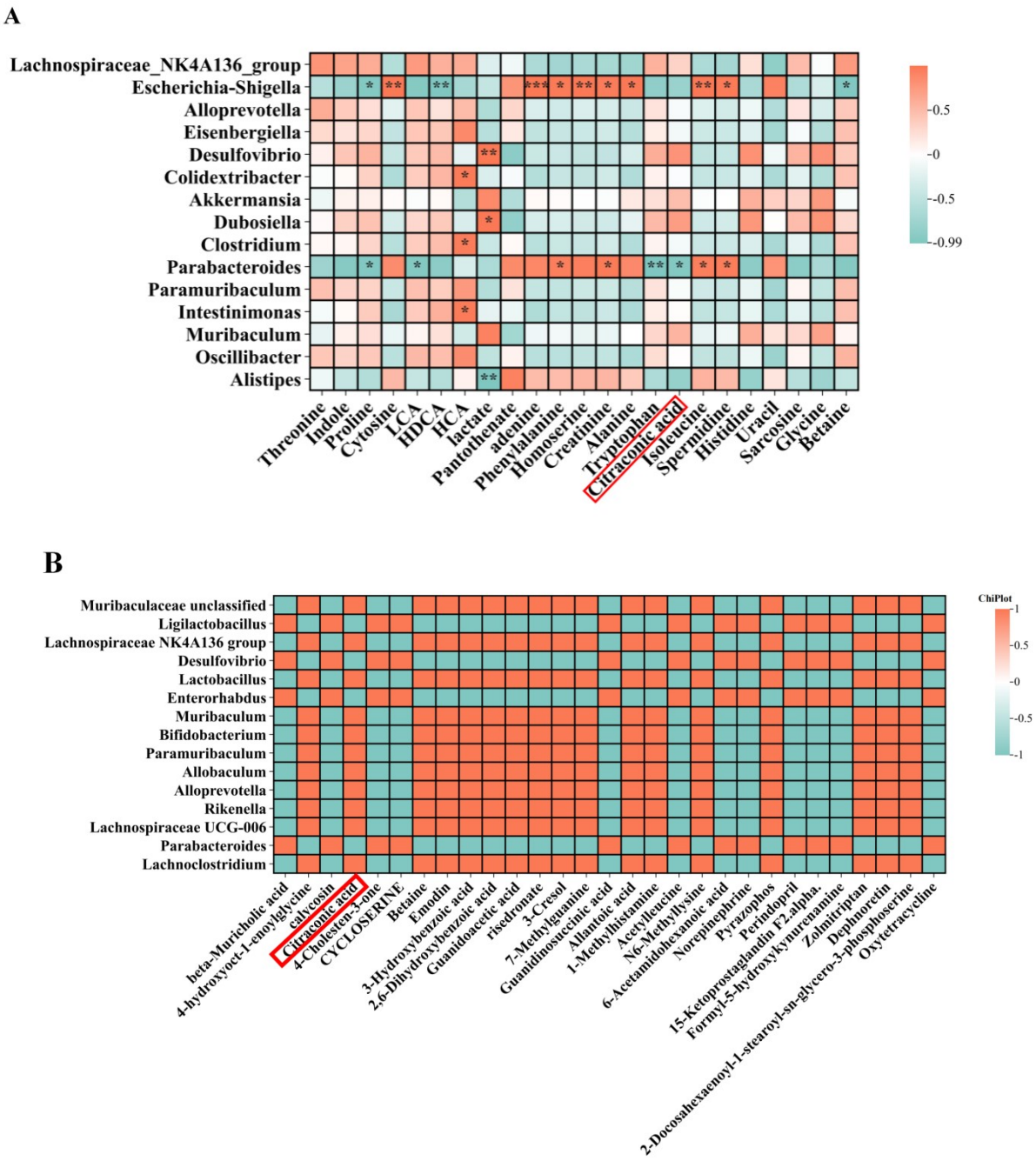

Fig. S2 Spearman correlation analysis between key bacteria and metabolites in serum (A) and feces (B).

Fig. S3

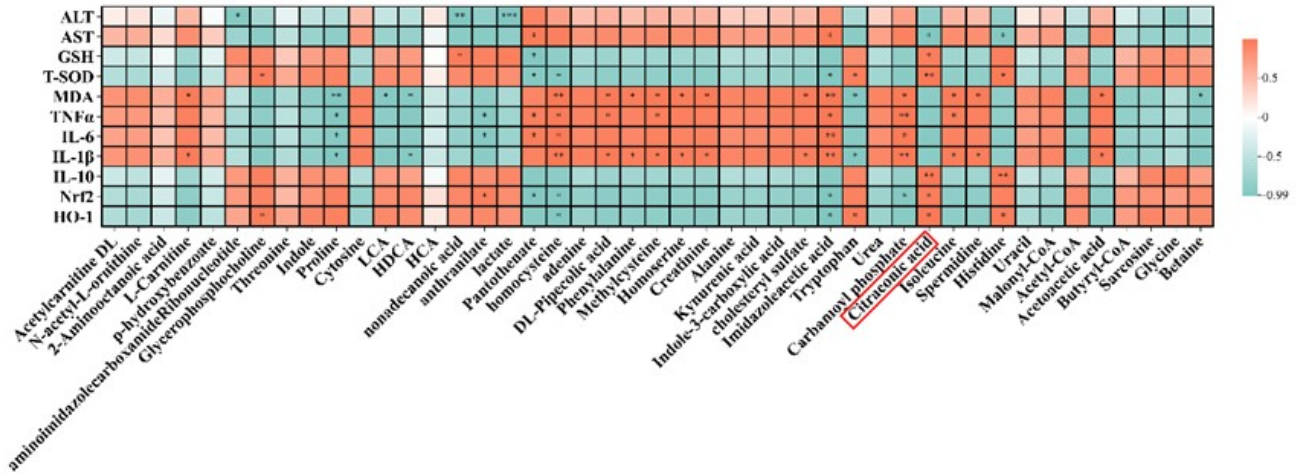

Fig. S3 Spearman correlation analysis between key metabolites and the levels of ALT, AST, inflammatory markers, and oxidative stress markers.

Fig. S4

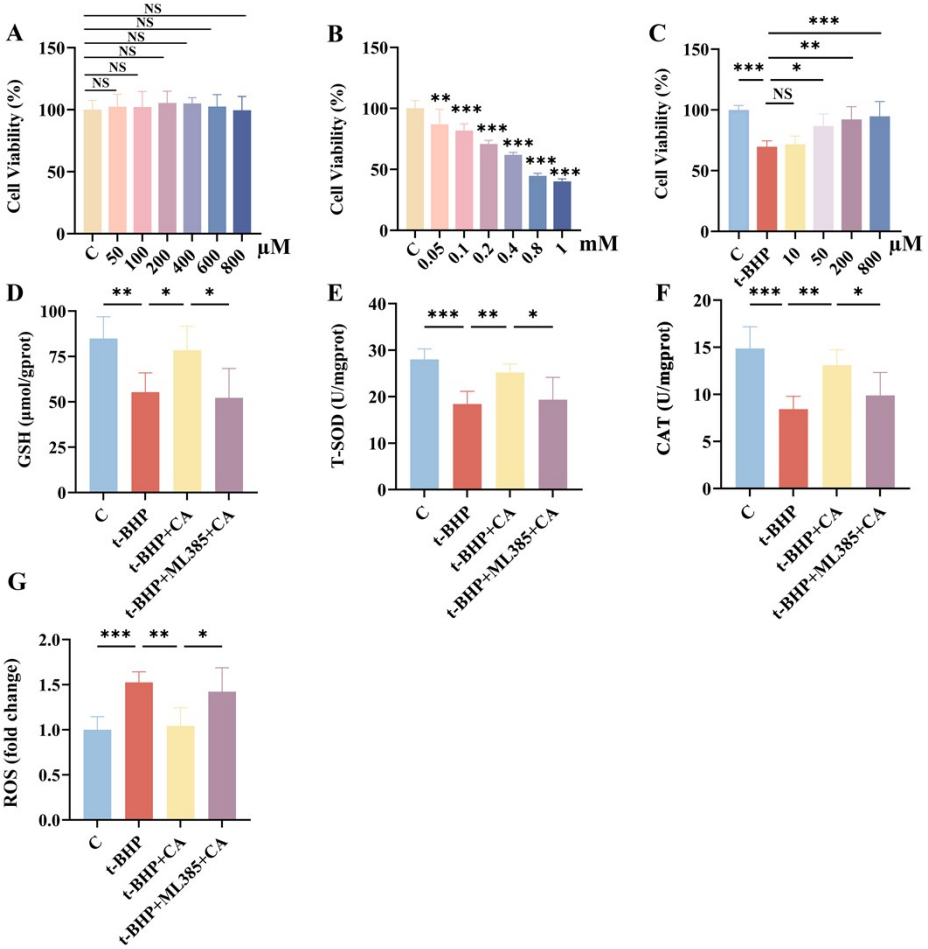

Fig. S4 CA alleviated t-BHP-induced oxidative stress in primary hepatocytes. Viability of cells after treatment with CA (50-800 μM, A) for 9 h or t-BHP (0.05-1mM, B) for 3 h. (C) Viability of cells after treatment with CA (10-μM) for 9 h, followed by t-BHP stimulation (150 μM) for another 3 h. (D-F) Effect of CA on GSH (D), T-SOD (E), and CAT (F) levels. Primary hepatocytes were sequentially pretreated with ML385 (10 μM) for 24 h and CA (50 μM) for 9 h, followed by stimulation with t-BHP (150 μM) for 3 h. (G) ROS levels. Intracellular ROS levels were determined using a commercial ROS assay kit. Results are expressed as mean ± SD. *P*-values were determined by one-way ANOVA, followed by Tukey's post hoc test. **p* <0.01, ***p* <0.01 ****p* <0.001. NS means no significance (*p* >0.05).

Primary hepatocytes were isolated as previously described [1] with slight modifications. Briefly, mice were anesthetized with pentobarbital sodium, the abdomen was opened, and the liver was perfused via the portal vein. The initial perfusion was carried out with HBSS containing 50 mM HEPES and 0.05 mM EGTA until the liver turned pale yellow. This was followed by perfusion with collagenase-containing HBSS (0.04% collagenase IV, 50 mM HEPES, 0.5 mM $CaCl_2$) for 5-8 min until the liver became softened. Hepatocytes were released by gently pipetting the digested liver in complete medium, filtered by a 100 μm strainer, and purified by Percoll density gradient centrifugation. The resulting hepatocytes were seeded on collagen-coated plates and cultured in high-glucose DMEM supplemented with 10% FBS, 1% penicillin-streptomycin, 2 mM L-glutamine, 0.1 μM insulin, and 0.1 μM dexamethasone under standard culture conditions (37 °C, 5% CO_2).

Reference

[1] H. Lyu, H. Wang, L. Li, J. Zhu, F. Chen, Y. Chen, C. Liu, J. Fu, B. Yang, Q. Zhang, Y. Xu, J. Pi, Hepatocyte-specific deficiency of Nrf2 exacerbates carbon tetrachloride-induced liver fibrosis via aggravated hepatocyte injury and subsequent inflammatory and fibrogenic responses, Free Radic Biol Med, 2020, **150**, 136-147, http://doi.org/10.1016/j.freeradbiomed.2020.02.015.