Supplementary File 1: Experimental details.

RT-qPCR quantifications of tetA and acrB gene expressions: Reverse transcription of 1 μg of extracted RNA was performed using the PrimeScript RT reagent Kit with gDNA Eraser (Takara, Beijing, China) following the manufacturer's protocol, and 10 ng of cDNA was used as a template for subsequent RT–PCR tests. The optimized primers for *tetA* (F: GCGCGATCTGGTTCACTCG; R: AGTCGACAGYRGCGCCGGC), *AcrB* (F: AAGAAGCTACCCGTAAGTCG; R: AGTAGAACCGCCAAAGAAGG) and *16S rRNA* (F: GTGYCAGCMGCCGCGGTAA; R: GGACTACNVGGGTWTCTAAT) were used. Thermal cycling was performed using a three-step PCR amplification standard procedure: 94 °C for 30 s, followed by 40 cycles of 94 °C to 72 °C for 5 s, 55 °C for 30 s, and 40 cycles of 95 °C to 55 °C for 5 s. RT–PCR was performed using CFX Connect (Bio-Rad, USA). The fold changes in gene expression were determined using the $2^{-\Delta\Delta Ct}$ method.

Transcriptomic analysis: The raw sequencing reads were subjected to quality control filtering with fastqc version 0.11.9 and then mapped to the E. coli MG1655/RP4 genome with Bowtie 2-2.2.4. The quantitative analysis was performed using featureCounts v1.6.0 in subread 2.0.3 software. For the biological replicates DESeq2 v1.34.0, the normalization method used DESeq, and the differential gene screening criteria were $|\log2(\text{FoldChange})| > 0$ & $p_{adj} < 0.05$; for the nonbiological replicates edgeR v3.36.0, the normalization method used TMM, and the differential gene screening criteria were $|\log2(\text{FoldChange})| > 1$ & $p_{adj} < 0.05$. FoldChange)| > 1 and $p_{adj} < 0.05$ for expression difference analysis and screening of differentially expressed genes.

Molecular docking between phenolic acids and *AcrB*: The *AcrB* protein structure (PDB ID: 2DRD) was obtained from the Protein Data Bank (http://www.rcsb.org/pdb/home/home.d o.PDB ID: 2DRD). The protein processing software used was PyMOL 3.7.0, VMD 194a. The spatial orientation of the ligand was calculated for the *AcrB* 2DRD protein using PyMOL 3.7.0. The box size was set to 40 Å, and rigid docking was used with AutoDock and AutoDock Vina. Sybyl-X 2.0 used the Surflex-Dock (SFXC) docking mode, ligand-protein structure, and a self-contained ligand as the active pocket for molecular docking. The Ligand Source is a self-built compound database, and Surex dock scores (kcal/mol) are calculated. The Total_Score (consensus score) integrates comprehensive ligand evaluations from many popular scoring functions and serves as the main score for judging docking results. Phenolic acids were plotted using ChemDraw 19.1, and the 3D spatial structure with minimum energy was calculated and plotted using MM. In addition, LeDock and Discovery Studio 2019 molecular docking software were used.

Knockout of the *AcrB* gene using CRISPR-B™: The *AcrB* gene was knocked down in the *E. coli C4313* strain according to the NCBI NC_000913.3:c484403-481254 *AcrB* (GeneID = 945108) gene sequence. The CRISPR-B _CR plasmid, which has enzymes expressing Cas9 nuclease and Red recombination system, was electrotransferred into *E. coli C4313* using the CRISPR-B™ technology system developed by Genjing, and colony PCR was used to identify whether the CRISPR-B _CR *E. coli C4313* was successfully transferred into CRISPR-B _CR, and colony PCR was performed to identify whether CRISPR-B _CR was successfully transferred into *E. coli C4313*. The targeting plasmid CRISPR-B_G and the repair template of the plasmid

CRISPR-B _D were electrotransferred into the receptor strain with stable CRISPR-B _CR, and the CRISPR system was combined with the Red recombination system to edit the bacterial genome, in which the electrotransfer conditions were 1.8 kV, 5 ms, and 1 pulse. The CRISPR-B _G plasmid contains a gRNA expressing the target gene with the following gene sequences: AcrB-gRNA1, GCAAGAAGTT CAGCAGCAAGGGG; AcrB-gRNA2, TGGTTGTGAGCAGGCCTACCTGG; and the CRISPR-B _D plasmid contains a DNA repair template. Finally, a single clone was selected for PCR and sequencing, and the CRISPR-B™ plasmid was removed to obtain a positive E. coli C4313 clone with the AcrB gene knocked out. The primer sequences used for PCR were JD-AcrB-F (CTCTCAGGCAGCTTAGCCC) and JD-AcrB-R (CGGTTATAGCTCCGAGA CGGTTATAGCTCCGAAAGCG). The MIC and FIC of *E. coli C4313 ΔacrB* against tetracycline and phenolic acids were re-assayed.