

Supplementary material
for
**Discovery of quercetin and its analogs as potent OXA-48
beta-lactamase inhibitors**

Yuejuan Zhang^{a,b}, Cheng Chen^c, Bin Cheng^d, Lei Gao^{a,b}, Chuan Qin^{a,b}, Lixia Zhang^e,
Xu Zhang^{a,b}, Jun Wang^{a,b}, Yi Wan^{a,b*}

^a Microbiology Institute of Shaanxi, Xi'an, Shaanxi 710043, PR China;

^b Engineering Center of Qinling Mountains Natural Products, Shaanxi Academy of Sciences, Xi'an, Shaanxi 710043, PR China;

^c College of Forestry, Northwest A&F University, Yangling, Shaanxi 712100, PR China;

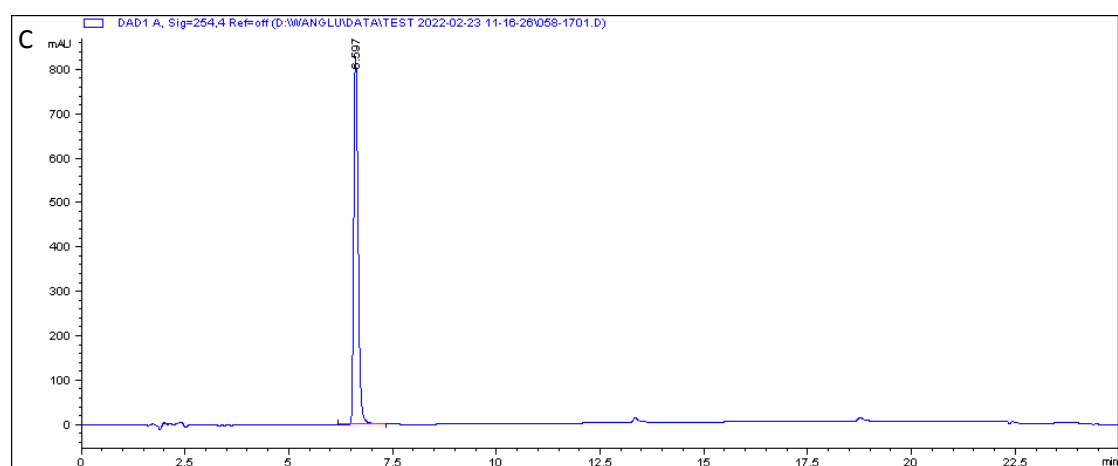
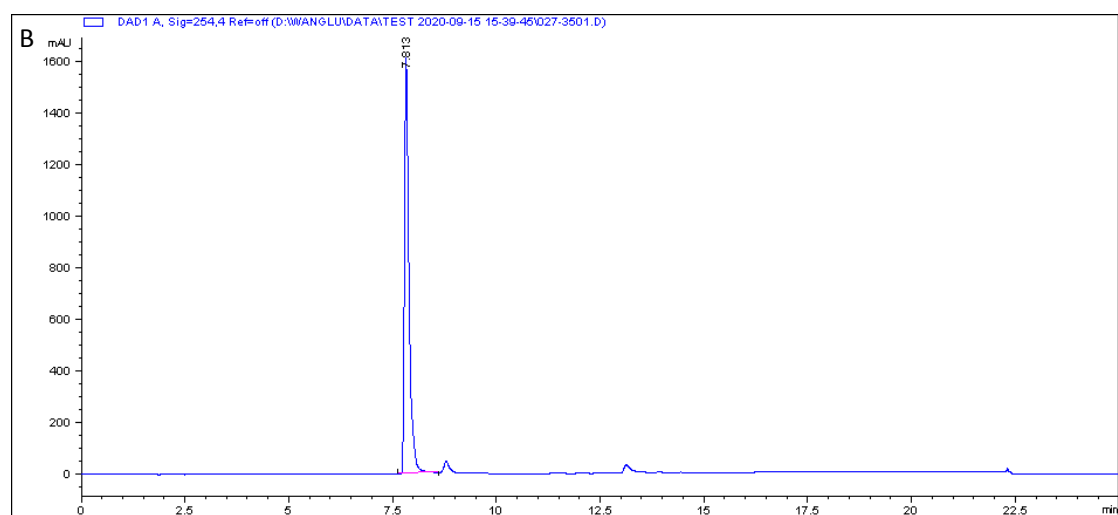
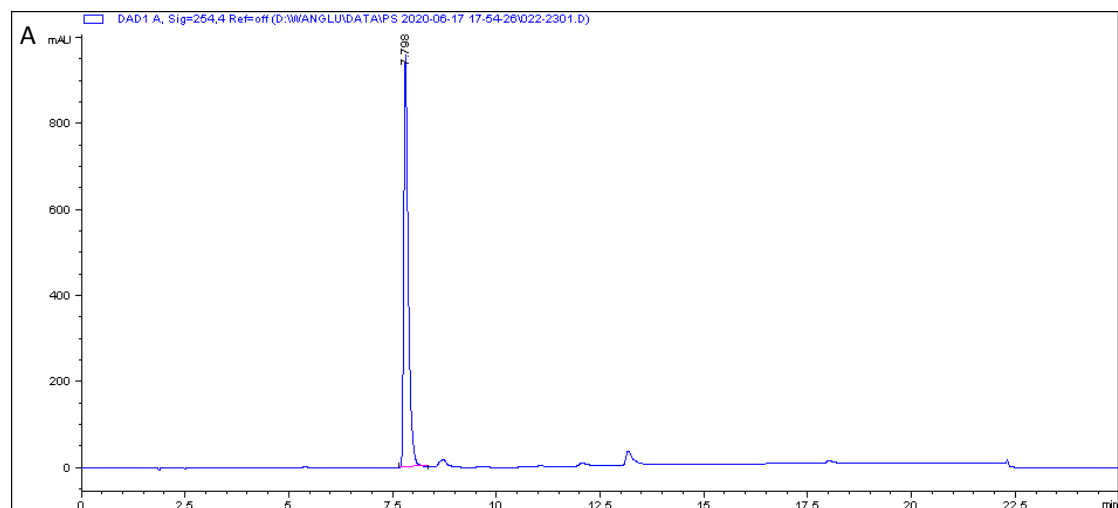
^d MOE Key Laboratory of Cell Activities and Stress Adaptations, School of Life Sciences, Lanzhou University, Lanzhou, Gansu 730000, PR China;

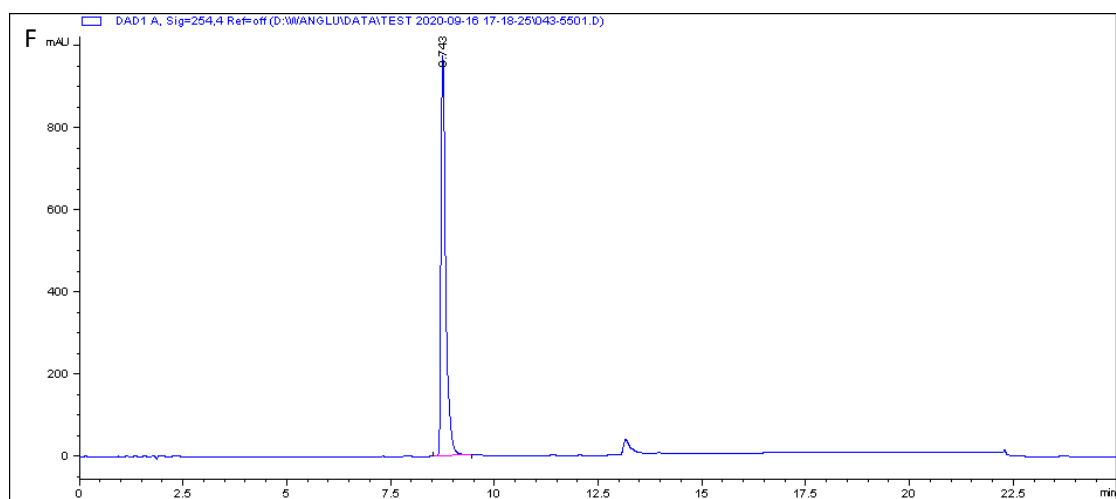
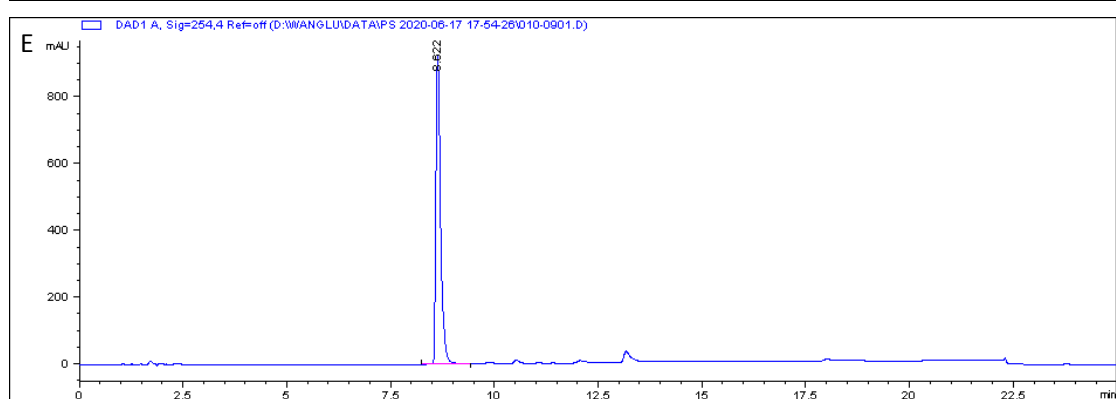
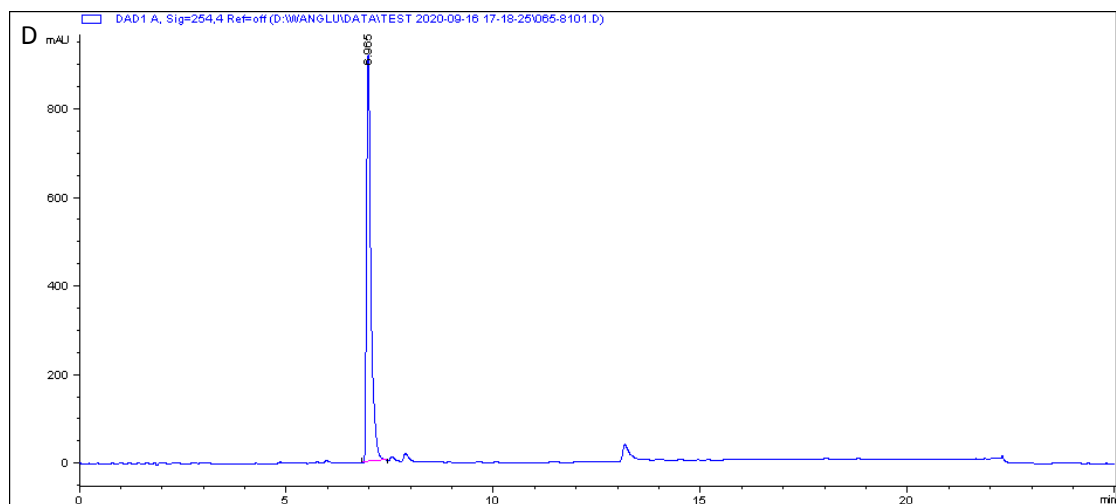
^e Clinical Laboratory, Shaanxi Provincial People's Hospital, Xi'an, Shaanxi 710068, PR China.

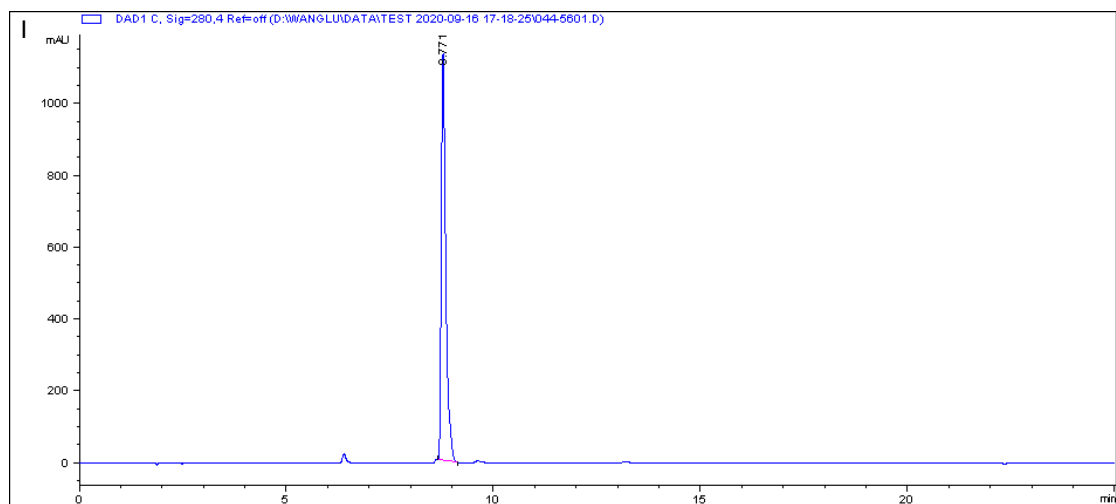
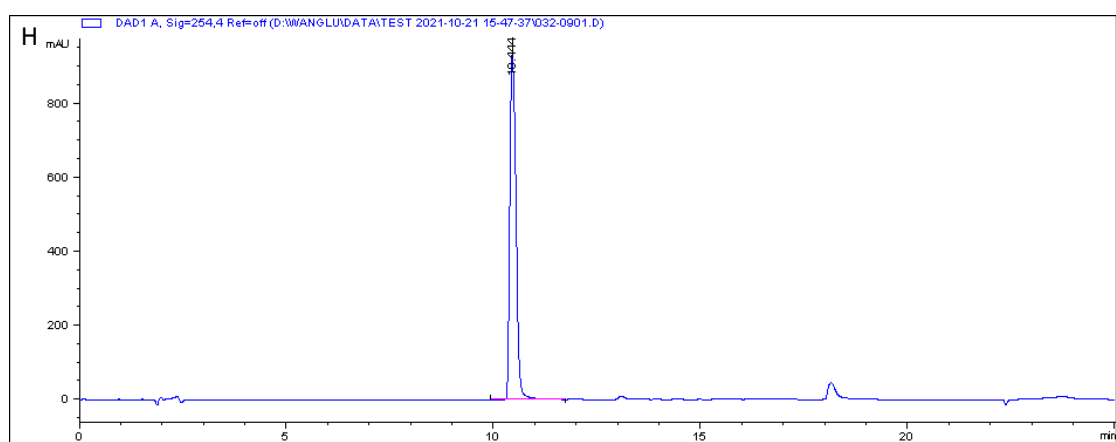
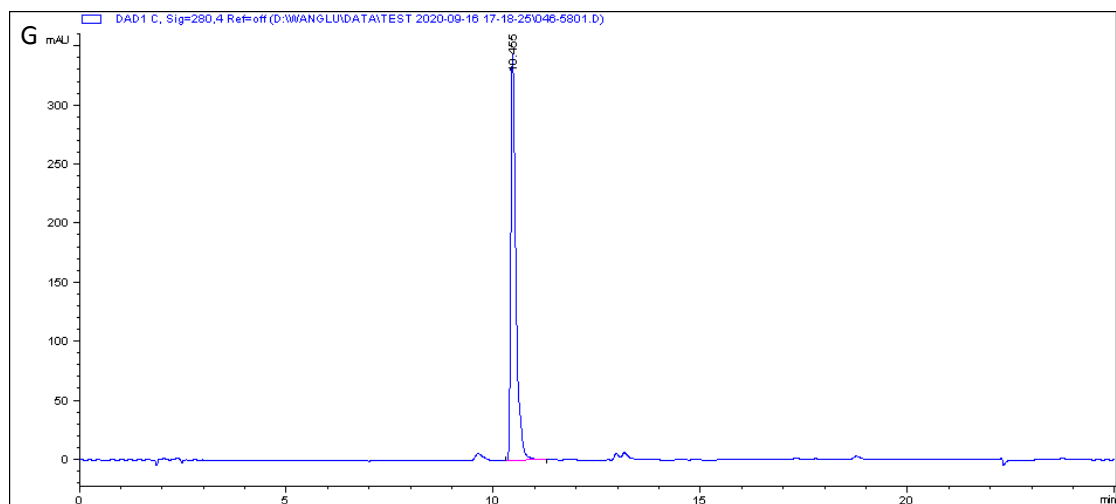
* Corresponding author: Yi Wan, Phone/fax: +86-29-8235-7035, E-mail: wanyi6565@163.com.

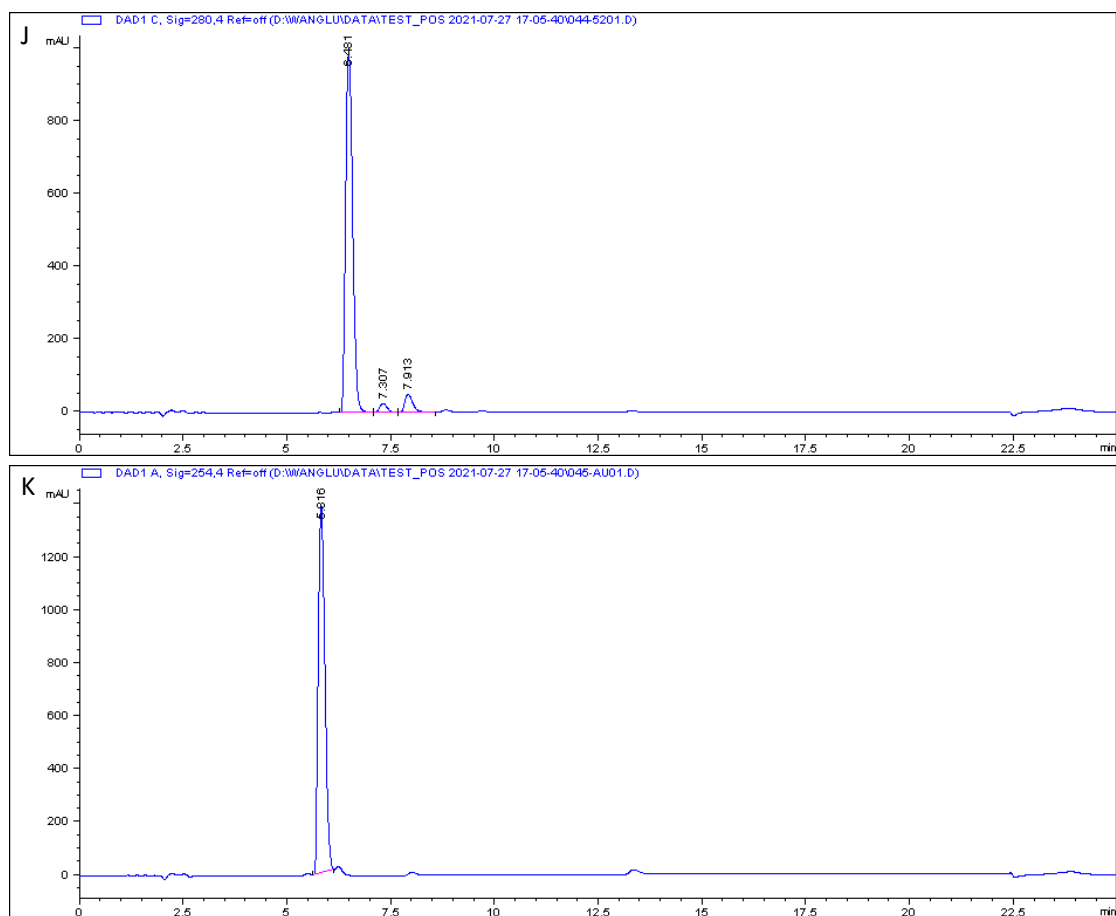
Table of contents

Supplementary Figure S1	The HPLC chromatograph of flavonoids	S2
Supplementary Table S1	The oligonucleotides used for cloning in the study	S5
Supplementary Figure S2	The growth curve of OXA-48-positive <i>E. coli</i> with different concentrations of piperacillin.	S6
Supplementary Figure S3	Profile of OXA-48 inhibition by flavonoids	S6
Supplementary Figure S4	Lineweaver–Burk plots of inhibition of OXA-48 by fisetin (A) and luteolin (B)	S8





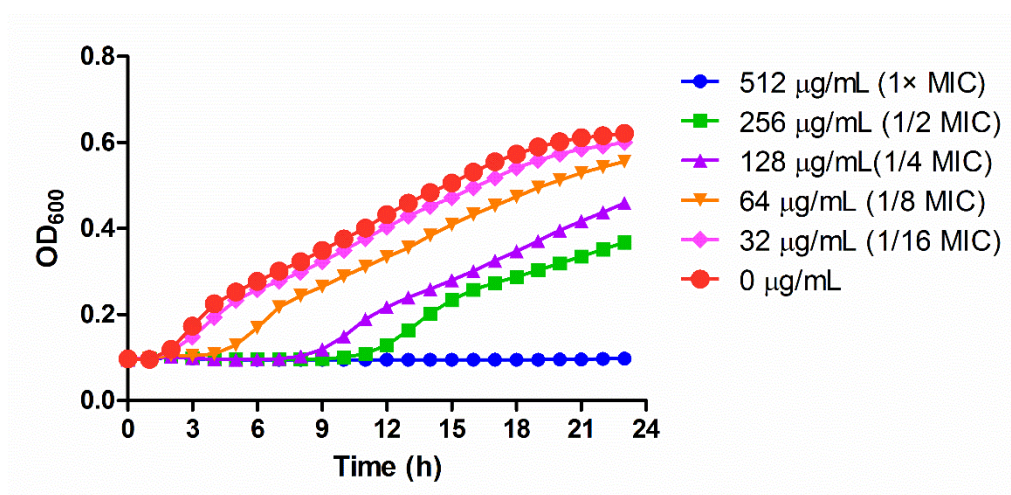




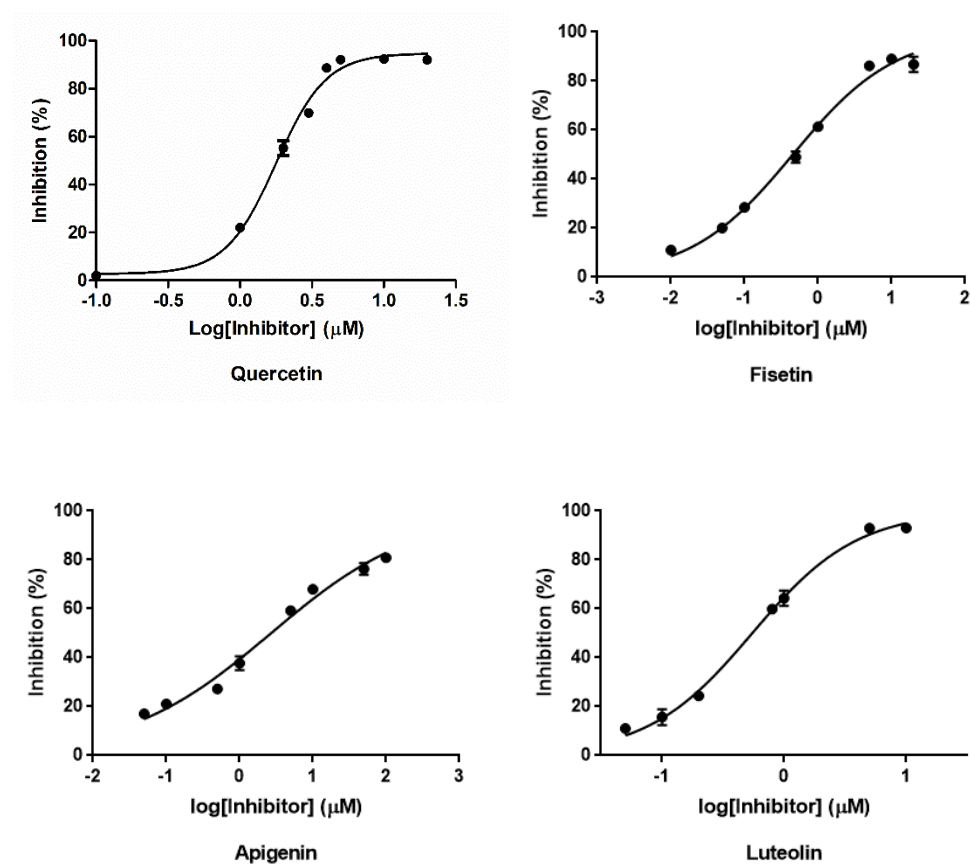
Supplementary Figure S1. The HPLC chromatograph of flavonoids. A: luteolin; B: quercetin; C: 3',4',7-trihydroxyflavone; D: fisetin; E: apigenin; F: kaempferol; G: Chrysin; H: galangin; I: naringenin; J: taxifolin; K: isoquercitrin.

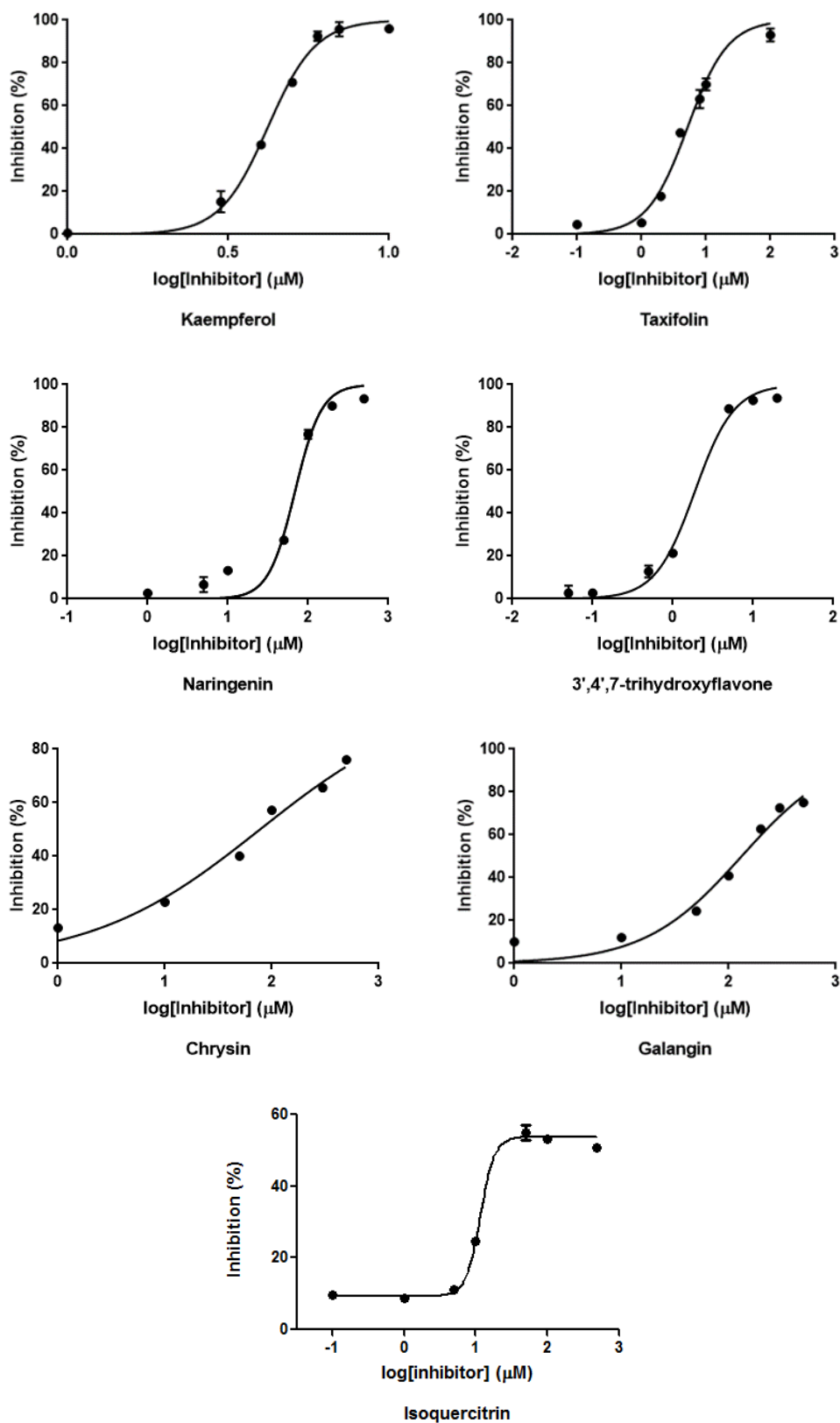
Supplementary Table S1. The oligonucleotides used for cloning in the study.

Primer	DNA sequence 5'-3'
acrB-Fw	ATTTGTTTCAGCTCATTCCGGGTTCA
acrR-Rv	AGAGATTACGTTGTGCCTGTTGC
pBla-Fw	CCTTTAGATCTGGCCTATTGGTTAAAA AATG
pBla-Rv	CCTTTTCTAGAGAAGCATTATCAGGG TTATTG

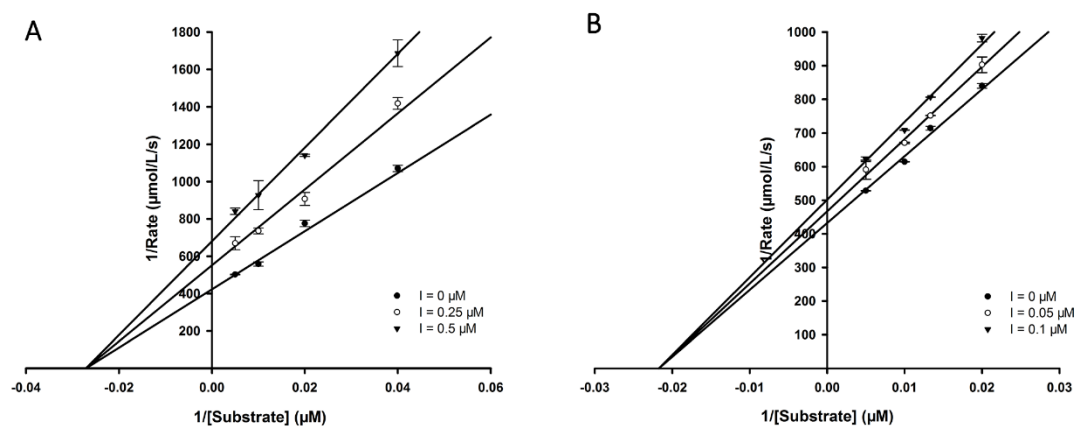


Supplementary Figure S2. The growth curve of *E. coli* BW25113 Δ acrA Δ bamB expressing OXA-48 with different concentrations of piperacillin.





Supplementary Figure S3. Profile of OXA-48 inhibition by flavonoids.



Supplementary Figure S4. Lineweaver–Burk plots of OXA-48 catalyzed hydrolysis of the substrate in the absence and presence of fisetin (A) and luteolin (B) at various concentrations.