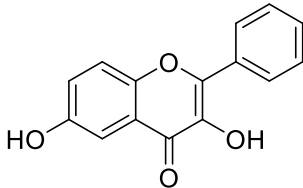
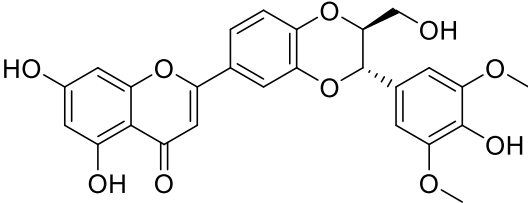
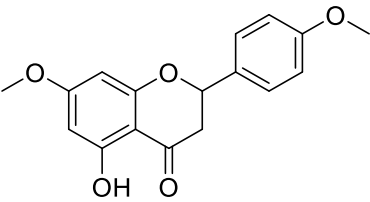
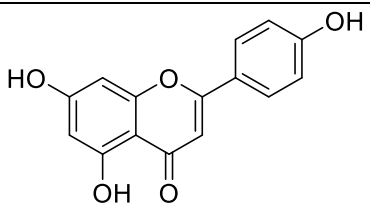
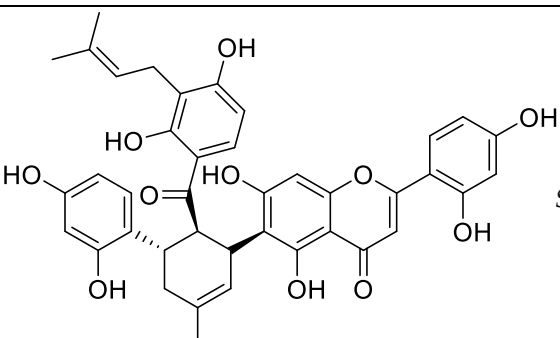
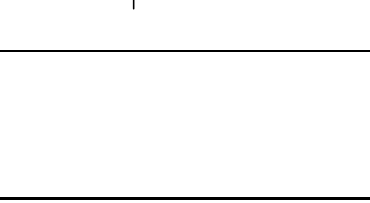
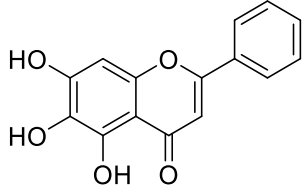
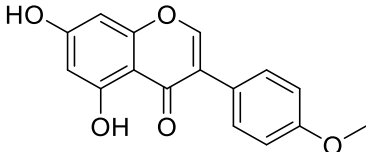
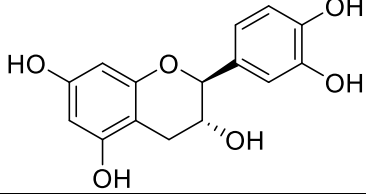
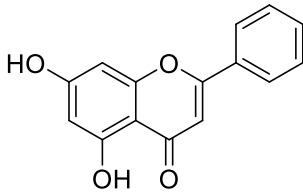
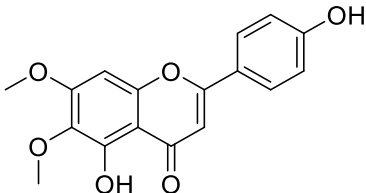
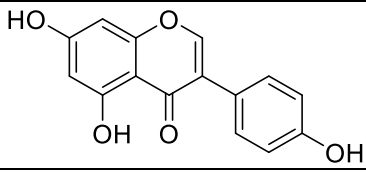
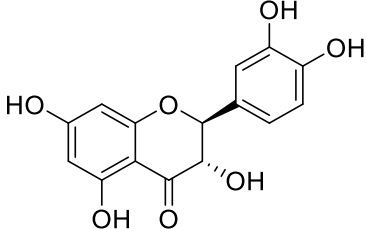
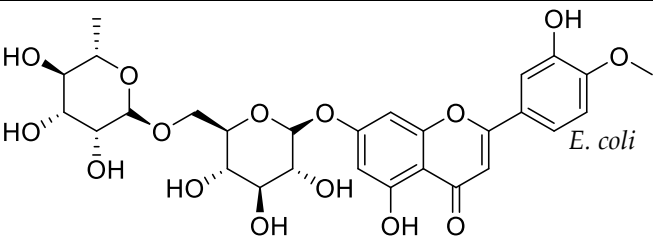


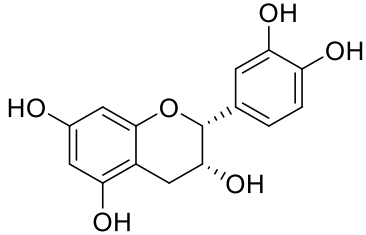
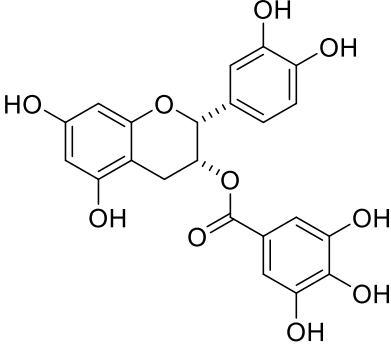
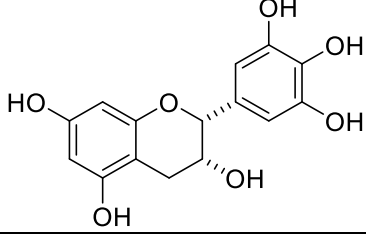
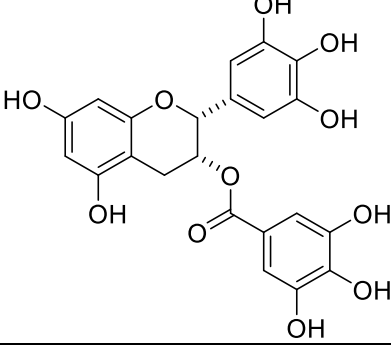
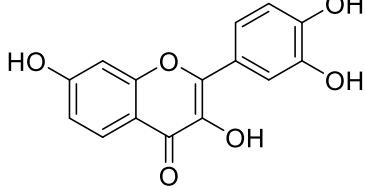
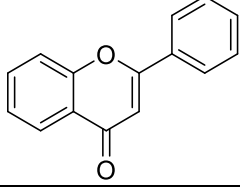
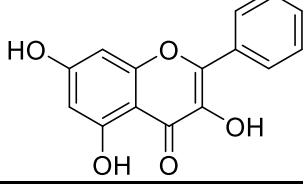
Supplementary Materials: Interactions with Microbial Proteins Driving the Antibacterial Activity of Flavonoids

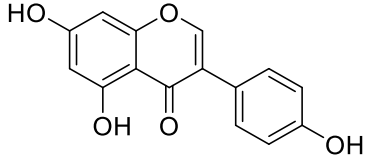
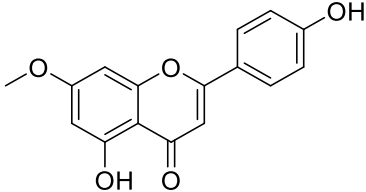
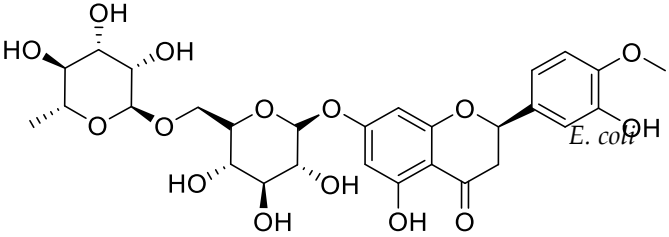
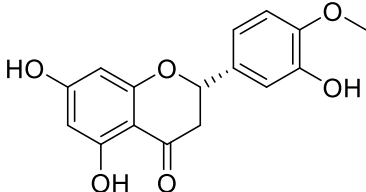
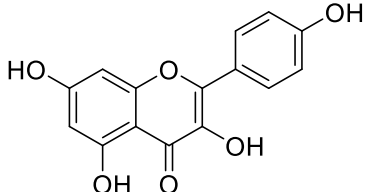
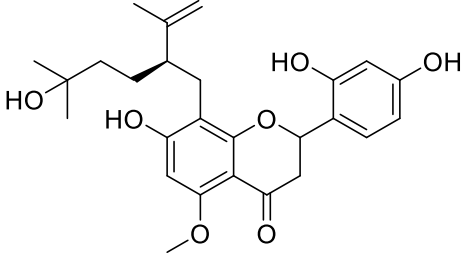
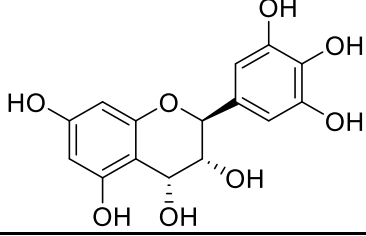
Giuliana Donadio, Francesca Mensitieri, Valentina Santoro, Valentina Parisi, Maria Laura Bellone, Nunziatina De Tommasi, Viviana Izzo and Fabrizio Dal Pia

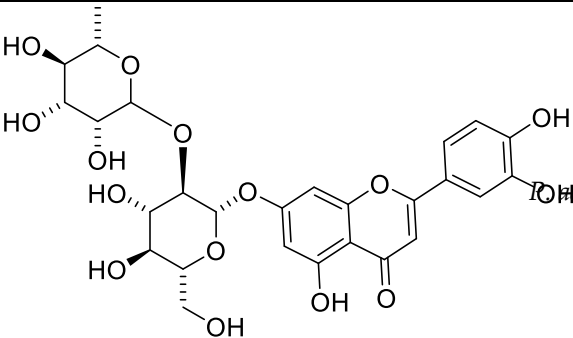
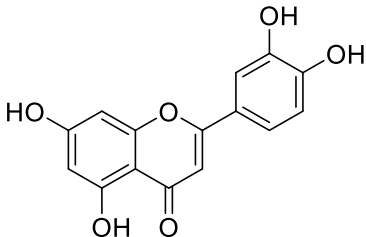
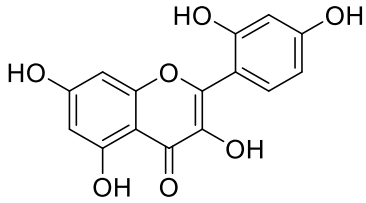
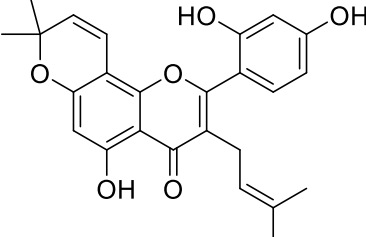
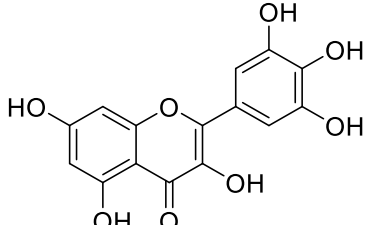
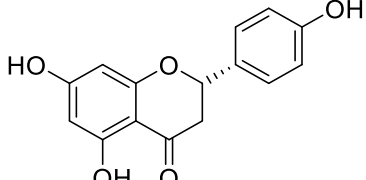
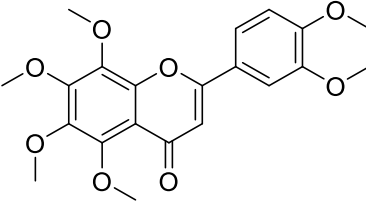
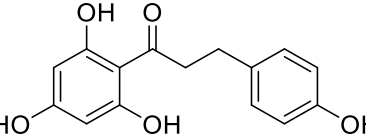
Table 1. Antimicrobial flavonoids and their respective molecular targets.

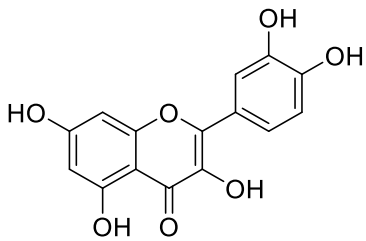
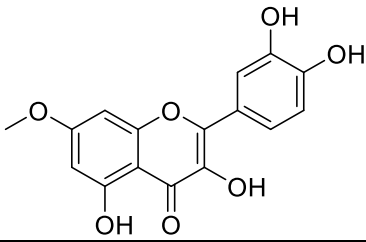
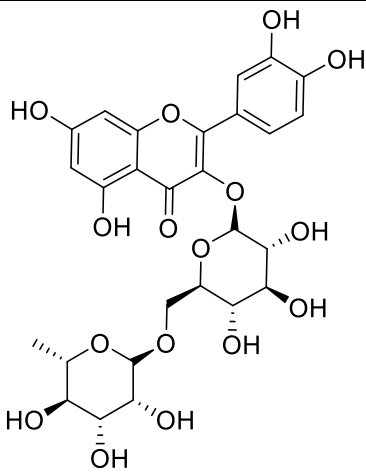
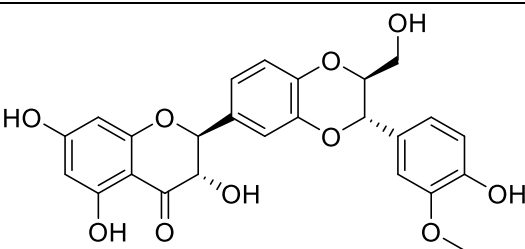
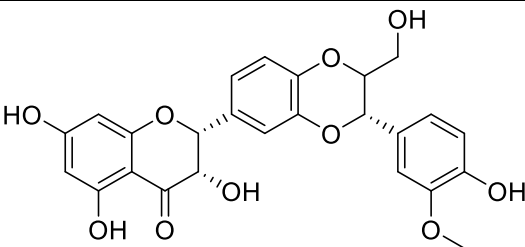
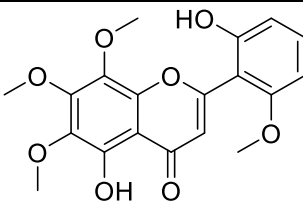
| Compound name | Structure | Bacterial strain | Target | Reference |
|-----------------------|---|---|--|-----------|
| 3,6-dihydroxyflavone |  | <i>E. coli</i> | Inhibition of β -ketoacyl acyl carrier protein (ACP) synthases | [83] |
| 5'-methoxyhydnocarpin |  | <i>S. aureus</i> | Inhibition of MDR-NorA efflux pump | [57] |
| 7,4'-dimethylapigenin |  | <i>S. aureus</i> | Inhibition of NorA efflux pump | [53] |
| Apigenin |  | <i>E. coli</i> | Partial inhibition of ATP synthase | [81] |
| | | <i>S. aureus</i> | Inhibition of efflux pump | [44] |
| | | <i>S. aureus</i> | Inhibition of NorA efflux pump | [53] |
| Artonin I |  | <i>S. aureus</i> | Inhibition of efflux pump Membrane damage | [56] |
| Baicalein |  | <i>M. smegmatis</i> , <i>M. aurum</i> and <i>M. bovis</i> | Inhibition of efflux pump | [58] |
| | | <i>E. coli</i> | Inhibition of ATP synthase | [81] |

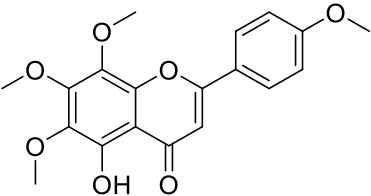
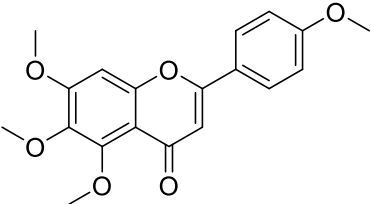
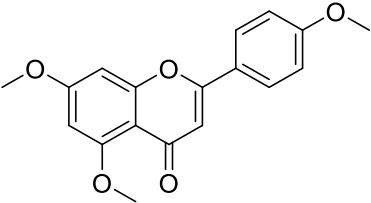
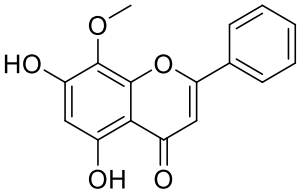
| | | | | |
|------------------|---|---------------------------------------|---|-------|
| |  | <i>L. monocytogenes</i> | Inhibition of listeriolysin O | [98] |
| | | <i>P. aeruginosa</i> | Interaction with LasR and PiIT | [109] |
| Biochanin A |  | <i>M. smegmatis</i> | Inhibition of MDR efflux pump | [44] |
| | | <i>E. coli</i> | Membrane perturbation | [69] |
| (+) -Catechin |  | <i>B. subtilis</i> and <i>E. coli</i> | ROS regulation Membrane perturbation | [63] |
| | | MRSA MSSA <i>S. aureus</i> | Decrease of SOD and CAT activity | [64] |
| | | <i>E. coli</i> | Membrane perturbation | [69] |
| Chrysin |  | <i>E. coli</i> | Partial inhibition of ATP synthase | [81] |
| | | <i>L. monocytogenes</i> | Inhibition of listeriolysin O | [98] |
| | | <i>P. aeruginosa</i> | Interaction with LasR and PiIT | [109] |
| Cirsimaritin |  | <i>S. aureus</i> | Inhibition of NorA efflux pump | [53] |
| Daidzein |  | <i>E. coli</i> | Weak Inhibition of ATP synthase | [81] |
| Dihydroquercetin |  | <i>E. coli</i> and <i>S. aureus</i> | Inhibition of β -ketoacyl ACP reductase, 3R-hydroxyacyl ACP dehydratase and trans 2-enoyl ACP reductase | [68] |
| | | <i>C. violaceum</i> | Interaction with CviR protein | [112] |
| Diosmin |  | <i>E. coli</i> | Partial inhibition of ATP synthase | [81] |

| | | | | |
|------------------------------|---|-------------------------|---|---------|
| (-)-Epicatechin |  | <i>E. coli</i> | Inhibition of ATP synthase | [78,81] |
| (-)-Epicatechin gallate |  | <i>E. coli</i> | Inhibition of DNA gyrase (sub GyrB) | [115] |
| (-)-Epigallocatechin |  | <i>E. coli</i> | Inhibition of DNA gyrase (sub GyrB) | [115] |
| (-)-Epigallocatechin gallate |  | <i>E. coli</i> | Inhibition of DNA gyrase (sub GyrB) | [115] |
| Fisetin |  | <i>L. monocytogenes</i> | Inhibition of listeriolysin O | [98] |
| Flavone |  | <i>S. aureus</i> | Inhibition of expression of the gene encoding for α -hemolysin (Hla) Inhibition of staphyloxanthin production | [96] |
| Galangin |  | <i>E. coli</i> | Weak inhibition of ATP synthase | [81] |

| | | | | |
|------------------|---|------------------------------|---|------|
| Genistein |  | <i>E. coli</i> | Partial Inhibition of ATP synthase | [81] |
| Genkwanin |  | <i>S. aureus</i> | Inhibition of NorA efflux pump | [53] |
| Hesperidin |  | <i>E. coli</i> | Partial inhibition of ATP synthase | [81] |
| Hesperetin |  | <i>E. coli</i> | Membrane perturbation | [69] |
| Kaempferol |  | <i>E. coli</i> | Partial inhibition of ATP synthase | [81] |
| | | <i>E. coli and S. aureus</i> | Membrane perturbation | [68] |
| | | <i>E. coli</i> | | [69] |
| | | <i>S. aureus</i> | Inhibition of efflux pump | [52] |
| Kurarinol |  | <i>S aureus</i> | Inhibition of Sortase A | [91] |
| Leucodelphinidin |  | <i>E. coli and S. aureus</i> | Inhibition of β -ketoacyl ACP reductase, 3R-hydroxyacyl ACP dehydratase and trans 2-enoyl ACP reductase | [68] |

| | | | | |
|------------|---|---|---|------------|
| Lonicerin |  | <i>P. aeruginosa</i> | Inhibition of alginate production protein AlgE | [92] |
| Luteolin |  | <i>E. coli</i> | Weak inhibition of ATP synthase | [81] |
| | | <i>S. aureus</i> | Inhibition of staphyloxanthin production | [96] |
| | | <i>E. coli</i> | Inhibition of assembly of amyloid curli fibers | [111] |
| Morin |  | <i>E. coli</i> | Inhibition of ATP synthase | [78,79,81] |
| | | <i>L. monocytogenes</i> | Inhibition of listeriolysin O | [98] |
| | | <i>E. coli</i> | Inhibition of assembly of amyloid curli fibers | [111] |
| Morusin |  | <i>S. aureus</i> and <i>S. enterica</i> | Downregulation of expression levels of different subunit of the fatty-acid-synthase (fabD, fabF, fabG and fabH) | [74] |
| Myricetin |  | <i>L. monocytogenes</i> | Inhibition of listeriolysin O | [98] |
| | | <i>S. aureus</i> | Inhibition of efflux pump | [44,51] |
| | | <i>E. coli</i> | Inhibition of assembly of amyloid curli fibers | [111] |
| | | <i>E. coli</i> | Inhibition of cellular functions of DnaK | [102] |
| Naringenin |  | <i>B. subtilis</i> | Inhibition of assembly of amyloid curli fibers | [111] |
| Nobiletin |  | <i>M. smegmatis</i> , <i>M. aurum</i> , and <i>M. bovis</i> | Inhibition of efflux pump | [58] |
| Phloretin |  | <i>B. subtilis</i> | Inhibition of assembly of amyloid curli fibers | [111] |

| | | | | |
|--------------------|---|---|---|---------|
| Quercetin |  | <i>E. coli</i> and <i>S. aureus</i> | Inhibition of β -ketoacyl ACP reductase, 3R-hydroxyacyl ACP dehydratase and trans 2-enoyl ACP reductase | [68] |
| | | <i>E. coli</i> | Inhibition of assembly of amyloid curli fibers | [111] |
| | | <i>E. coli</i> | Inhibition DNA gyrase (sub GyrB) | [72] |
| | | <i>E. coli</i> | Inhibition of ATP synthase | [78,79] |
| | | <i>P. aeruginosa</i> | Interaction with PilT and LasR | [109] |
| Rhamnetin |  | <i>S. aureus</i> | Inhibition of efflux pump | [52] |
| Rutin |  | <i>E. coli</i> | Partial inhibition of ATP synthase | [81] |
| Silibinin |  | <i>E. coli</i> | Inhibition of ATP synthase | [81] |
| Silymarin |  | <i>E. coli</i> | Inhibition of ATP synthase | [81] |
| Skullcapflavone II |  | <i>M. smegmatis</i> , <i>M. aurum</i> , and <i>M. bovis</i> | Inhibition of efflux pump | [58] |

| | | | | |
|-------------------------|--|---|--------------------------------|------|
| Tangeretin |  | <i>M. smegmatis</i> , <i>M. aurum</i> , and <i>M. bovis</i> | Inhibition of efflux pump | [58] |
| Tetramethylscutellarein |  | <i>S. aureus</i> | Inhibition of NorA efflux pump | [53] |
| Trimethylapigenin |  | <i>S. aureus</i> | Inhibition of NorA efflux pump | [53] |
| Wogonin |  | <i>M. smegmatis</i> , <i>M. aurum</i> , and <i>M. bovis</i> | Inhibition of efflux pump | [58] |