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## Antibacterial modes of herbal flavonoids combat resistant bacteria

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The increasing dissemination of multidrug resistant (MDR) bacterial infections has endangered a global crisis in public health. Currently, the infections caused by Gram-negative (G-) bacteria are more than Gram-positive (G+) bacteria in the clinic. A report from China Antimicrobial Resistance Surveillance System (CARSS) showed that G- bacteria accounted for 71.1%, while Gram-positive (G+) bacteria about 28.9 % from the 3,249,123 isolated strains. How to develop the effective antibacterial agents against resistant bacteria is becoming the most urgent demands in the resistant era. Herbal flavonoids with multi-target antibacterial actions are emerging arsenal to overcome resistant bacterial infections. In this work, we focus mainly on the antibacterial mechanisms of herbal flavonoids. Advances in herbal flavonoid compounds distribute in heat-clearing Chinese medicine show the prospect therapy of resistant bacteria. Additionally, we summarize the targets of recent flavonoid compounds and divide into direct antibacterial compounds (DACs) and host-acting antibacterial compounds (HACs) based on their modes of action. We also discuss associated functional groups of flavonoid compounds and highlight recent pharmacological activities against diverse resistant bacteria to treat the clinical infection of resistant pathogens.

**Keywords:** Herbal flavonoids; heat-clearing Chinese medicine; antibiotic resistance; multidrug resistant bacteria; antibacterial modes