Spatholobus suberectus metabolites inhibit sortase A and sortase A-mediated cell aggregation of Gram-positive bacteria

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The sortase enzymes are a family of Gram-positive transpeptidases responsible for anchoring surface protein virulence factors to the peptidoglycan cell wall layer. Numerous genetic knockout experiments have shown that the sortase A (SrtA) isoform plays a critical role in the pathogenesis of Gram-positive bacteria by modulating the ability of the bacterium to adhere to host tissue via the covalent anchoring of adhesions and other virulence-associated proteins to cell wall peptidoglycan. In this study, 20 flavonoids were isolated from the stem of the medicinal plant Spatholobus suberectus. The SrtA activity was determined by quantifying increased fluorescence intensity upon cleavage of a synthetic peptide substrate containing the LPETG motif. Among these isolated compounds, 7-hydroxy-6-methoxyflavanone and formononetin were identified as compounds with promising SrtA inhibitory activity. These compounds also exhibited inhibitory activity against Staphylococcus aureus cell clumping to fibrinogen and saliva-induced cell aggregation in Streptococcus mutans. The suppression of cell-aggregation activity indicates the potential of these compounds in the treatment of Gram-positive bacterial infections via the inhibition of SrtA.

Biography

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