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Effects of steroidal alkaloids from *Holarrhena antidysenterica* and conessine as efflux pump inhibitors against *Pseudomonas aeruginosa*

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The *Pseudomonas aeruginosa* MexAB-OprM, MexXY-OprM, MexCD-OprJ and MexEF-OprN are well characterized efflux systems of the Resistance-Nodulation-Cell Division (RND) family and are able to export a wide variety of structurally diverse compounds, including many clinically administered antibiotics. The pumps are expressed upon exposure to antibiotics and mutations in local or global regulator genes can occur, leading to overexpression of these efflux pumps and to Multidrug Resistance (MDR) phenotypes. To overcome MDR, efflux pump inhibitors are a potential solution. Efflux pump inhibitors from natural products have been extensively explored as potential sources because of fewer adverse effects, low cost and traditional medicine. Many plant alkaloids have been previously reported as efflux pump inhibitors such as curcumin, reserpine, capsaicin and piperine. This study has determined the effects of steroidal alkaloids from *Holarrhena antidysenterica* and its major steroidal alkaloid conessine as efflux pump inhibitors against *P. aeruginosa*. Steroidal alkaloids and conessine combined with various antibiotics were investigated for synergistic activity against *P. aeruginosa* PAM1020 (WT), *P. aeruginosa* PAM1032 (nalB), *P. aeruginosa* PAM1033 (nfxB), *P. aeruginosa* PAM1034 (nfxC) and *P. aeruginosa* PAM1626 (Δ mex). Conessine (32 mg/L) reduced MICs of Piperacillin, Meropenem and Levofloxacin in MexEF-OprN overexpressed strain (*P. aeruginosa* PAM1034). However, synergistic activity obtained from steroidal alkaloids at 1024 mg/L demonstrated less effects than conessine. The results suggested that conessine could be applied as an efflux pump inhibitor to restore antibiotic activity by inhibiting efflux pump system in *P. aeruginosa*.

Biography

Thanyaluck Siriyong is a PhD candidate in Microbiology from Prince of Songkla University, Thailand. She has completed her BSc and MSc in Thai Traditional Medicine from Prince of Songkla University. She is currently a Visiting Doctoral Researcher at the University of St Andrews, Scotland, UK. Her project is supported by the Thailand Research Fund through the Royal Golden Jubilee PhD Program co-funded by the British Council through Newton Fund.

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