

Lavender essential oil induces oxidative stress which modifies the bacterial membrane permeability of carbapenemase producing *Klebsiella pneumoniae*

ABSTRACT

Misuse of antibiotics in the clinical and agricultural sectors has caused the emergence of multidrug-resistant (MDR) *Klebsiella pneumoniae* which contributes a threat to human health. In this study, we assessed the feasibility of lavender essential oil (LVO) as an antimicrobial agent in combinatory therapy with meropenem in suppressing the growth of carbapenemase-producing *K. pneumoniae* (KPC-KP). Synergistic interactions between LVO and meropenem were detected, which significantly reduce the inhibitory concentration of both LVO and meropenem by 15 and 4-fold respectively. Comparative proteomic profiling identified a disruption in the bacterial membrane via oxidative stress that was indicated by loss of membrane and cytoplasmic proteins and the upregulation of oxidative regulators. As a proof of concept, zeta potential measurements showed a change in cell surface charge while outer membrane permeability measurement indicated an increase in membrane permeability following exposure to LVO. This was indicative of a disrupted outer membrane. Ethidium bromide influx/efflux assays demonstrated no significant efflux pump inhibition by LVO, and scanning electron microscopy revealed irregularities on the cell surface after exposure to LVO. Oxidative stress was also detected with increased level of ROS and lipid peroxidation in LVO-treated cells. In conclusion, our data suggest that LVO induced oxidative stress in *K. pneumoniae* which oxidizes the outer membrane, enabling the influx of generated ROS, LVO and meropenem into the bacterial cells, causing damage to the cells and eventually death.