

Disruption of KPC-producing *Klebsiella pneumoniae* membrane via induction of oxidative stress by cinnamon bark (*Cinnamomum verum* J. Presl) essential oil

ABSTRACT

Klebsiella pneumoniae (KP) remains the most prevalent nosocomial pathogen and carries the carbapenemase (KPC) gene which confers resistance towards carbapenem. Thus, it is necessary to discover novel antimicrobials to address the issue of antimicrobial resistance in such pathogens. Natural products such as essential oils are a promising source due to their complex composition. Essential oils have been shown to be effective against pathogens, but the overall mechanisms have yet to be fully explained. Understanding the molecular mechanisms of essential oil towards KPC-KP cells would provide a deeper understanding of their potential use in clinical settings. Therefore, we aimed to investigate the mode of action of essential oil against KPC-KP cells from a proteomic perspective by comparing the overall proteome profile of KPC-KP cells treated with cinnamon bark (*Cinnamomum verum* J. Presl) essential oil (CBO) at their sub-inhibitory concentration of 0.08% (v/v). A total of 384 proteins were successfully identified from the non-treated cells, whereas only 242 proteins were identified from the CBO-treated cells. Proteins were then categorized based on their biological processes, cellular components and molecular function prior to pathway analysis. Pathway analysis showed that CBO induced oxidative stress in the KPC-KP cells as indicated by the abundance of oxidative stress regulator proteins such as glycyl radical cofactor, catalase peroxidase and DNA mismatch repair protein. Oxidative stress is likely to oxidize and disrupt the bacterial membrane as shown by the loss of major membrane proteins. Several genes selected for qRT-PCR analysis validated the proteomic profile and were congruent with the proteomic abundance profiles. In conclusion, KPC-KP cells exposed to CBO undergo oxidative stress that eventually disrupts the bacterial membrane possibly via interaction with the phospholipid bilayer. Interestingly, several pathways involved in the bacterial membrane repair system were also affected by oxidative stress, contributing to the loss of cells viability.

Keyword: *Klebsiella pneumoniae*; Cinnamon bark essential oil; Antimicrobial resistance

