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Quorum sensing inhibition may mediate anti-microbial efficacy of Quellthera EPQ-100 botanical drug candidate against multi-drug resistant ESKAPE pathogens

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According to the Center for Disease Control (CDC) 1 out of 25 patients, contracts a hospital acquired infection (HAI). These infections are often from Multi-drug resistant (MDR) bacteria. The species of MDR bacteria that are responsible for most HAIs are known as the "ESKAPE" pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species*). Although there are a few promising antimicrobial agents, currently in preclinical stages, there is still an urgent and immediate need for novel anti-infective agents with activity against these pathogens. Polyphenols in fresh cut plant tissues are involved in significant antimicrobial activity that is not exhibited once extracted. The short-lived biologic activity of these metabolites has been a foundation of traditional medicines used successfully by many cultures for the treatment of human diseases caused by microorganisms. We evaluated the antimicrobial activity of a novel botanical drug candidate developed by Quellthera Inc., to mimic *in-vivo* levels of plant antimicrobial activity. Our results show that the test material is effective against the MDR strains of ESKAPE at surprisingly low concentrations. Evidence further suggests this anti-microbial activity is significantly mediated by quorum sensing inhibition. The bacterial strains used for the study were the multidrug resistant (MDR) ESKAPE pathogens; *Enterococcus faecium* (MDR1674620), MRSA *Staphylococcus aureus* (ATCC 33591), MDR Klebsiella pneumoniae (ATCC BAA-2473), *Acinetobacter baumannii* (MDR 1674627), *Pseudomonas aeruginosa* (MDR 1674623), and *Enterobacter cloacae* (ESBL 1744299). The following susceptible wildtype QC strains were used for Broth Microdilution Minimal Inhibitory Concentration (MIC) assays to determine the antimicrobial susceptibility of the test articles: *S. aureus* ATCC 29213, and *Escherichia coli* ATCC 25922. *Chromobacterium violaceum* strain 12472 was used to study inhibition of quorum sensing by test product. Quellthera material showed growth inhibition of the ESKAPE pathogens at low concentrations. Low concentrations of Quellthera's EPQ-100 demonstrated effective inhibition of various MDR bacteria. Preliminary data suggest further investigations of its novel non-antibiotic mechanism of action and its potential to obviate drug resistance while promoting stability of the normal gut microbiome.

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