

Title: Monitoring anti-virulence effects of phenolic extracts from upcycled products using pseudo-targeted metabolomics

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The threat of antibiotic-resistant bacterial strains because of unregulated antibiotic use requires new strategies to combat microbial pathogenicity. This study aimed to investigate the potential of phenolic extracts from grape, pomegranate, and persimmon to modulate bacterial virulence factors through pseudo-targeted metabolomics. The effect of sub-inhibitory concentration of phenolic extracts on bacterial quorum sensing was assessed by monitoring the interaction of extracts and extracellular autoinducers of *Pseudomonas aeruginosa* and *Chromobacterium violaceum*. Also, the interaction of extracts, bacteria and colon cells were determined. A neutral loss pattern of the lactone ring at 102.1 *m/z* revealed the presence of acyl-homoserine lactones (AHLs) expressed by *C. violaceum* and *P. aeruginosa*. Multiple reaction monitoring allowed the annotation of 21 molecules of AHLs and 8 molecules of 2-alkyl-4(1*H*)-quinolones (AQs). MRM allowed tracking these compounds which were significantly downregulated by the extracts, indicating their potential to attenuate bacterial virulence such as biofilms, bacterial motility, and pigment production by phenolics was correlated with the downregulation of AHLs and AQs. This study highlights phenolic extracts from upcycled products as candidates to modulate bacterial pathogenicity and mitigate bacterial virulence. The use of pseudo-targeted metabolomics as a monitoring tool allows for the annotation of both virulence molecules and bioactive compounds within the extracts, shedding light on their mechanisms of action.