# DISARMING *PSEUDOMONAS AERUGINOSA* VIRULENCE: INHIBITORY EFFECTS OF METAL-BASED COMPOUNDS ON ELASTASE B ACTIVITY

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*Pseudomonas aeruginosa* is a notorious nosocomial and opportunistic human pathogen, which exhibited high pathogenicity due to its genetic/metabolic plasticity and expression of virulence factors. Elastase B is a metalloprotease that plays a pivotal role promoting tissue damage, immune system evasion and pseudomonal infection establishment in the host. The failure of classical anti-*P. aeruginosa* antibiotic approaches represents a growing threat to public health, which lead to increase of morbidly and mortality of infectious illness. Therefore, anti-virulence strategy has been outstanding as a promissory alternative therapeutic, attenuating the virulence of pathogens. Due to the key roles played by elastase B in pseudomonal virulence, this extracellular enzyme is a potential target for the development of an inhibitor as an antimicrobial agent. The aim of this study was to (i) evaluate the *in silico* interactions of 1,10-phenanthroline-5,6-dione (phendione), $[Ag(phendione)_2].ClO_4$ (Ag-phendione) and $[Cu(phendione)_3](ClO_4)_2.4H_2O$ (Cu-phendione) on the active site of elastase B, (ii) examine the *in vitro* effects of these compounds on the elastase B activity, (iii) investigate the effects of these compounds on *lasB* gene expression, and (iv) evaluate the ability of these compounds to block the damages induced by elastase B on host cells. Molecular docking assays revealed that 1,10-phenanthroline and its derivatives can interact with the active site of lasB, especially Cu-phendione that showed more favorable interaction energy value. Similarly, the *in vitro* assays revealed that these compounds were effective inhibitors of the LasB activity, particularly Cu-phendione that exhibited the highest inhibitory activity using purified elastase B (Ki = 0.09 μM). Also, these compounds, at sub-inhibitory concentrations, blocked the expression of *lasB* gene as well as this mature protein production/secretion. Finally, Ag-phendione and Cu-phendione presented protective effects against elastase B on lung epithelial cell damage, being able to restore 32.42% and 42.02% of host cell viability, respectively. Collectively, our data highlight elastase B as a potential therapeutic target. Additionally, these compounds could interact with the catalytic site, inhibit the enzymatic activity and the gene expression of the elastase B, besides neutralizing cell-damage action of elastase B. In this context, phendione and particularly its metal-based derivatives are emerging as potential anti-virulence drugs against *P. aeruginosa* infection.

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