Abstract

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Project Title : Antivirulence agents against *Pasteurella multocida* in swine

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Abstract:

Pasteurella multocida is the causative agent of fowl cholera in poultry, hemorrhagic septicemia in ungulates and atrophic rhinitis in swine. This study aims to discover the antivirulence agents against *P. multocida* in order to treat swine. Outer membrane protein A (OmpA), HldE-kinase and Fis transcription factor, are the virulence factors of *P. multocida* which are the targets for this research. Libraries of small molecules were downloaded from the ZINC database and docked against those virulence factors using virtual screening approach. The three dimensional structures of three proteins were constructed by homology modeling. The FDA-approved drug category was selected to perform virtual screening. Deferoxamine mesylate, Mycophenolate mofetil, Famciclovir, Orlistat, Neomycin C, Letrozole, Indocyanine green, Prostaglandin, Vidarabine monohydrate, Ribavirin, Fludarabine phosphate, N-methyl-D-glucamine and Adenosine monohydrate were purchased. The small compounds, Deferoxamine mesylate, Mycophenolate mofetil, Orlistat, Letrozole, Neomycin C, could inhibit the formation of biofilm in the different concentrations with no effect to the growth of *P. multocida* serotype A. Mycophenolate mofetil showed its highest efficacy with the IC_{50} at 7.3 nM. For serotype D, the Indocyanine green showed the highest effect at the IC_{50} value 11.7 nM. The amount of LPS of *P. multocida* serotype A and D were found higher than that of control after adding the compounds, Deferoxamine mesylate, Orlistat, Neomycin C. These results revealed the relationship of LPS and biofilm formation in *P. multocida*. No candidate compound was found to inhibit Fis activity. This study offers an alternative way to combat *Pm*, which could also be applied to combat other pathogens.

Keywords: *Pasteurella multocida*, outer membrane protein A, biofilm formation, FDA-approved drugs, virtual screening