Computer-aided identification of recognized drugs as Pseudomonas aeruginosa quorum-sensing inhibitors

Attenuation of Pseudomonas aeruginosa virulence by the use of small-molecule quorum-sensing inhibitors (referred to as the antipathogenic drug principle) is likely to play a role in future treatment strategies for chronic infections. In this study, structure-based virtual screening was used in a search for putative quorum-sensing inhibitors from a database comprising approved drugs and natural compounds. The database was built from compounds which showed structural similarities to previously reported quorum-sensing inhibitors, the ligand of the P. aeruginosa quorum-sensing receptor LasR, and a quorum-sensing receptor agonist. Six top-ranking compounds, all recognized drugs, were identified and tested for quorum-sensing-inhibitory activity. Three compounds, salicylic acid, nifuroxazide, and chlorzoxazone, showed significant inhibition of quorum-sensing-regulated gene expression and related phenotypes in a dose-dependent manner. These results suggest that the identified compounds have the potential to be used as antipathogenic drugs. Furthermore, the results indicate that structure-based virtual screening is an efficient tool in the search for novel compounds to combat bacterial infections.