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Finding a new therapeutic target of an old drug: An efficient route for drug discovery

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The road map of drug discovery is a daunting endeavor which is full of several uncertainties. Although several large and diversified chemical libraries of 'drug like compounds' are readily screened to yield the lead compounds which can be transformed into drugs. A more efficient approach involves the screening of approved drugs and off-patent medications for the alternative therapeutic targets which can yield compounds that can be evaluated immediately in clinical trials. This technique was utilized for identifying inhibitors of quorum sensing in pathogens which causes production of virulence factors and formation of biofilms, thus leads to bacterial resistance. Several quorum sensing inhibitors were developed in the recent past but none of them managed to reach in clinic due to toxicity issues which is a major hassle in drug discovery. Virtual screening of several drugs were carried out and based on similarity scoring function and putative drug-macromolecular interactions in the active site pocket of CviR and LasB receptor several drugs were recognized as quorum sensing inhibitor. Further, the *in vitro* activity of the recognized drugs has been evaluated using violacein production and biofilm based bioassays. Further, the efficacy of the most effective drug candidate was also analyzed in combination with tobramycin (an antibiotic shows resistance against *P. aeruginosa*) where the combined drug therapy proves to be highly effective in reducing the bacterial load. Hence, it is concluded that screening of approved drugs for identifying their new therapeutic uses proves to be an efficient tool in the area of drug discovery.

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