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Virtual Screening of Potential Inhibitors against Efflux Pumps of Mycobacterium tuberculosis

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Abstract : Mycobacterium tuberculosis was described as 'captain of death' with an inherent property of multiple drug resistance majorly caused by the competent mechanism of efflux pumps. In this study, various open source tools combining chemo-informatics with bioinformatics were used for efficient in-silico drug designing. The efflux pump, Rv1218c, belonging to the ABC transporter superfamily, which is predicted to be a tetronasin-transporter in M. tuberculosis was targeted. Recent studies have shown that Rv1218c forms a complex with two more efflux pumps (Rv1219c and Rv1217c) to provide multidrug resistance to the bacterium. The 3D structure of the protein was modeled (as the structure was unavailable in the previously collected databases on this gene). The TMHMM analysis of this protein in TubercuList has shown that this protein is present in the outer membrane of the bacterium. Virtual screening of compounds from various publically available chemical libraries was performed on the M. tuberculosis protein using various open source tools. These ligands were further assessed where various physicochemical properties were evaluated and analyzed. On comparison of different physicochemical properties, toxicity and docking, the ligand 2-(hydroxymethyl)-6-[4, 5, 6-trihydroxy-2-(hydroxymethyl) tetrahydropyran-3-yl] oxy-tetrahydropyran-3, 4, 5-triol was found to be best suited for further studies.

Keywords : drug resistance, efflux pump, molecular docking, virtual screening
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