Abstract

Structure Guided Design of *Xanthomonas oryzae* pv. *oryzae* Topoisomerase I Inhibitors [†]

Lakindu Samaranayake P. K. * and Inoka C. Perera

Department of Zoology and Environment Sciences, University of Colombo, Colombo 00700, Sri Lanka; icperera@sci.cmb.ac.lk

* Correspondence: lakyspk@gmail.com

[†] Presented at the 1st Molecules Medicinal Chemistry Symposium, Barcelona, Spain, 8 September 2017.

Published: 23 October 2017

Topoisomerase inhibitors initiate the cell killing process by either stabilizing or increasing the amount of the covalent complex formed between the enzyme and cleaved DNA. In our study, we have attempted to identify structure based *Xanthomonas oryzae* pv. *oryzae* (*Xoo*) topo I inhibitors by in silico analysis of the binding affinities (BA) of a set of small ligands with the protein. In order to identify novel inhibitors of topoisomerase I, a 3D model of the *Xoo* topoisomerase is created based on the *Mycobacterium tuberculosis* (PDB ID-5d5h) by using the SWISS-MODEL workspace. The final model is obtained in high quality as assessed by SAVeS server, which shows that the refined model is reliable. With this model, a flexible docking with screen compounds from MayBridge and known topoisomerase I inhibitors such as Tn5 and ofloxacin were performed by AutoDock in PyRx Virtual Screening tool. The resulted BA were ordered and the top hundred molecules were selected. The binding pockets in the protein were assessed by POCASA1.1 and the active-site of the modelled protein was predicted. Out of the top hundred molecules, two molecules named HTS09044 and HTS11914 were bound with the assumed active-site with a better BA than Tn5 or ofloxacin. The binding interactions of the compound with the active-site of the model suggested that the amino acid residues (tyr495, asp546, pro492, arg491, thr265 and ser267) play a key role in drug design. The pharmacological properties were predicted and these two selected compounds showed a good drug profile. Hence, they would represent an intriguing step towards the development of potent inhibitor molecules against *Xoo* topo I.

© 2017 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<http://creativecommons.org/licenses/by/4.0/>).