Molecular Enzymology and Drug Targets©
2 (9) 2023 : 001-003 • REVIEW ARTICLE

A knowledge from a molecular docking study on the mycobacterium tb arabinosyltransferase c enzyme as a possible therapeutic target

Sachita Varma*

Department of Cellular and Molecular Biology, University of Cincinnati, Saudi Arabia

AUTHORS' CONTRIBUTION: (A) Study Design · **(B)** Data Collection . **(C)** Statistical Analysis · **(D)** Data Interpretation · **(E)** Manuscript Preparation · **(F)** Literature Search · **(G)** No Fund Collection

ABSTRACT

One of the main obstacles to treating and curing tuberculosis is the fact that Mycobacterium tuberculosis is multi-drug resistant. Numerous anti-tubercular medications lack effectiveness as a result of M. tab's established drug resistance mechanism. Therefore, research has been done globally to create potent anti-TB medications to enhance the treatment of these strains. Due to a lack of a structure-based approach, traditional drug development methods have been shown to be ineffective in the development of broad-spectrum drugs. In this context, numerous researches have been carried out and a number of drug target sites that affect drug-resistant Mtb strains have been found. The goal of this study was to determine how the two current medicines and five modified compounds produced from ethambutol interacted with the protein Arabinosyltransferase C. With Auto Dock, a molecular docking study can determine affinities and modes of binding. Emb1 and Emb3, which have different binding affinities, can be thought of as potential inhibitors of Arabinosyltransferase C in Mycobacterium TB, which is in charge of cell wall formation, according to analysis of a comparison study of the available medication. The information presented may be further tested experimentally for use in the development of new drugs to fight tuberculosis and further the study of effective antimyco bacterial techniques.

Keywords: Pharmaceutical chemistry; Binding affinity; Multi-drug resistant; Molecular docking; Anti-TB drugs; Tuberculosis

Address for correspondence:

Sachita Varma,
Department of Cellular and Molecular Biology, University of Cincinnati, Saudi Arabia
E-mail: Sachitavarma32@gmail.com

Word count: 1568 **Tables:** 00 **Figures:** 00 **References:** 10

Received: 3.04.2023, Manuscript No. Ipmedt -23-13674; **Editor assigned:** 05.04.2023, PreQC No. P-13674; **Reviewed:** 19.04.2023, QC No. Q-13674; **Revised:** 21.04.2023, Manuscript No. R-13674; **Published:** 28.04.2023

INTRODUCTION

One of the deadliest and most contagious diseases in the world, tuberculosis is brought on by the Mycobacterium tuberculosis, which affects about one-fourth of the world's population [1]. WHO estimates that around 10.4 million individuals in 2016 have TB, which is a leading cause of death for those who are HIV [2]. One of the most pervasive public health problems wreaking havoc globally is multidrug resistance bacteria. 4,90,900 of the 6,00,000 cases of TB are multidrug resistant [3]. INH, an anti-mycobacterial antibiotic that is commonly used to treat tuberculosis, has recently been discovered to be resistant to other anti-mycobacterial treatments [4]. According to the most recent assessment, 2.3% and 3.8% of patients with new and recurrent tuberculosis in the United States exhibit EMB resistance, respectively. A total of 63 surveys of ant tuberculosis drug resistance were done between 1985 and 1994, and the results showed that the rate of newly acquired EMB resistance was higher than 13.7% in only a few countries [5]. The transferase enzyme arabinosyltransferase C reacts with arabinose that is found in the farinose form and is involved in the polymerization of arabinogalactan, a significant and vital component of the cell wall of mycobacterium [6]. By acting through three arabinose transferase and EmbC, EMB is used in combination with isoniazid, pyrazinamide, and rifampin (rifampicin) to block the formation of cell walls and the synthesis of arabinogalactan and lipoarabinomannan [7]. A member of glycosyltransferase superfamily C is EmbA, EmbB, and EmbC. The biosynthesis of arabinogalactan is aided by EmbA and EmbB, whereas LAM synthesis is aided by EmbC [8]. LAM is a crucial element in offers a variety of perspectives on the interactions between Mycobacterium species and host cells [9]. Since there is a significant correlation between EmbC activity and the amount of LAM species produced by the overexpression of an embCmutant of M. smegmatis with embCMtb, EmbC is regarded as a high grade target for ethambutol. These M [10]. tuberculosis Emb enzymes have 13 transmembrane helices, which is a common design, and a hydrophilic C-terminal domain made up of residues from the full-length enzyme. Computational drug discovery using a structure-based method provides an invaluable replacement for the costly and random screening is a time-consuming process, however ligand-based computational virtual screening methods, along with other approaches, are proven to be crucial for de novo characterization, finding

new inhibitors, and medication repurposing. The purpose of the current work is to use molecular docking to assess the binding affinity of the existing antibiotic Isoniazid and several functional variants of ethambutol against Arabinosyltransferase C of Mycobacterium TB. The target enzyme's and its ligands' three-dimensional structures were obtained for the current inquiry from the Protein Data Bank and the PubChem databases. One of the main obstacles to treating and curing tuberculosis is the fact that Mycobacterium tuberculosis is multi-drug resistant. Numerous anti-tubercular medications lack effectiveness as a result of M. tb's established drug resistance mechanism. Therefore, research has been done globally to create potent anti-TB medications to enhance the treatment of these strains.

DISCUSSION

The information presented may be further tested experimentally for use in the development of new drugs to fight tuberculosis and further the study of effective ant mycobacterial techniques. In order to determine the binding affinity and interaction of ligands taken with various important amino acid residues on the C-terminal domain of EmbC, a molecular docking research was conducted utilising the enzyme Arabinosyltransferase C. Strong intermolecular interactions, like H-bonds, or even other noncovalent interactions, like ionic interactions, hydrophobic interactions, and van der Waals forces, which are crucial in protein ligand interaction, stabilise a specific ligand energetically at a specific binding site of the protein structure. According to the WHO, TB is one of the top 10 global killers, and in 2015 and 2016, it claimed more lives than HIV. The first study on STR monooresistance in M. tuberculosis was published. In the beginning, combined therapy using STR, INH, and para-amino salicylic acid was used to combat the development of drug resistance. Later, pyrazinamide and rifampicin were added. However, medication resistance can develop and escalate to incorporate both RIF and INH-MDR-TB due to poor physician prescription, poor patient adherence, poor drug quality/supply, and factors not frequently seen or generally known. Jointly reporting XDR-TB MDR-TB with added bacillary resistance to any fluoroquinolone and at least one of the three second-line drugs in 2006, the Centres for Disease Control and Prevention and WHO Amikacin, Kanamycin, and Capreomycin, three injectable medicines In the recent past, "XXDR-TB" was proposed in Italy for XDR strains of M. tuberculosis that were found to be resistant to standard first-line treatments and second-line drugs as well as rifabutin, clofazimine, dapsone, clarithromycin, and thiacetazone. Iranian researchers suggested the moniker "TDR-TB" to characterise the "XXDR-TB" (Velayati et al., 2009). Later, TDR-TB cases were also noted in South Africa Since M. tuberculosis grows slowly, medication susceptibility tests on solid media take 4 to 6 weeks to complete, compared to 1 to 2 weeks for tests on liquid media. Because the use of ineffective medications during the initial treatment phase may promote the formation of drug-resistant profiles, the absence of quick diagnostic techniques might be recommended as a risk factor for the prevalence of MDR-, XDR-, and TDR-TB. In this regard, the WHO recommends the TB Biochip platform, additional molecular methods, and the quick and more sophisticated in vitro growth monitoring system, MGIT 960, as well as the nucleic acid amplification method, Xpert MTB/RIF, for early identification of PZA-resistant and RIF-resistant TB, respectively. Each approach was put forth to deliver both faster and more trustworthy outcomes for detecting medication resistance early. Cost and infrastructure requirements for each treatment should be taken into account, as they are the main factors that will ultimately restrict their clinical application in many parts of the world.

CONCLUSION

The failure of TB patients to adhere to treatment regimens and the expense of a full recovery are likely the two main causes of the development of medication resistance. In fact, the majority of patients had previously received treatment for TB either ineffectively or for an inadequate amount of time, which led to an incomplete sterilisation of the lungs and the regrowth of "persisters" that became more resistant to the medications that had previously been used and transformed them into XDR-/TDR-TB, respectively. Another study found that the main cause of drug resistance is spontaneous mutations in drug targets, which promote acid resistance, drug adaptations, drug inactivation or degradation by enzymes encoded by M. tuberculosis genes, molecular simulation of drug targets, and epigenetic drug tolerance to ensure the survival of TB bacilli at very low pH. It is also important to note that the term "resistance" should be used carefully because misunderstanding or improper application may create the impression that it is a binary phenotype while, in reality, it can be assessed at various levels, including low, moderate, and high-level drug resistance. Due to a lack of a structure-based approach, traditional drug development methods have been shown to be ineffective in the development of broad-spectrum drugs. In this context, numerous researches have been carried out and a number of drug target sites that affect drug-resistant M.tb strains have been found. The goal of this study was to determine how the two current medicines and five modified compounds produced from ethambutol interacted with the protein Arabinosyltransferase C. Using an analysis of molecular docking with Auto Dock 4. Emb1 and Emb3, which have binding affinities and, respectively, can be analysed as potential inhibitors of Arabinosyltransferase C in Mycobacterium tuberculosis, which is in charge of cell wall synthesis, based on the comparison study of the existing drug and the five proposed modified molecules.

REFERENCES

1. **Pahor AL.** Ear, nose and throat in ancient Egypt. *J Lar Otol Lond*. 1992; 106: 677-687.
2. **Sullivan R.** the identity and work of the ancient Egyptian surgeon. *J R Soc Med.* 1996; 89: 467-473.
3. **Ruetsch YA, Böni T, Borgeat A.** from cocaine to ropivacaine: the history of local anesthetic drugs. **Curr Top Med Chem.** 2001; 1: 175-182.
4. **Brill S, Gurman GM, Fisher A, et al.** A history of neuraxial administration of local analgesics and opioids. *European Journal of Anaesthesiology*. 2003; 20: 682-689.
5. **Reddy S, Patt RB**. the benzodiazepines as adjuvant analgesics. *J Pain Symptom Manag*. 1994; 9: 510-514.
6. **Mallinson T.** Fascia iliaca compartment block: a short how-to guide. *J Paramed Pract.* 2019; 11: 154-155.
7. **Lewis Sharon R, Price Anastasia, Walker Kevin J, et al.** Ultrasound guidance for upper and lower limb blocks. *Cochrane Database Syst Rev*. 2015; 9: 6459.
8. **Ullah H, Samad K, Khan FA, et al.** Continuous interscalene brachial plexus block versus parenteral analgesia for postoperative pain relief after major shoulder surgery. *CDSR*. 2014; 2: 7080.
9. **Klomp T, Van Poppel M, Jones L, et al.** Inhaled analgesia for pain management in labour. *CDSR.* 2012; 12: 9351.
10. **Radvansky BM, Shah K, Parikh A, et al.** Role of ketamine in acute postoperative pain management: a narrative review. BioMed Research International.