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Elucidating the binding mode and binding interactions of 1,2,4-triazole-5-thione derivatives as InhA inhibitor using molecular docking calculations

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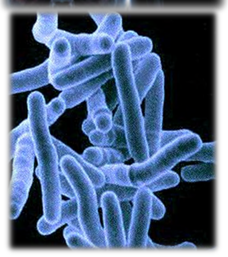
Introduction

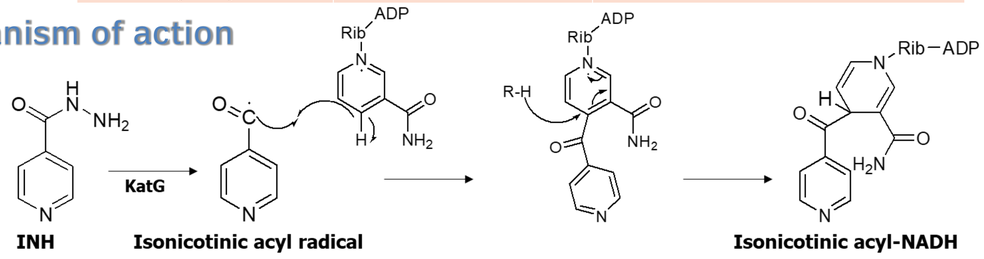


Mycobacterium tuberculosis (Mtb)

World Health Organization (WHO) data, 2021

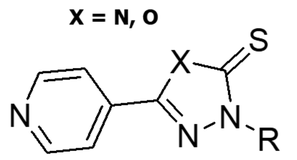
Infectious disease	People deaths with TB	People newly infected with TB
Tuberculosis (TB)	1.5 (million)	9.9 (million)

Mechanism of action

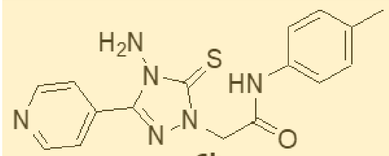
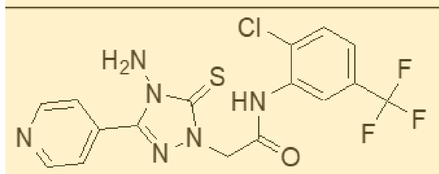
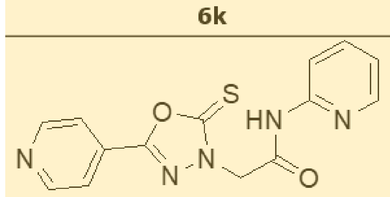


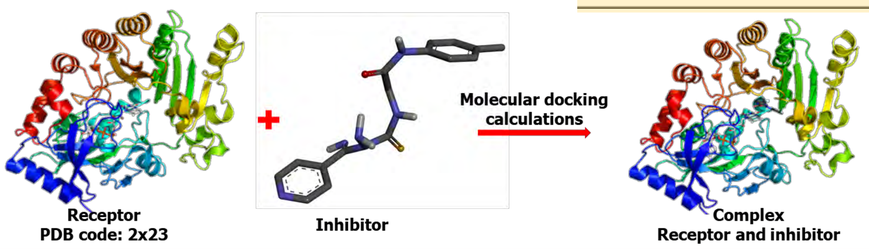
Materials and method

Table 1. Structure of 1,2,4-triazole-5-thione derivatives and different biological activity



Compound were selected with different InhA IC_{50}

Code name	InhA IC_{50} (μM)
 6b	0.09
 6k	6.36
 7a	50



Conclusion

- 1,2,4-triazole-5-thione derivatives formed hydrogen bond interaction with Met199.
- Hydrophobic interactions were found with Met161, Pro156, Ala198, Ala157 Met155, Leu218 residue.
- The obtained results from these studies are fruitful to further design the promising InhA inhibitors to overcome tuberculosis drug resistance.

Results

Table 2. The crucial interaction of 1,2,4-triazole-5-thione derivatives and different biological activity

Code name	InhA IC_{50} (μM)	H-bonding interaction	Hydrophobic interaction
6b	0.09	Met199	Met161, Pro156, Ala198, Tyr158, Ala157 Met155, Leu218
6k	6.36	Met199	Met161, Pro156, Ala198, Ile194, Leu218, Met199, Ala157
7a	50	-	Met161, Pro156, Ala198, Val203, Ile202, Leu218, Met199, Ala158, Phe149, Ala157

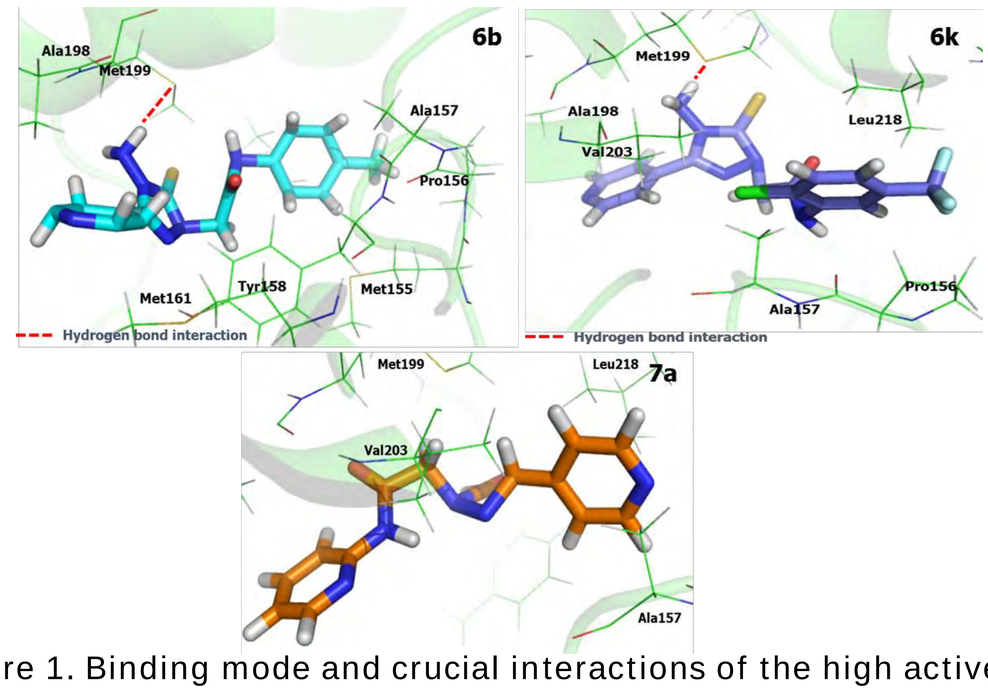


Figure 1. Binding mode and crucial interactions of the high active compound (6b), moderate active compound (6k) and low active compound (7a)

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