

MOLECULAR DOCKING OF THE INHIBITORY ACTIVITIES OF SYZYGIUM CORDATUM AGAINST MYCOBACTERIUM TUBERCULOSIS

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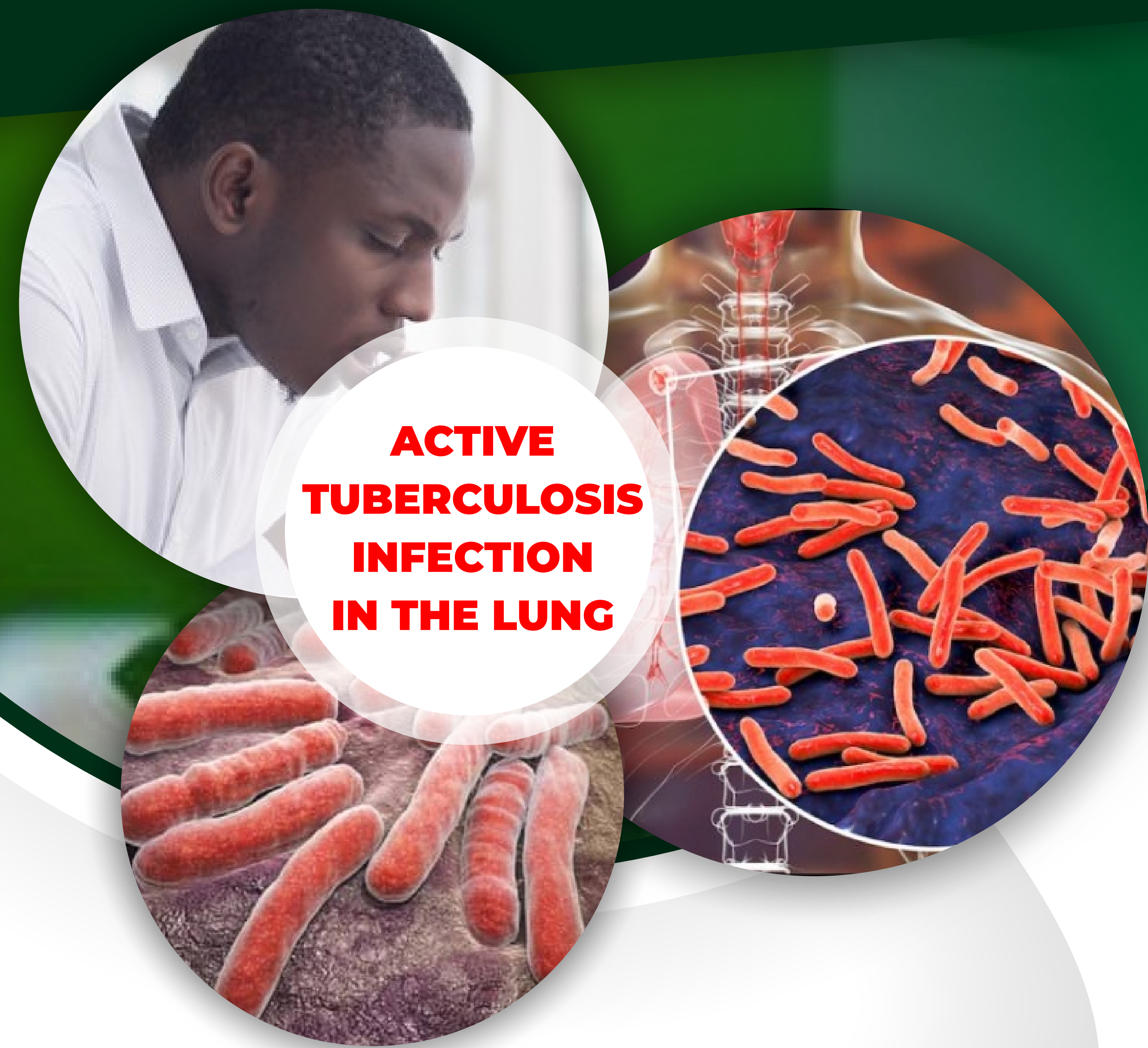
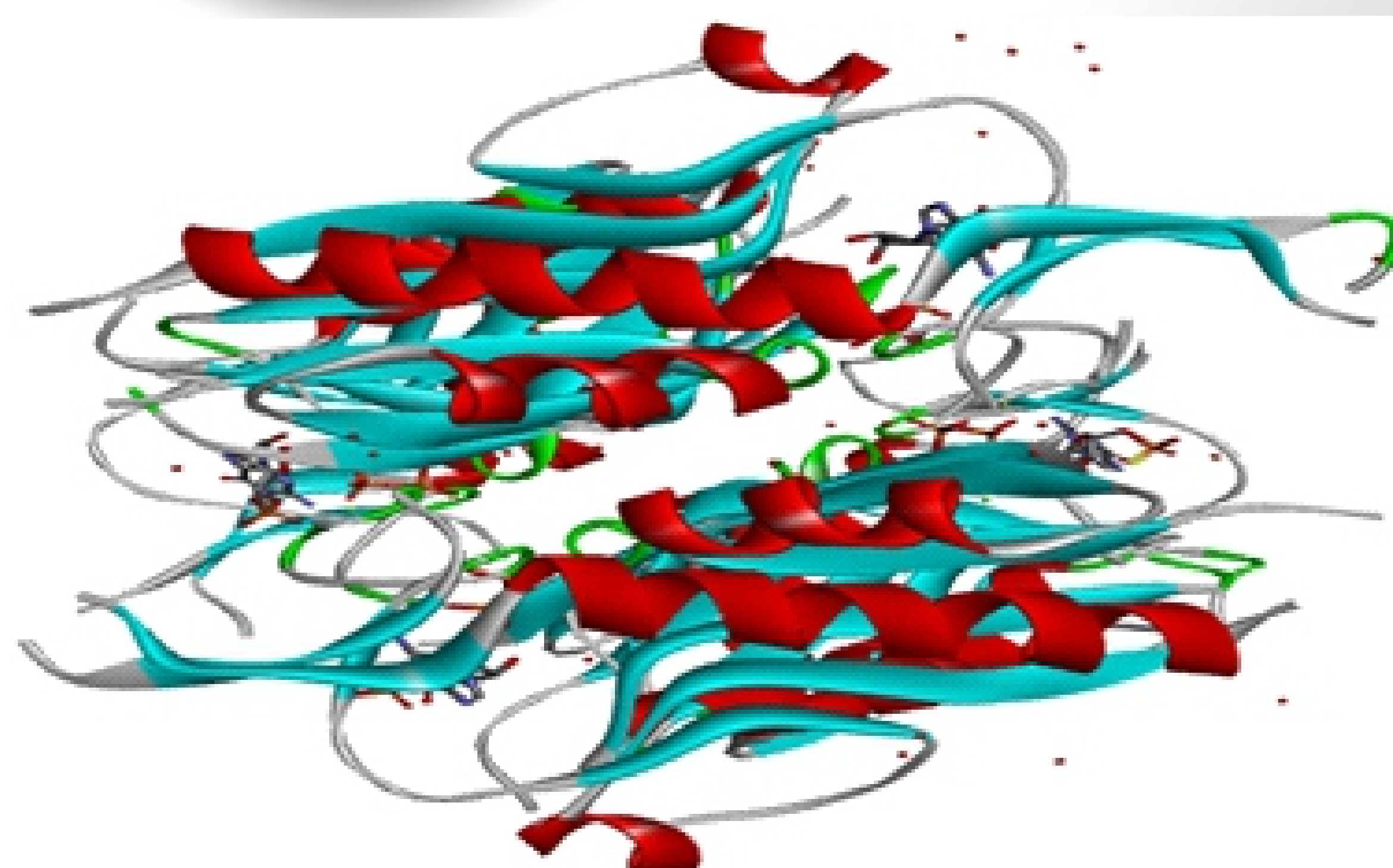


Fig 1. CRYSTAL STRUCTURE OF MYCOBACTERIUM TUBERCULOSIS

INTRODUCTION

- Tuberculosis remains one of the significant infectious diseases causing over 1.8 million deaths a year, making it the world's most deadly human pathogen (Gordon & Parish, 2018).
- 10 million people were estimated to fell ill with tuberculosis in 2019 globally.
- Men ≥ 18 years = 56% while women and children ≤ 15 = 44%.
- Despite 9% and 14% cumulative reduction between 2015 to 2019 in the incidence rate and death rate of tuberculosis respectively (WHO, 2020).
- Tuberculosis (TB) remains a major public health problem especially in the developing and low-income countries.
- WHO has recommended these four first-line drugs: Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for treating active, drug-susceptible TB in a 6-month regimen treatment.
- But research has shown that tuberculosis has proven to be multi-drug resistant and extensively drug resistant to at least two of the first-line drugs: isoniazid and rifampicin.
- Search for novel chemical compounds in treating this life-threatening human diseases is now paramount.
- Natural Products is a safe option due to low production costs, less-toxic, structural diversity, and multiple uses of active compounds to treat various diseases.
- Syzygium cordatum, water berry (Fig. 2), is a valuable medicinal plant which researcher have identified phytochemicals in its bark as promising cure against tuberculosis.
- Molecular docking is a Structure Based Drug Design (Fig. 3) technique that is used in predicting the binding interaction of these ligands to the Mycobacterium tuberculosis Protein (4RHT) (Fig. 1).

METHODOLOGY

- The Ligands and drug compounds were retrieved from Pubchem and converted to pdb with Biovia Discovery Studio
- The crystal structure of (MTB-H37Rv)PDB ID: 4RHT was retrieved from the RCSB Protein Data Bank in PDB format with atomic resolution of 2.76Å. Alpha Beta – chain (D chain) was used for the docking study.
- CASTp & Biovia Discovery Studio were used to validate the active sites.
- AutoDock Vina of PyRx virtual screening software was used for the docking simulation.
- PyMol & Biovia used in viewing the interaction.
- ADMETSar2, Molinspiration, swissADME webserver were used in assessing the pharmacochemical properties.



Fig 2. SYZYGIUM CORDATUM (Water Berry)

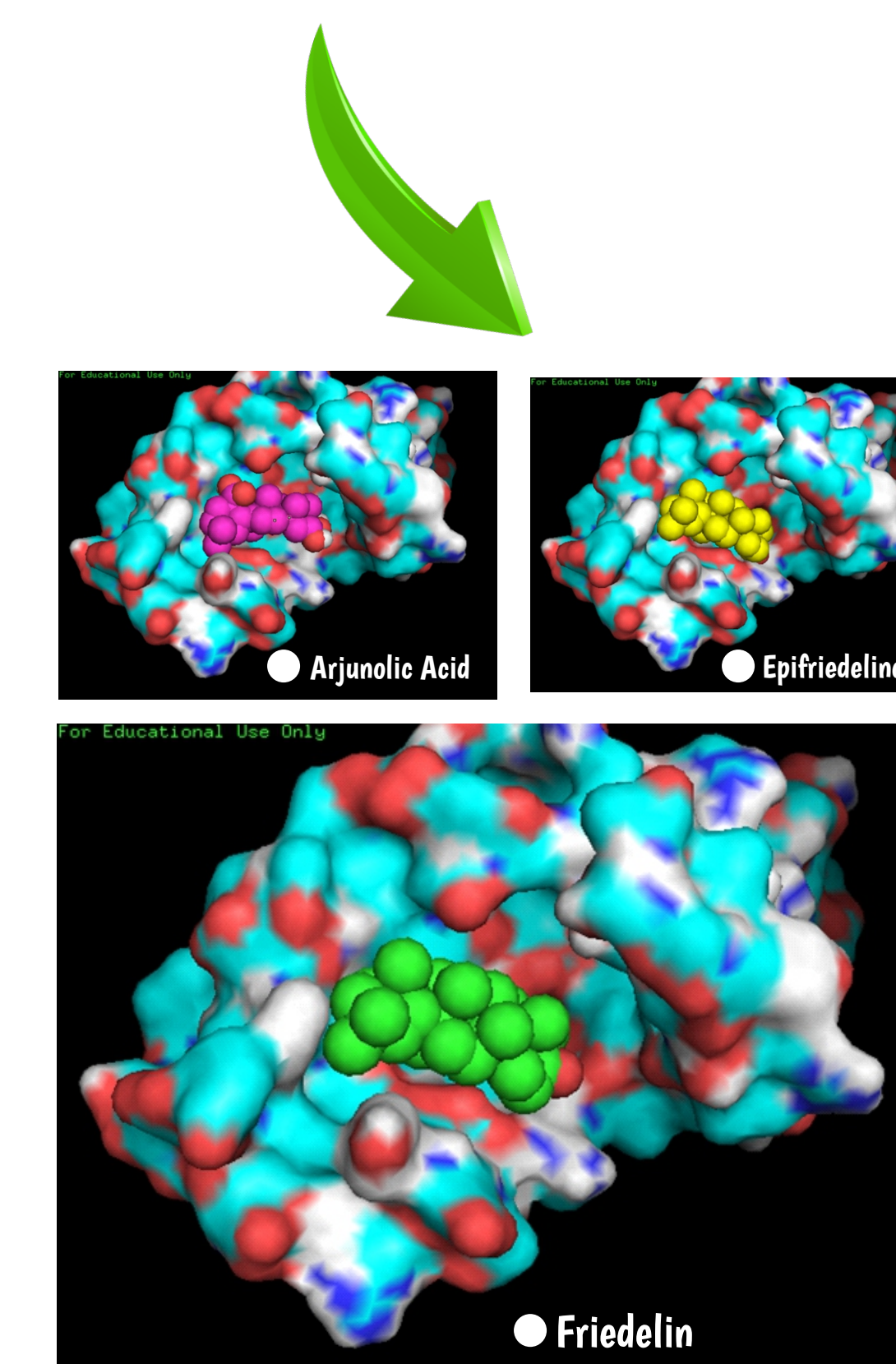


Fig 3. Inhibitory Interaction of Arjunolic Acid, Epifriedelinol & Friedelin against 4RHT



Fig 4. Drug Designing

RESULTS AND DISCUSSION

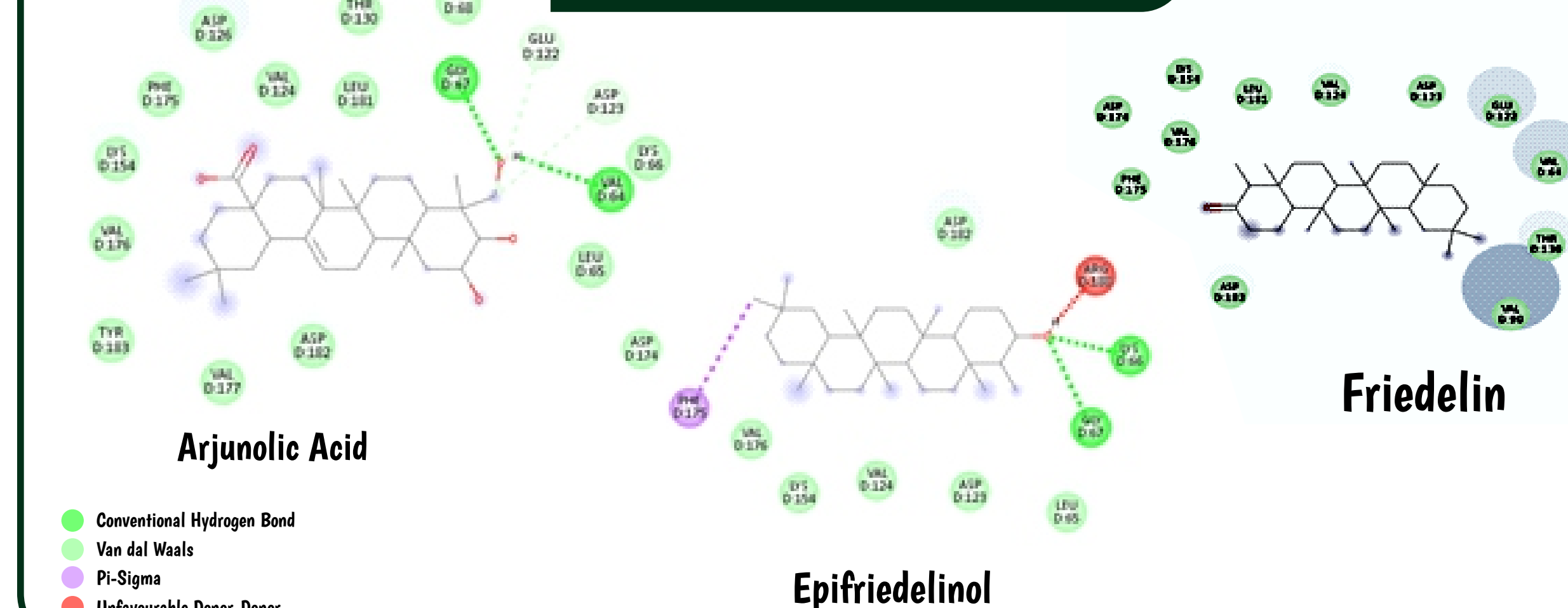
- All the Ligands interact better with 4RHT than all the first-line drugs except Rifampicin
- Arjunolic acid, Caffeic acid, Cinnamic acid, Epifriedelinol, Friedelin, Hexahydroxydiphenic acid and Sinapic acid have good pharmacochemical properties
- Arjunolic acid, Epifriedelinol and Friedelin (Fig. 3) have K_i values (0.97, 0.30, 0.35 respectively) close to that two Acyclic Nucleoside Phosphates (0.69, 0.77) proposed as potent inhibitors of 4RHT.
- Thus, have low ligand efficiency values which indicates that the ligands bond closely to the protein.

CONCLUSION

Arjunolic acid, Epifriedelinol and Friedelin show excellent results as potential inhibitors of 4RHT. However, with low ligand efficiency values and better pharmacochemical properties, Caffeic acid, Cinnamic acid, Hexahydroxydiphenic acid and Sinapic acid can also be considered.

If these promising drug candidates for tuberculosis are explored through interdisciplinary collaboration between medicinal chemists and pharmaceutical professionals, the incidence and death rate of this deadly diseases would be substantially reduced. Healthy life and well-being for all as goal 3 of the sustainable development goals (SDG) will be achieved successfully.

2D INTERACTION



REFERENCES

- Gordon, S., and Parish, T. (2018). Microbe Profile: Mycobacterium tuberculosis: Humanity's deadly microbial foe. *Microbiology*, 164, 437-439.
- World Health Organization (2020). *Global tuberculosis report*, Geneva, Switzerland: WHO.