



IN SILICO-PREDICTION OF HIT ANTISARS- COV-2 DRUGS FROM AFRICA FLORA

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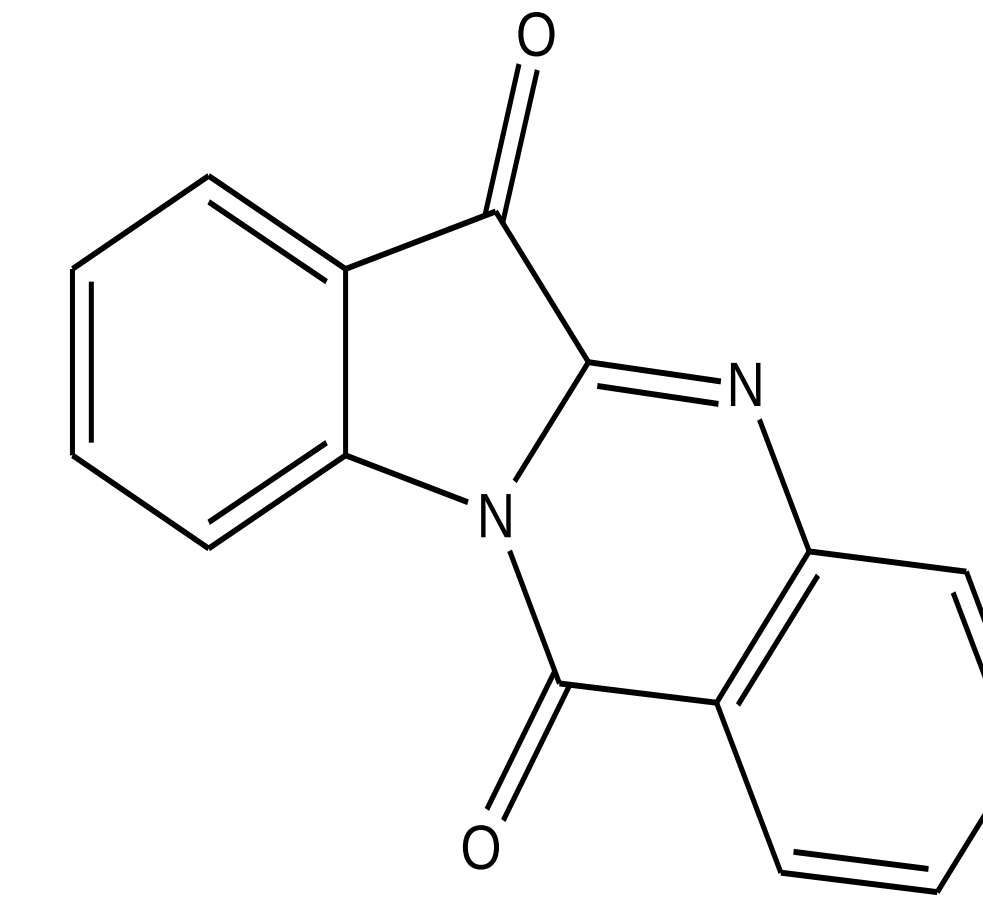


ABSTRACT

RNA-dependent RNA polymerase (RdRp), is a key component of the Coronavirus' replication machinery which is being exploited for drug targets (Dai *et al.*, 2020). We built a chemical library based on a similarity of anti-covid-19 ethnobotanically from 42 bioactive molecules divided into eight families (Alkaloids, Diarylheptanoids, Flavonoids, Phenolics, Saponin, Diterpenoids, Triterpenoids, Xanthone) (Oyere et al., 2021). A molecular screening was carry out throug the analysis of the pharmacokinetic and toxicity parameters (ADMET) by calculating the values of the descriptors of each parameter which we then analyzed using tools of Rapid medicinal screening constraints (Lipinski, opreah and verdonk rules successively) The tryptanthrin was the unique molecule meeting all these initial constraints, such as the ability to diffuse in a passive way, the crossing of the blood brain barrier, a good penetration into kidney cells and easy elimination. The human ether-a go-go related gene encoding a potassium ion (HERG K⁺) reveals the fact that the tryptanthrin is not potentially toxic for the heart. In addition, the binding to human serum albumin (log K_{HSA}) parameter indicates an adequate binding of the tryptanthrin to plasma-protein. Its circulation in the blood stream is appreciable. The logarithm of IC₅₀ of the tryptanthrin (0.06) lower than that of the remdesivir (0.07) and the galidesivir (0,31 μM) justifies its lower toxicity compared to these two market reference drugs. The interaction between tryptanthrin and the target protein (RdRp) by the mean of the Docking guarantees its good binding of the molecule in the pocket and consequently its anti-SARS-COV2 good activity.

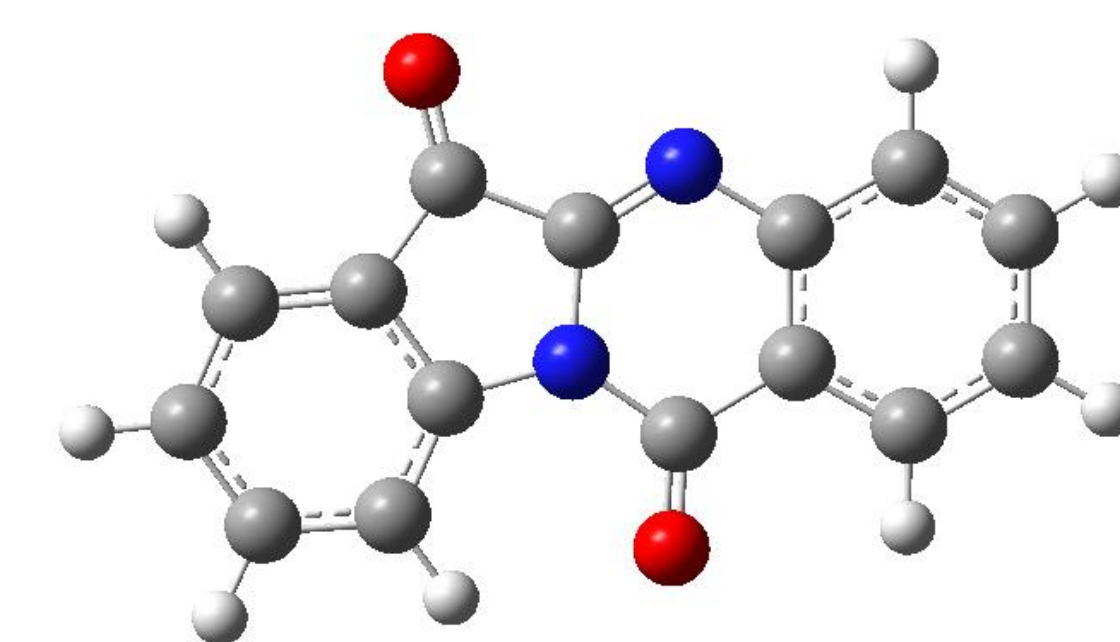
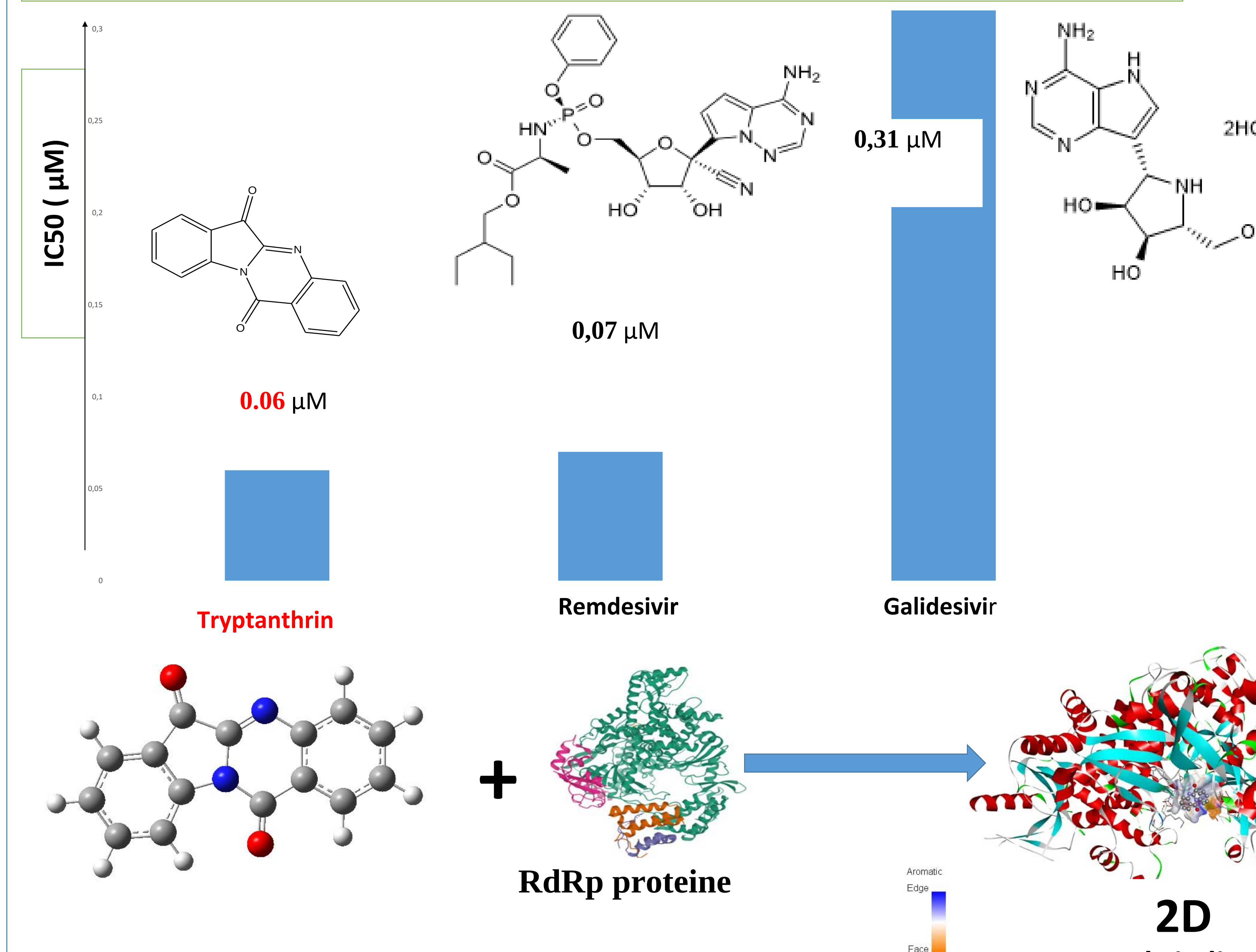
Chemical library
42 compound

Screening process

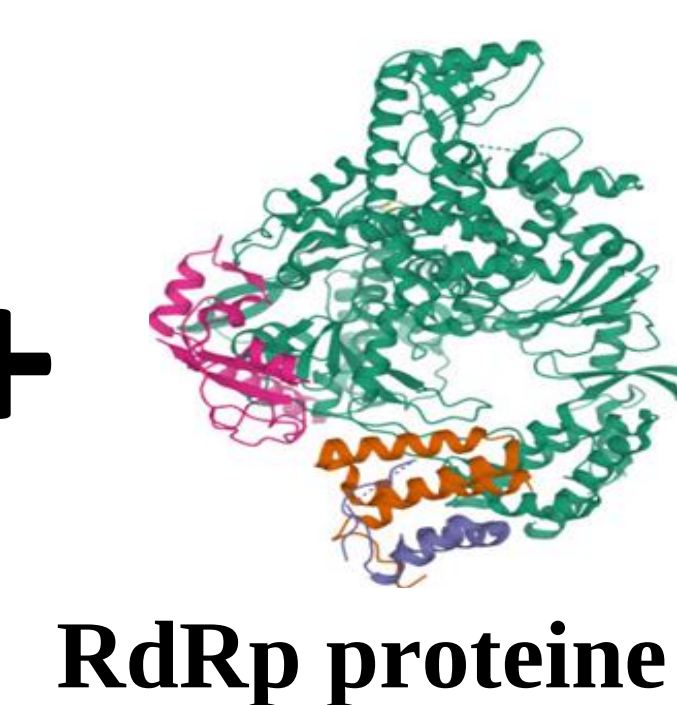


Tryptanthrin (Indolo[2,1-b]quinazoline -6,12-dione)
as the potential anti COVID-19 drug

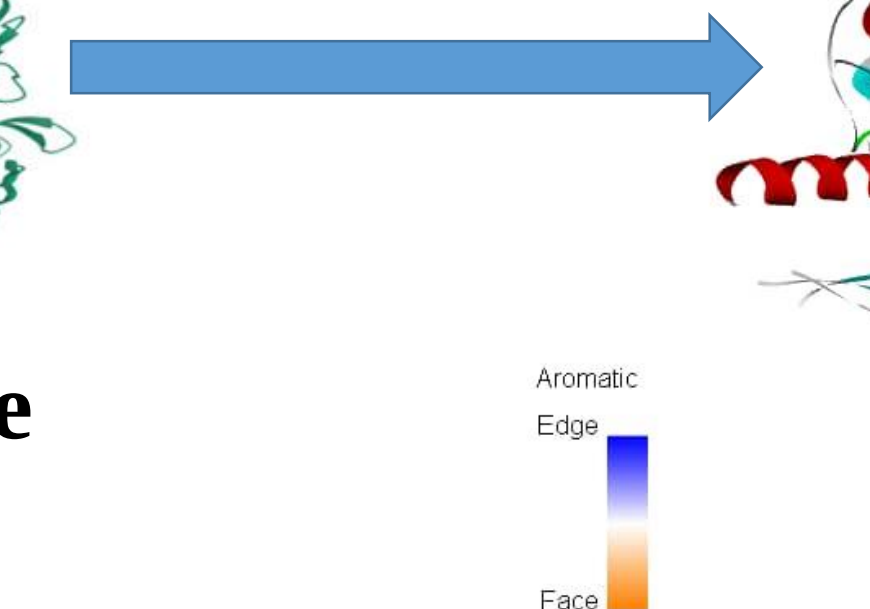
BIOLOGICAL ACTIVITY :Antiviral activities of the lead compound compared to two of the bests antivirals on the market



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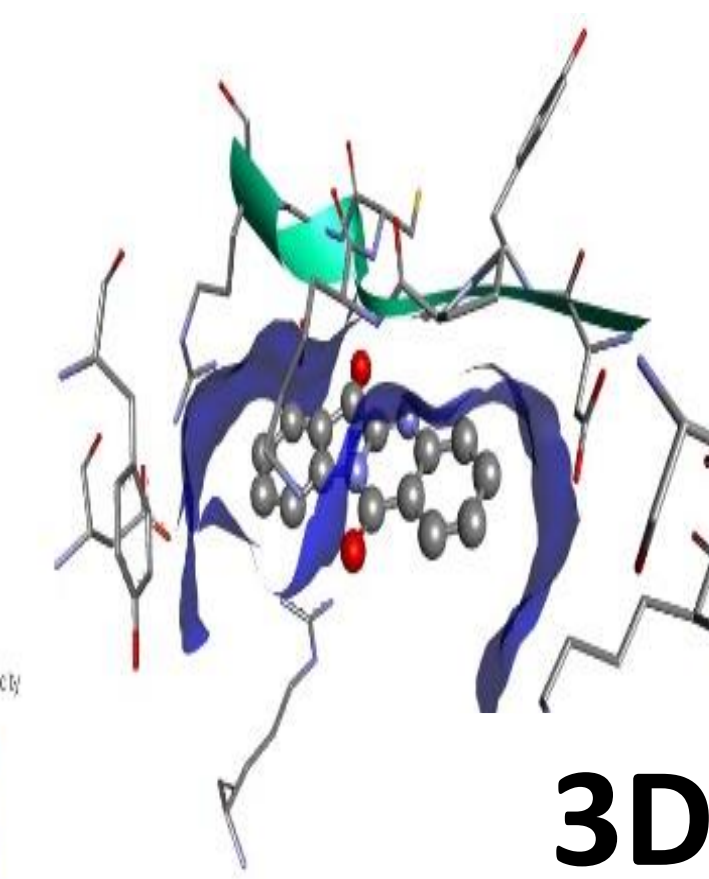
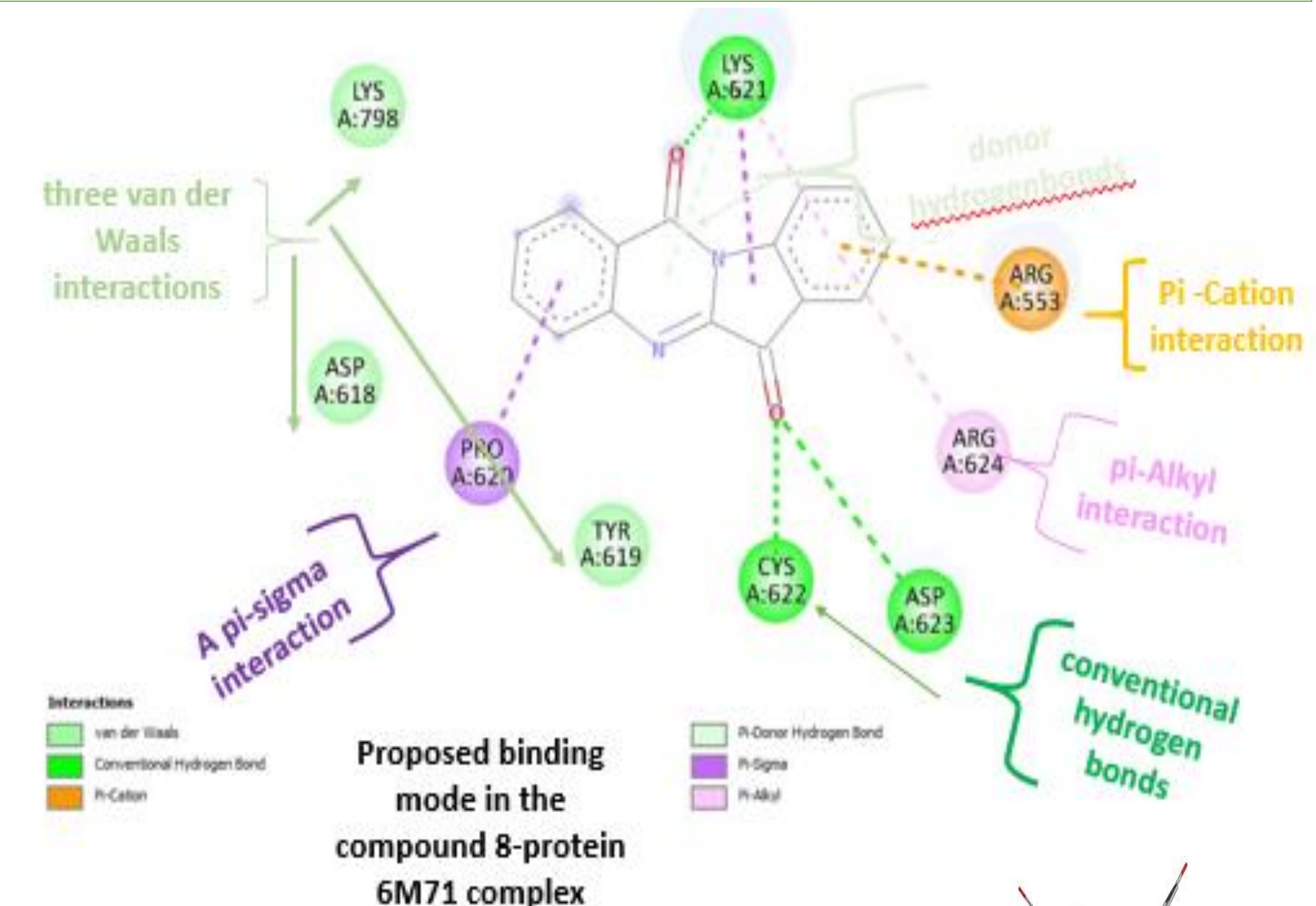
RdRp proteine



2D
Tryptanthrin ligand (8) –
6M71 protein binding
complexe

References

1. Dai, W., Zhang, B., Jiang, X.-M., Su, H., Li, J., Zhao, Y., Xie, X., Jin, Z., Peng, J., Liu, F., Li, C., Li, Y., Bai, F., Wang, H., Cheng, X., Cen, X., Hu, S., Yang, X., Wang, J., Liu, X., Xiao, G., Jiang, H., Rao, Z., Zhang, L.-K., Xu, Y., Yang, H., Liu, H., 2020. Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease. Science 368, 1331–1335. <https://doi.org/10.1126/science.abb4489>
2. Oyere T. E., Smith B. B, Fidele NK. 2021. Natural Products as Potential Lead Compounds for Drug Discovery Against SARS-CoV-2. Natural Products and Bioprospecting 11:611–628. <https://doi.org/10.1007/s13659-021-00317-w>



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