IOCT 2025 Conference
The 3rd International Online Conference on Toxins
10–12 September 2025 | Online
MDPI

First Insight into the Binding of Microcystin-LR and Cylindrospermopsin to Estrogen and Androgen Receptors via *In Silico* Molecular Docking

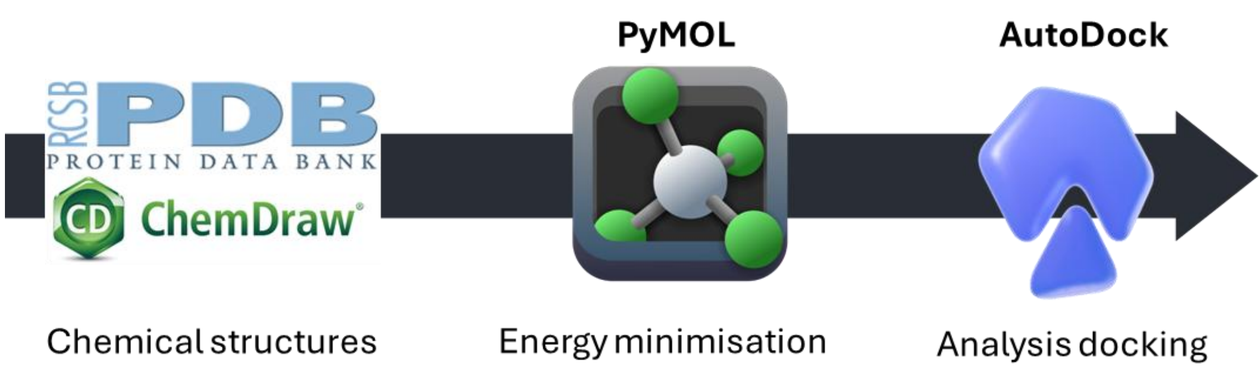
Antonio Casas-Rodríguez, Antonio Cascajosa-Lira, María Puerto, Ana María Cameán, Angeles Jos
Area of Toxicology, Faculty of Pharmacy, Universidad de Sevilla, Spain

INTRODUCTION & AIM

Cyanotoxins are secondary metabolites produced by cyanobacteria that are attracting increasing scientific interest due to their global distribution, toxic potency, and ability to bioaccumulate. The potential endocrine-disrupting properties of cyanotoxins such as microcystin-LR (MC-LR) and cylindrospermopsin (CYN) are of particular concern given their increasing prevalence, the scarcity of research on this topic and their potential impact on human health.

This study therefore performed an in silico analysis for the first time to assess the potential of MC-LR and CYN to form stable complexes with the oestrogen receptor (ER) and the androgen receptor (AR).

METHOD



RESULTS & DISCUSSION

- CYN displayed a preference for agonist conformations (1ERE: -6.7 kcal/mol; 3ERD: -7.0 kcal/mol) over antagonist conformations (1ERR: -6.6 kcal/mol; 3ERT: -6.1 kcal/mol). Key interactions in 1ERE involved the CYN guanidine group with SER-305, ALA-307, GLY-366, and ASP-369 (**Figure 1**).
- MC-LR exhibited a stronger affinity for the agonist conformations (1ERE: -7.1 kcal/mol; 3ERD: -8.2 kcal/mol) compared to the antagonist conformations (1ERR: -6.4 kcal/mol; 3ERT: -7.8 kcal/mol). Specific interactions in the agonist conformations involved arginine nitrogen with ASP-321 and GLU-323 (**Figure 2**).
- MC-LR showed a binding energy of -7.2 kcal/mol with AR, with the leucine nitrogen interacting with PRO-682. CYN exhibited a higher affinity for AR (-8.2 kcal/mol), with interactions involving the guanidine group with GLN-798 (**Figure 3**).

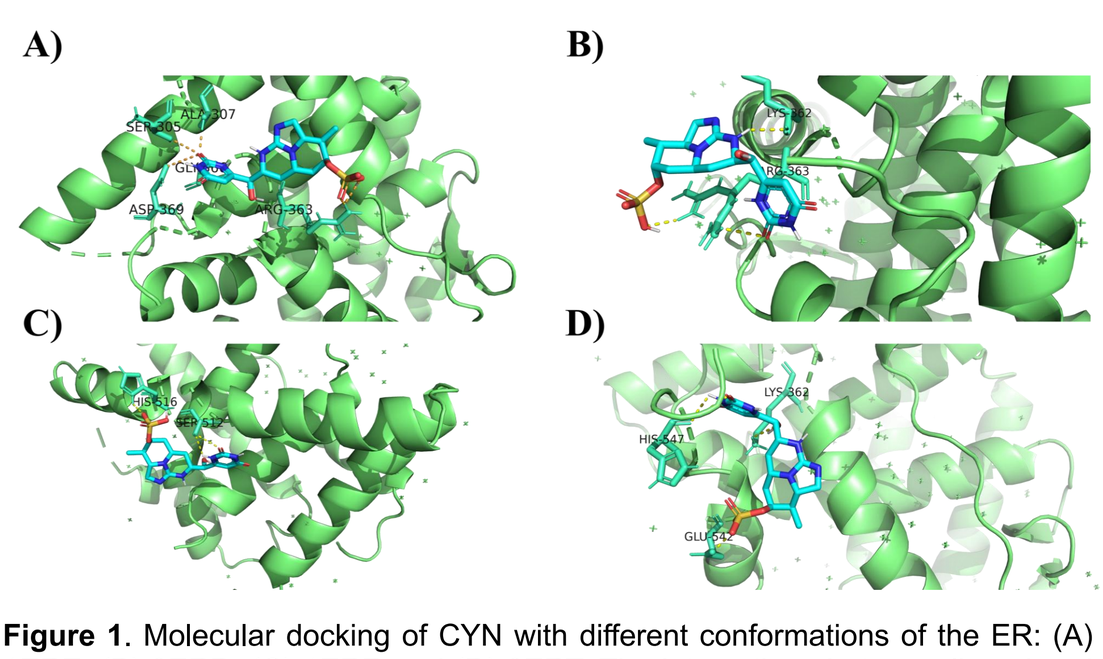


Figure 1. Molecular docking of CYN with different conformations of the ER: (A) 1ERE, (B) 3ERD, (C) 1ERR and (D) 3ERT. The interactions between ligand and receptors are represented by yellow lines.

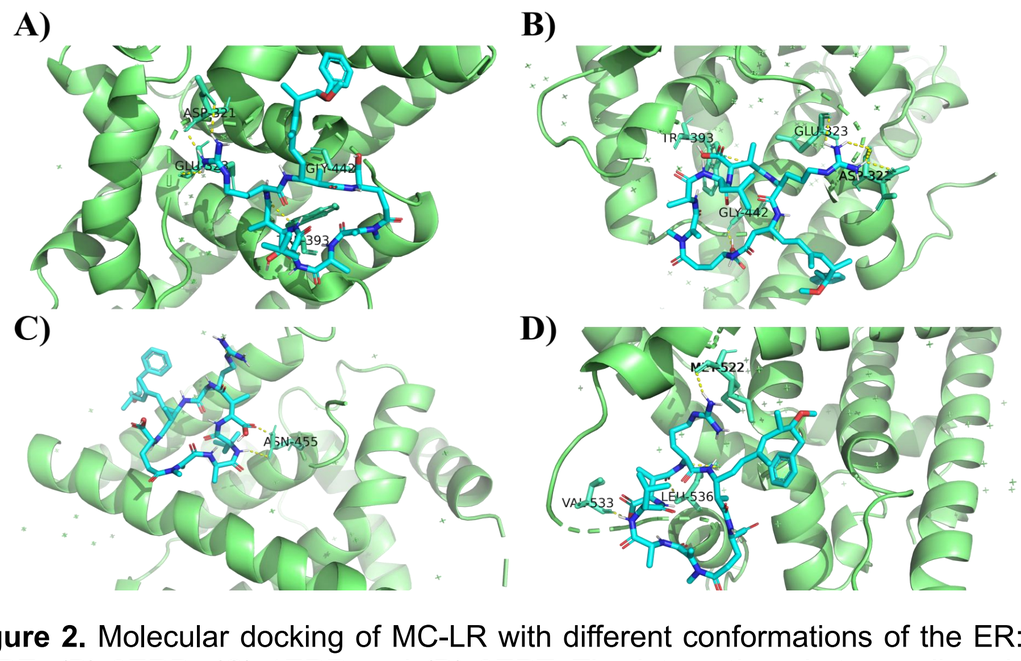


Figure 2. Molecular docking of MC-LR with different conformations of the ER: (A) 1ERE, (B) 3ERD, (C) 1ERR and (D) 3ERT. The interactions between ligand and receptors are represented by yellow lines.

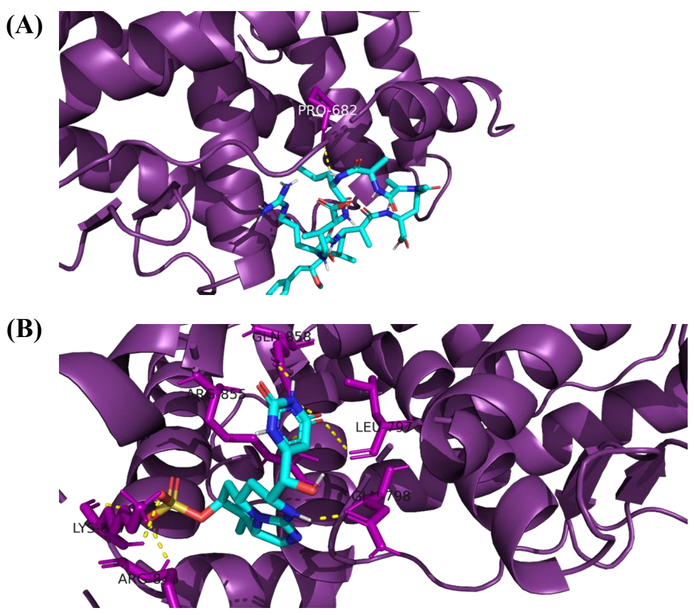


Figure 3. Molecular docking of (A) MC-LR and (B) CYN and AR. The interactions between ligand and receptors are represented by yellow lines.

CONCLUSION

Taking this into account, computational docking analyses indicated possible binding interactions between both toxins and both receptors.

ACKNOWLEDGEMENTS

The authors would acknowledge to the MICIU/AEI/10.13039/501100011033 and FEDER, project number PID2023-147444OB-I00. A.C.-R. acknowledges the Spanish MICINN for the predoctoral grant awarded (PRE-2020-094412).