I CONGRESSO INTERNACIONAL DE BIOLOGIA CELULAR E MOLECULAR
X CURSO DE INVERNO

PROSPECTING INHIBITORS OF THE PHOSPHOENOLPIRUVATE CARBOXYLASE *IN SILICO*

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Introduction

Resistant weeds have evolved due to the repeated use of herbicides with the same mechanism of action. This highlights the importance of discovering new active principles that act on different cellular targets. The inhibition of enzymes in charge of the C4 metabolism, such as phosphoenolpyruvate carboxylase (PEPC) are promising selective herbicide targets.

Objective

Here, we modelled the structure of *Zea mays* PEPC from (*Zm*PEPC) in order to identify potential inhibitors of its activity by virtual screening (VS) simulations.

Materials and methods

1st Molecular modeling by homology:

Modeled as a homotetramer bound to the cofactor Mg2+ and the inhibitor 3,3-dichloro-2-phosphonomethyl-acrylic acid (DCO) → Software: Modeller-10.2

2nd Energy minimized:

Generated 1200 models and the best scored had its energy minimized → Software: NAMD2

3rd Molecular docking:

Virtual Screening → Vitual library selected from similar to DCO → Virtual Docking → Validation
- ADMETOX / Toxicity
- Interaction number
- Energy score

→ Inhibitors selected

Softwares: Molegro; Autodock 4 and Vina (PyRx 0.9)

Results and discussion

The final structure of Phosphoenolpyruvate carboxylase:

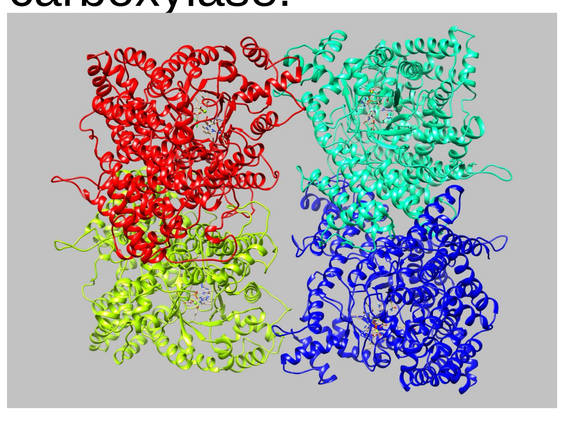


Figura 1: Homology modeling of Phosphoenolpyruvate carboxylase

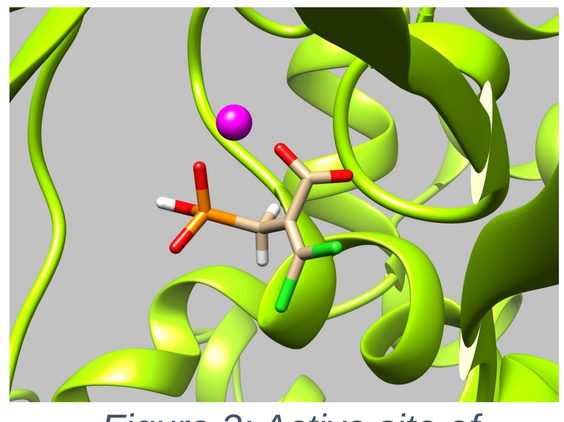
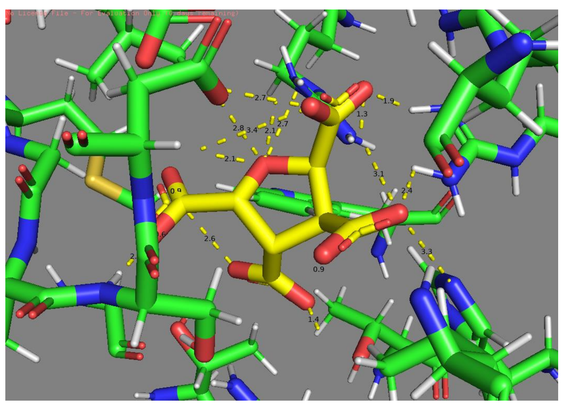


Figura 2: Active site of Phosphoenolpyruvate carboxylase

The molecule identified as ZINC12405021 had better interaction than the DCO inhibitor:



Energy score:
Vina: -7.5
Autodock: - 6.77
Molegro: - 174.121

Figura 3: Ligand ZINC12405021

Conclusion

This work identified the molecule ZINC12405021 as a potential inhibitor of the enzyme ZmPEPC. Our next step will be to acquire it for *in vitro* and *in vivo* tests.

Acknowledgments

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References

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