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

PROSPECTION OF POSSIBLE INHIBITORS OF THE ENZYME O-ACETYLSERINE (THIOL) LIASE BY *IN SILICO* TECHNIQUES

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Introduction

Weeds have developed great resistance to herbicides due to their indiscriminate use. To reduce this selective pressure, the development of herbicides with new and more efficient mechanisms of action is necessary. In this context, an interesting mechanism is the inhibition of the enzyme O-acetylserine(thiol)lyase (OAS-TL), responsible for the assimilation of sulfur in plants, an essential macronutrient for plant metabolism.

Objective

To use the OAS-TL enzyme structure in virtual scan (VS) simulations for the selection of inhibitor candidates.

Materials and methods

The structure of OAS-TL from Zea mays complexed with its substrate O-acetylserine (OAS) and the cofactor pyridoxal-phosphate was obtained in a previous work.

Vina and autodock-4 programs were used in VS.

The library of molecules used was assembled from the catalog of the company Acros Organics, using the Lipinski Rules as a filter and a ClogP interval between -0.4 and 3.0.

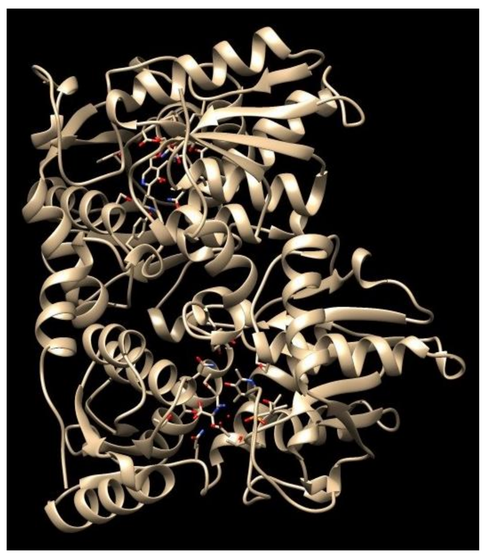

Figure 1: Three-dimensional structure of corn O-acetylserine(thiol) lyase (OAS-TL) (homodimer) modeled with O-acetylserine substrate (OAS) and pyridoxal-phosphate cofactor (PLP). FOLETTO-FELIPE, 2021.

Results and discussion

The VS of 4949 molecules by the two programs indicated that four of them (ZINC16892208, ZINC149993, ZINC159056 and ZINC2562555) have greater interaction with the enzyme compared to the OAS substrate. All compounds were successfully filtered by applying ADMETox criteria, indicating that they would not be toxic to mammalian cells and tissues. These molecules have not yet been described as inhibitors of the target enzyme.

Results and discussion

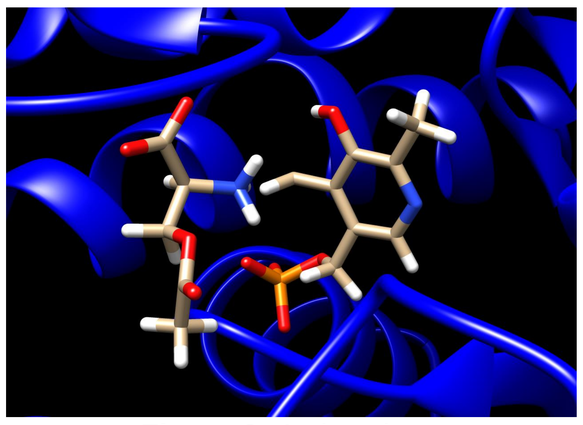

Figure 2: Active site

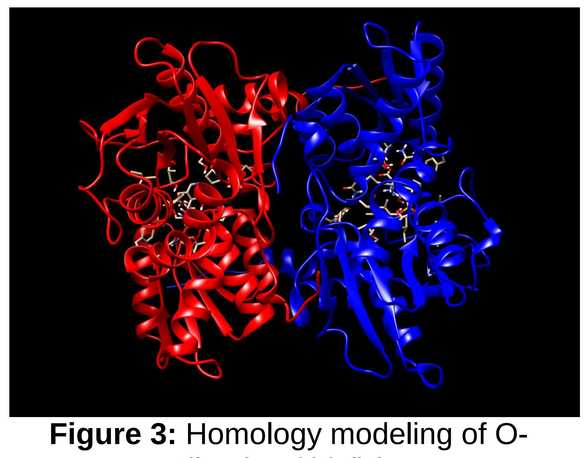

Figure 3: Homology modeling of O-acetilserine (thiol) lyase

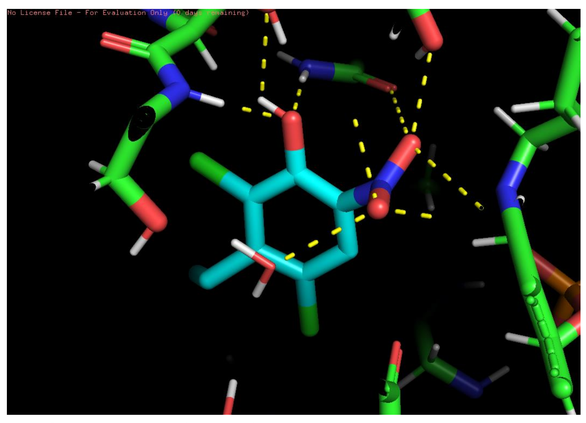

Figure 4: Ligand ZINC000002562555
Vina: -6,6
Autodock: -7,85

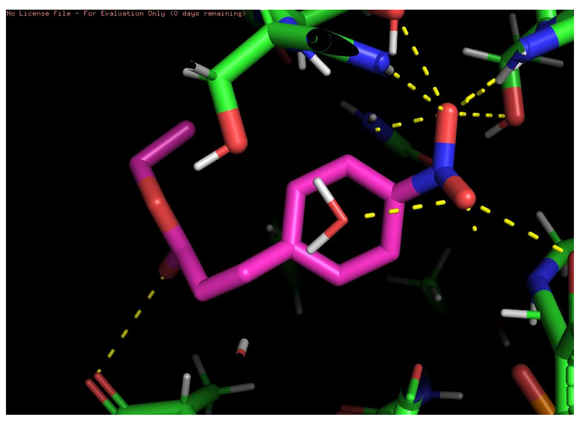

Figure 5: Ligand ZINC000016892208
Vina: -6,9
Autodock: -7,68

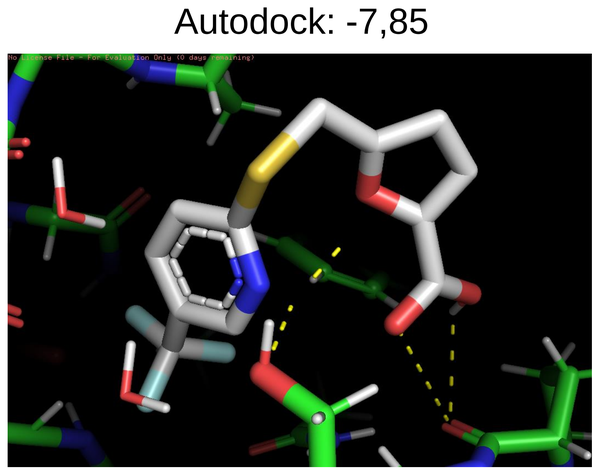

Figure 6: Ligand ZINC000000149993
Vina: -6,6
Autodock: -7,33

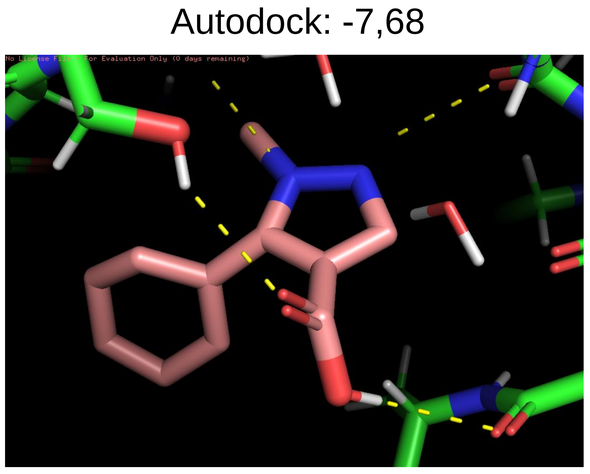

Figure 7: Ligand ZINC000000159056
Vina: -6,9
Autodock: -7,9

Conclusion

The results obtained in this research indicate that the selected molecules have potential characteristics to act as inhibitors of OAS-TL. However, to validate the results, the molecules will be acquired for in vitro and in vivo inhibition studies.

Acknowledgments

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References

FOLETTO-FELIPE, M.D.P. *O*-acetilserina(thiol) liase: estudos *in silico*, *in vitro* e *in vivo. Tese de Doutorado-Pós Graduação em Ciências Biológicas-Universidade Estadual De Maringá, 2021;*
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