NETWORK PHARMACOLOGY OF *ANNONA CRASSIFLORA* ALKALOIDAL FRACTION ON ALZHEIMER'S AND ITS EFFECT ON *DROSOPHILA MELANOGASTER* MODEL

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INTRODUCTION

Studies from *Annona crassiflora* has shown the potential of its metabolites and therapeutic use. Alkaloids have been identified in the *A. crassiflora* fruit and peel and therefore we aim to investigate these alkaloids using a *Drosphila melanogaster* model of Alzeheimer disease and an approach of pharmacology in silico network to harness the full potential of the alkaloid fraction of *A. crassiflora*.

OBJECTIVE

Thus, this work aims to search possible human targets for these alkaloids, and from the targets found evaluate the effect of the alkaloid fraction treatment on the Alzheimer model using *D. melanogaster* and predict its mechanism of action.

RESULTS AND DISCUSSION

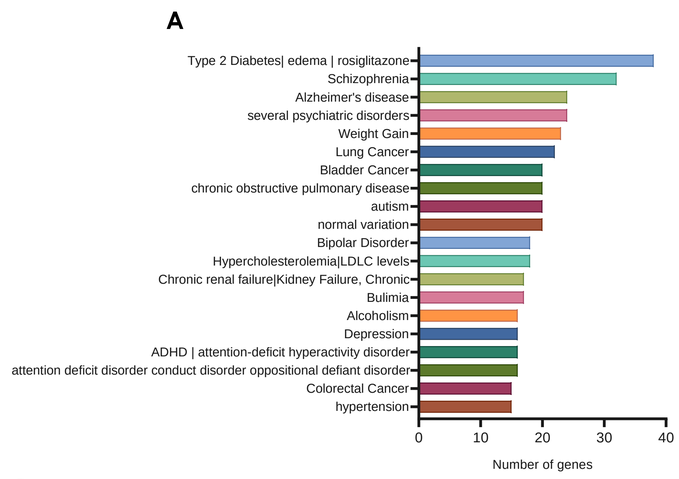
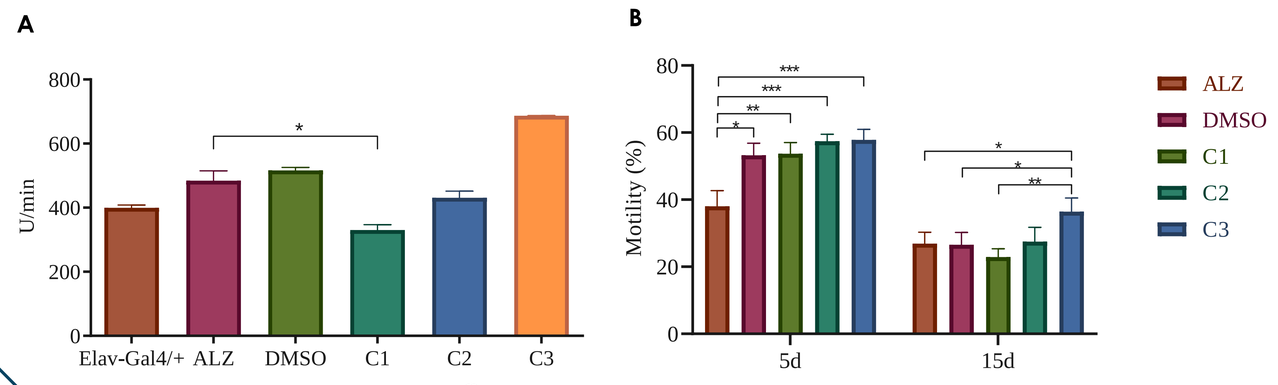
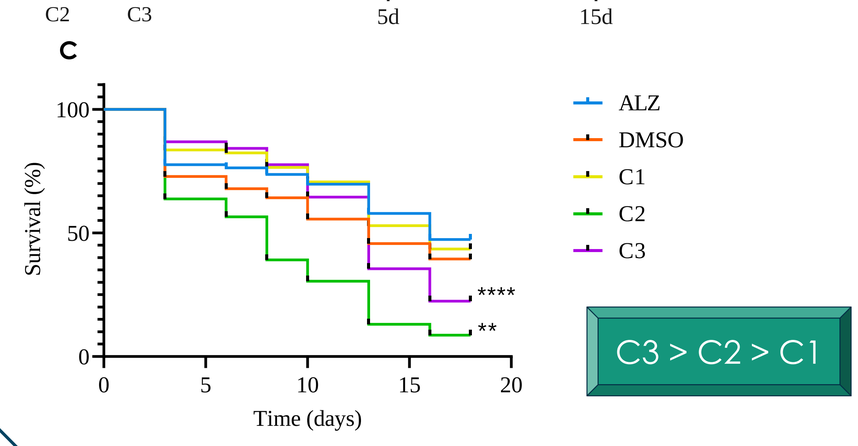


Fig1. (A) Main 20 diseases related with PPI target network. Y-axis, the name of diseases, X-axis, the number of target genes related to the diseases. (B) PPI targets network with gray edges and alkaloid-targets network related to AD with red edges.





C3 > C2 > C1

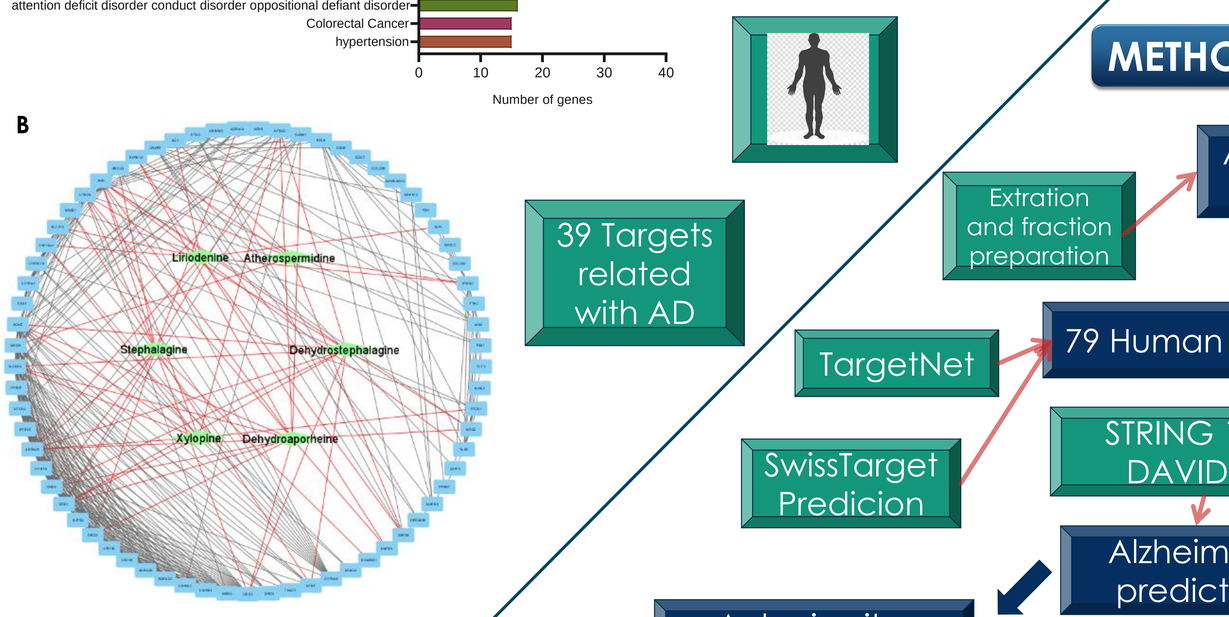
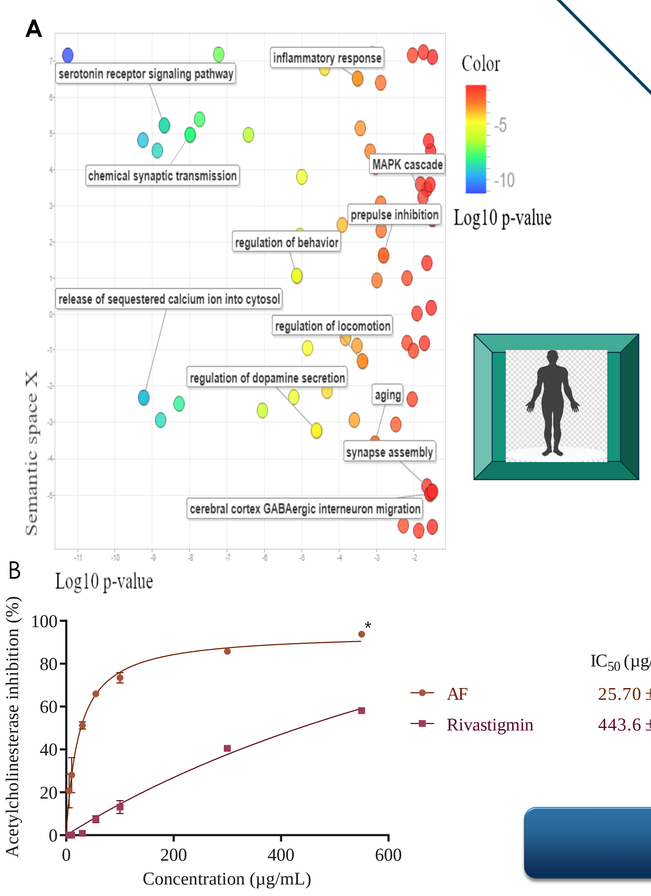


Fig 2. (A) GO analysis of *Homo sapiens* targets (B) Analysis of the inhibition of the enzyme acetylcholinesterase by the AF and the rivastigmine control.

Fig 3. (A) Evaluation of the AChE activity of control flies with Alzheimer genotype (ALZ) and flies without the Alzheimer genotype (Elav-Gal4 / +). ALZ flies treated with DMSO vehicle and with the alkaloidal fraction (AF) in C1- C3 concentrations (B) Evaluation of the motility of flies with the same groups. (C) Toxicity test (% survival) of flies groups



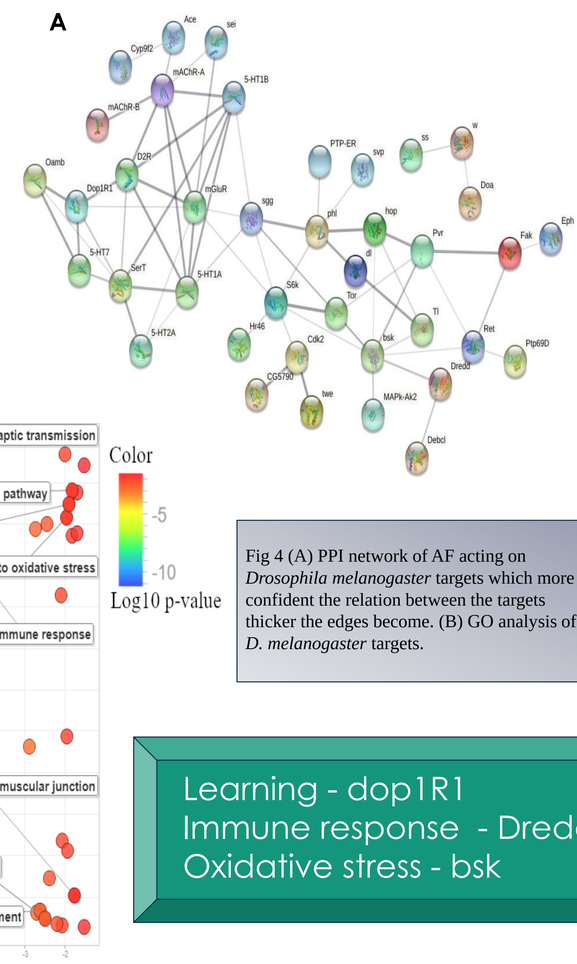


Fig 4 (A) PPI network of AF acting on *Drosophila melanogaster* targets which more confident the relation between the targets thicker the edges become. (B) GO analysis of *D. melanogaster* targets.

Learning - dop1R1
Immune response - Dredd
Oxidative stress - bsk

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Conclusion

In conclusion, the present study predicted alkaloids-target-disease interactions and multi-target mechanisms of the *A. crassiflora* alkaloidal fraction in the treatment of AD using the network pharmacology strategy, as well as validating the protective effect of AF against the AD model of D. melanogaster. Further studies are also necessary in order to deepen the knowledge about the interaction pathways and mechanisms of action of the alkaloids described for AF on AD, which may lead to the development of one of AF or its alkaloids as a potential candidate for the treatment of patients with AD.

FINANCIAL SUPPORT

CAPES

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CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico