DRUG REPOSITIONING FOR OROPOUCHE VIRUS TARGETS

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ABSTRACT

Background: Oropouche fever is caused by the Oropouche virus (OROV), an emerging arboviral disease that poses an increasing threat to public health in Latin America, particularly in Brazil and Peru, with outbreaks also reported in other countries such as Argentina, Bolivia, Colombia, and Ecuador. OROV belongs to the family *Peribunyaviridae* and the genus *Orthobunyavirus*, primarily transmitted by the mosquito *Culicoides paraensis* in urban areas, although it also exhibits a replication cycle in sylvan regions. With nonspecific febrile symptoms that may be confused with other arboviral infections, such as dengue, clinical diagnosis is challenging and may lead to severe systemic complications, including damage to the central nervous system. To date, there are no vaccines or antiviral treatments available against OROV. In light of this, drug repurposing emerges as a rapid strategy for identifying potential therapies targeted at OROV.

Objectives: This study aims to identify existing drugs that may inhibit the replication of the OROV, targeting four viral proteins: RNA polymerase, non-structural protein, envelope polyprotein, and nucleoprotein.

Methods: *In silico* assays were conducted using molecular docking with the GOLD software to identify potential drugs with binding affinity for the four proteins of the OROV. A total of 1,600 drugs were tested against these viral targets. The final ligands were selected based on the best binding scores for each target, prioritizing those with higher interactions, predictive specificity, and those that are administered orally.

Results and Discussion: Molecular docking identified several drugs with potential antiviral activity against the OROV. Among them, fosinopril emerged as a promising candidate, demonstrating high binding scores for three of the viral targets: nucleoprotein, envelope polyprotein, and RNA polymerase. These results highlight the potential of drug repurposing as a viable approach for the treatment of Oropouche fever. Further studies are necessary for experimental validation, elucidation of the mechanisms of action, and optimization of drug formulations for in vivo efficacy.

Conclusion: Drug repurposing identified promising ligands for OROV treatment, suggesting therapeutic potential and encouraging future experimental validation. This approach demonstrates the capacity to accelerate the development of antiviral therapies for neglected and emerging viral diseases, such as Oropouche fever, contributing to rapid outbreak response and reduced public health impact.