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STRUCTURE/DEPENDENCE ANTI-ARBOVIRAL ACTIVITY OF DI-CHLORINATED AND DI-BROMINATED DERIVATIVES OF L-TYROSINE.

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INTRODUCTION

Since none of the three most important arboviruses DENV, ZIKV and CHIKV have specific licensed antiviral drugs to treat or prevent the infection, the aim was to evaluate the potential anti-arboviral *in vitro* activity of di-halogenated L-tyrosine derived compounds with structural differences.

MATERIAL AND METHODS

Eight synthetic di-brominated and di-chlorinated L-tyrosine derived compounds with different substitutions were tested and classified in four groups: PH (Phenolic), O-ME (methylation in the phenolic hydroxyl), PH/EST (Phenolic esterified) and O-ME/EST (O-ME esterified). Antiviral strategies were accomplished in VERO cells against CHIKV/Col, ZIKV/Col and DENV-2/S16803. The inhibitory effect was quantified by plaque assay, RT-qPCR and Cell-ELISA; and the *in sílico* approach were made with Autodock Vina ®

RESULTS

In the antiviral screening, CHIKV/Col viral particles were inhibited by PH, PH/EST and O-ME/brominated compounds. ZIKV/Col was inhibited by PH/EST, O-ME and chlorinated O-ME/EST compounds. DENV-2/S16803 was inhibited by O-ME/brominated and O-ME/EST chlorinated compounds. According to the groups, in the individual antiviral strategies, PH compounds inhibit CHIKV-viral protein in pre-treatment and viral genome and particles depending on the halogen. PH/Esterified compounds inhibited CHIKV/Col Viral particles in pre-treatment and CHIKV and ZIKV viral protein and genome in post-treatment; O-ME/brominated compound inhibited ZIKV-viral protein and genome in pre and post-treatment; and DENV-viral particles and genome both strategies. O-ME/esterified compound inhibited ZIKV-viral particles, protein and genome in pre-treatment, and viral protein of both flaviviruses in post-treatment. Finally, PH/esterified and O-ME-brominated compounds had virucidal activity against ZIKV/Col and O-ME/esterified-Chlorinated compound against DENV-2/S16803. None of compounds had virucidal activity against CHIKV/Col.

CONCLUSIONS

Small structural differences may affect activity and mechanisms of action depending on the arboviral model.

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