

TITLE: *IN VITRO* EVALUATION OF THE ANTIVIRAL EFFECT OF DERIVATIVE COMPOUNDS OF XANTHEDIONE AGAINST ZIKA VIRUS.

AUTHORS: ÍTALO ESPOSTI POLY DA SILVA, MILENE LOPES DA SILVA, EDJON GONÇALVES SANTOS, ROBERTO SOUSA DIAS, ANDRÉ SILVA DE OLIVEIRA, ANA FLÁVIA C. DA SILVEIRA OLIVEIRA, RÓBSON RICARDO TEIXEIRA AND SÉRGIO OLIVEIRA DE PAULA.

INSTITUTION: UNIVERSIDADE FEDERAL DE VIÇOSA, VIÇOSA-MG (AVENIDA PETER HENRY ROLFS, S/N - CAMPUS UNIVERSITÁRIO, VIÇOSA - MG, 36570-900- BRAZIL)

The World Health Organization (WHO) and the Brazilian Ministry of Health estimates that a new outbreak of Zika can occur in 2017/2018, specially on Northeast of Brazil. Similar to other flaviviral arboviruses, there is still no specific treatment for Zika to date. Considering the high number of possible infections, the risks it has to the brain and the fact that there is no vaccine or specific prophylaxis available to date, an effective treatment able to prevent the infection would be extremely desirable. Xanthene derivatives have attracted the attention of several research groups because of their diverse properties and biological activities such as antiviral, antibacterial and anti-inflammatory. The cytotoxicity of xanthenedione derivatives were evaluated in VERO cells. Cell viability was measured by MTT method, and the CC_{50} value was determined. Considering the 31 xanthenedione derivatives, only 5 presented high cytotoxicity in the highest concentrations, the other are few toxic to the cells. Concentrations used in subsequent neutralization assays do not present a reduction in cell viability. The screening assay for the xanthenedione compounds was made using the highest non-toxic dilution in VERO cells, and the cell viability was measured by MTT method. From the 31 compounds tested, 9 presented antiviral activity higher than 50%, and two (compounds #06 and #23) were selected for the next steps. To evaluate if the xanthenedione derivatives acts under the viral infection, PRNTs were performed. A viral activity reduction of 99,9% in the number of lysis plaques was observed for the compound #06 ($CC_{50} = 27,64$ M) on the highest non-toxic dilution and a reduction of 99,9% for the compound #27 ($CC_{50} = 224,4$ M) even under a dilution of 1:8. Based on dose-response viral activity reduction the IC_{50} value was determined, $9,715 \mu\text{M}$ and $7,466$ M for the compounds #06 and #27 respectively. With CC_{50} and IC_{50} value it is possible to calculate the selectivity index (SI) which determine if is possible to neutralize the virus before killing the host. According to the literature, a good SI value is equal or higher than 4, considering the values of 2.85 and 30.05 respectively for the compounds #06 and #27, we can conclude that the compound #27 can be a promising candidate against ZIKV infection. Further assays will be carried out to verify which are the compounds inhibition mechanism.

Keywords: Zika Virus, Antiviral, Xanthenedione

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