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Evaluation of the Antiviral Activity of Dermaseptin Analogs Against Zika Virus

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Abstract : Zika virus represents the primary cause of infection during pregnancy and can lead to various neurological disorders, such as microcephaly and Guillain-Barré syndrome, affecting both children and adults. This infection is also associated with urological and nephrological problems. So far, evidence of mosquito-borne Zika virus infection has been reported in a total of 89 countries and territories. However, surveillance efforts primarily concentrate on outbreaks that this virus can cause, yet the measures implemented are typically limited. Currently, there are no specific treatments or vaccines designed for the prevention or treatment of Zika virus infection or its associated disease. The development of effective therapeutic agents presents an urgent need. Importantly, an alternative for advancing the discovery of molecules could be dermaseptins, a family of antimicrobial peptides known for their potential antiviral properties. In this study, we carried out the synthesis of dermaseptins and their analogs and subsequently assessed the bioactivity tests against Zika virus (ZIKV PF13) of dermaseptins B2 and S4 and their derivatives. The cytotoxicity of these peptides was investigated on the HMC3 cell line and HeLa cells by CellTiter-Glo® Luminescent Cell Viability Assay. Thereafter, we evaluated the antiviral activity caused by the action of our dermaseptins on the viral envelope using the Fluorescence Activated Cell Sorting (FACS). The cytotoxicity of our molecules was concentration-dependent at microgram concentrations except for dermaseptin B2 and its derivative, which present no toxicity against HeLa and HMC3 cell lines. It was observed that all tested analogs from the S4 family exhibited antiviral activity with low concentrations ranging from 3 to 12.5 µg/mL, unlike the native B2 and its derivative, which increased the infectivity. Pre-incubating of dermaseptins with ZIKV PF13 before infection revealed that these derivatives inhibit the initial stages of virus infection. In summary, these results suggest that dermaseptins could serve as lead structures for the development of potent antiviral agents against Zika virus infections.

Keywords : dermaseptin B2, dermaseptin S4, analogs, zika virus, neurological infections, antiviral activity
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