Porphyrrin-Membrane Interactions and Their Antiviral Activity Against SINV and VSV

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INTRODUCTION: Porphyrins are amphipathic cyclic molecules composed by a tetrapyrrole ring that can bear a metal atom in the center. We demonstrated that porphyrins are potent antiviral compounds that inactivate some viruses including flaviviruses, Sindbis (SINV) and Vesicular Stomatitis (VSV) viruses. Since these viruses are enveloped viruses and porphyrins are amphipathic molecules that intercalate cell membranes, we hypothesized that they could interact with viral envelope, impairing virus infection. The fluorescent porphyrins PPIX, MesoPPIX and ZnPPIX were used to study porphyrin-membrane interactions. As porphyrins fluorescence emission spectra are affected by changes from aqueous to hydrophobic environment, we evaluated the partitioning of these compounds to membranes using fluorescence spectroscopy. MATERIAL AND METHODS: Progressive LUV (Large Unilamellar Vesicles) addition to a solution containing porphyrins resulted in fluorescence emission curves from which partition coefficients (Kp) were calculated. Porphyrin partition to PC(100%), PC:PE(4:1), PC:PS(4:1), PC:Chol(3:1), PC:Sph(3:1) and PC:Sph:Chol(1:1:1) as well as LUVs mimicking SINV and VSV envelopes were tested. To correlate membrane partition with porphyrins antiviral activity, viruses were incubated with 50, 100, 200 and 300 µM of each porphyrin for 1 hour and virus infectivity was accessed by plaque assay in BHK cells. RESULTS AND DISCUSSION: PPIX and MesoPPIX showed higher Kp values (14,9-25,9x10³ for MesoPPIX and 10,6-14,1x10³ for PPIX) than ZnPPIX (1,6-3,6x10³) in all LUVs tested. Kp values from porphyrin partition to SINV or VSV synthetic envelopes were: 3x10³ and 1,9x10³ for ZnPPIX, 16,8x10³ and 19,2x10³ for MesoPPIX and 10,6x10³ and 12x10³ for PPIX, respectively. ZnPPIX and MesoPPIX inactivated both SINV and VSV in concentrations up to 200 and 300 µM in a dose dependent manner, whereas PPIX impaired only SINV replication. CONCLUSION: Using porphyrin fluorescent properties, it was possible to calculate their partition coefficient for different model membranes and to correlate these values to their antiviral activity.

Keywords: porphyrin, Large Unilamellar Vesicles, antiviral activity
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