Inhibitory effects of the tempol on the proliferation of murine hepatitis virus strain A59 (MHV-A59)

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Introduction: Recently, we showed that tempol greatly attenuates multiple sclerosis in an experimental model of multiple sclerosis induced by murine hepatitis virus, neurotropic strain MHV-A59. In parallel, tempol decreased the viral titers in the CNS of treated mice. Considering the lack of knowledge about nitroxide effects on viral replication, we investigated the effects of tempol on MHV-A59 proliferation in cell cultures. Materials and methods: Tempol treatment was performed in astrocytoma DBT cells before and after virus adsorption. The cultures were infected with MHV-A59 (MOI 0.04), treated with 500 \(\mu\)M tempol and incubated at 37°C for 8h. The numbers of MHV-infected cells were determined by counting the number of syncytia. The expression levels of the N gene of MHV-A59 were determined by Taqman RT-PCR. Remaining concentrations of tempol were monitored by EPR spectroscopy. The cytotoxicity of tempol was checked by trypan blue exclusion test. Results and discussion: Significant reduction of viral production (54 ± 6.8%, \(p<=0.007\)) and of viral RNA synthesis (45.67 ± 6.50%, \(p=0.029\)) were observed when the cells were treated with tempol after viral adsorption. Marginal differences were observed when the cells were treated before viral adsorption as shown by the relative % of infected cells (90.31 ± 3.71%, \(p = 0.2\)) and the % of viral RNA (91.33 ± 13.22%, \(p = 0.38\)). In DBT cell cultures infected with MHV-A59 or mock infected, tempol was almost entirely metabolized to products that are not oxidized by ferricyanide. Conclusions: These preliminary results suggest that tempol at a non cytotoxic concentration interferes with viral RNA synthesis and with production of infective particles when added after virus adsorption.

Keywords: Tempol, MHV A59, viral replication

Support: FAPESP