

Pre-treatment with pravastatin at low concentrations associated with conventional drugs reduces the intracellular proliferation of *T. Gondii* tachyzoites in HeLa cells

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Toxoplasma gondii, the etiological agent of toxoplasmosis, is a mandatory intracellular protozoan capable of infecting birds and mammals. Due to the toxicity of the conventional drugs sulfadiazine and pyrimethamine used in the treatment of toxoplasmosis, other compounds have been researched as an alternative treatment, between them pravastatin. Therefore, the objective of the study was to evaluate the effect of the combination of pravastatin with conventional drugs at low concentrations against infection by the *T. gondii* RH strain in HeLa cells using experimental models of tachyzoite infection pre-treated for 30 minutes. Tachyzoites (5×10^5) were pre-treated with combination of sulfadiazine and pyrimethamine (50 e 25 µg/mL, respectively) and pravastatin (12 µg/mL) associated with pyrimethamine (8 µg/mL,) and / or sulfadiazine (16 µg/mL), for 30 minutes. Tachyzoites that received only RPMI medium were considered negative control. After the treatment, the tachyzoites were washed and transferred to 24-well plates containing culture of HeLa cells (1×10^5) adhered to the 13mm round coverslips, remaining in the oven for 24 hours at 37 °C at 5% CO₂. After fixation and staining, 200 cells per slide were analyzed for infection index and intracellular proliferation of the parasite. Statistical analysis was performed by analysis of variance (One Way ANOVA) and post-test Bonferroni, ($\neq p < 0,05$). Regarding the number of infected cells and intracellular proliferation all treatments promoted a significant reduction, except for the association of pravastatin (12 µg/mL) + sulfadiazine (16 µg/mL), when compared to the negative control ($P=0,0001$). In addition, the intracellular proliferation of parasites treated with all of the associations tested was significantly reduced. The parasites pre-treated with the combination of pravastatin (12 µg/mL) + pyrimethamine (8 µg/mL) + sulfadiazine (16 µg/mL) were similar to the reduction observed in the positive control, reducing 54.72% of intracellular proliferation ($P=0,001$) When compared to the negative control. Pravastatin associated with reduced concentrations of conventional drugs had a significant antiproliferative effect on previously pre-treated forms of tachyzoites, demonstrating promising results as an alternative compound in the treatment of toxoplasmosis.

Key words: HeLa cells, pravastatina, *Toxoplasma gondii*

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