Effect of N-salicyloyltryptamine (STP) on parameters of cell viability and immunomodulation in RAW 264.7 macrophages

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INTRODUCTION: Tryptamines constitute a wide group of endogenous (e.g. melatonin and serotonin) as well as synthetic (e.g. anti-migraine triptans) compounds exhibiting a diverse range of biological effects. Immunomodulatory actions exerted by some classes of tryptamines, such as benzoyltryptamine analogues, suggest these molecules as promising candidates to develop new therapies to treat conditions associated to acute and chronic pain and inflammation. N-salicyloyltryptamine (STP) was observed to act as an anticonvulsive agent and exert antinociceptive effects in mouse. MATERIAL AND METHODS: We performed a screening of cytotoxic, cytoprotective, immunomodulatory and redox properties of STP in RAW 264.7 macrophages challenged with hydrogen peroxide and LPS. To assess cell viability, MTT reduction, SRB incorporation and cell morphology (contrast phase microscopy) were evaluated. Intracellular reactive species production was assessed by monitoring DCFH oxidation in intact cells. Nitrite concentration in the incubation medium was assessed as parameter of NO production. TNF-α release to the incubation medium was evaluated by ELISA, and cellular levels of TNF-α and CD40 was assessed by western blot. RESULTS AND DISCUSSION: STP presents no cytotoxicity in the range of 0.001 to 1 µg/mL, but doses of 50 and 100 µg/mL caused loss of cell viability. Similarly, STP at 0.001 to 1 µg/mL did not cause oxidative stress to RAW 264.7 cells, although it did not prevent cell death induced by H₂O₂ 0.5 mM. At 0.05 and 1 µg/mL, STP caused a small increase in NO production under basal conditions, but it did not significantly change NO production induced by LPS. At these same doses, STP significantly decreased LPS-induced TNF-α release and protein upregulation of both TNF-α and CD40. CONCLUSION: These data indicate that STP is able to modulate inflammatory parameters at doses that do not interfere in cell viability, opening new therapeutic applications for this novel tryptamine.

Keywords: N-salicyloyltryptamine, inflammation, TNF-alpha, LPS, oxidative stress, RAW 264.7

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