Anti-inflammatory activity of secondary bile acids derivatives in murine macrophages

Poster

Otros

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Introduction: Bile acids (BA) and their synthetic derivatives have significant potential to regulate pathophysiological processes such as those related to the exacerbation of the inflammatory response and metabolic alterations. Modulation of the BA receptor TGR5 has been linked to the differentiation, adhesion, and cytokine production by immune cells, regulating various pathophysiological processes that can be used to assess the anti-inflammatory activity of different compounds. Objective: To evaluate the effect of BA and synthetic derivatives of BA on the activation of the TGR5 receptor in immune cells. Methods: The effect of BA and synthetic BA derivatives on TGR5-iNOS pathway in RAW 264.7 murine macrophages was evaluated. The derivatives evaluated exhibit structural modifications at positions C3 and C24. First, the cytotoxicity of the compounds was determined using MTT assay and nitric oxide production was measured using Griess reaction in macrophages stimulated with LPS, as a marker of iNOS activity. In both assays, the antagonist triamterene (TMT) was used to confirm TGR5 receptor dependence. Statistical analysis was performed, applying ANOVA or Kruskal-Wallis according to fulfillment of parametric assumptions. Results: BA C3-derivatives showed greater cytotoxicity than their reference compounds. Compounds modified at C24 of some of the BA reduced NO production in LPS-stimulated RAW 264.7 cells, with IC50 values between 5-15 µM. TMT was validated as a TGR5 competitive antagonist in this model, reversing the anti-

inflammatory activity of some compounds. Conclusion: The structural modifications evaluated influenced the cytotoxic activity of BA, and BA derivatives with modifications at positions C3 and C24 showed the greatest anti-inflammatory activity by generating lower NO production in this model. Furthermore, it was possible to suggest using TMT that the activity demonstrated in these assays is related to activity on the TGR5 receptor.

Palabras Clave

(1) Bile acids derivatives, (2) TGR5, (3) Anti-inflammatory.

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