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NOVEL PPARγ AGONISTS AND ITS MODULATORY EFFECTS ON MACROPHAGES AND NEUTROPHILS

Larissa Benvenutti[1]*, Fernanda C. Goldoni[1], Carlos R. Vaz[1], Elaine C. Kormann[1], Manuela S. Cozer Fátima de C. Buzzi[1], Nara L. M. Quintão[1], José R. Santin[1].

[1]*Universidade do Vale do Itajaí, Brasil.* *larabenv@gmail.com.

INTRODUCTION

Inflammation is a physiological response that occurs after tissue damage. Exacerbation of this process could be very harmful to the host. Peroxisome proliferator-activated receptors (PPAR) are important in the immune response, inhibiting the expression of inflammatory cytokines in several cell types, including neutrophils and macrophages. Thus, PPARγ agonists can be an alternative treatment to inflammatory diseases. In this context, we investigated the modulatory effects of new PPARγ agonists (D1, D2, D3, E2, E3, E4) in neutrophils and macrophages stimulated with LPS.

MATERIAL AND METHODS

The anti-inflammatory effects were evaluated in macrophages (Raw 264.7) and murine neutrophils stimulated with LPS (5 µg/mL) and treated with PPARγ agonists D1, D2, D3, E2, E3 or E4 (0,1, 1 or 10 µM). The PPARγ activation was evaluated in cells pretreated with GW9662 (PPARγ antagonist). The cell culture supernatant was used to measure nitric oxide (Griess reaction) pro-inflammatory cytokines (TNF, IL-1β and IL-6, ELISA). In addition, was evaluate the effects of agonist on neutrophils chemotaxis. CEUA: 015/22.

RESULTS

Treatment with agonists D1, D2, D3, E2, E3 and E4 in LPS-stimulated macrophages led to a significant inhibition of the production of inflammatory mediators such as nitric oxide, TNF, IL-6 and IL-1β compared to untreated cells. It was found that the use of the antagonist GW9662 as a pre-treatment significantly inhibited the anti-inflammatory activity of the compounds, demonstrating the involvement of PPARγ receptors in the anti-inflammatory activity. The compounds also led to a significant inhibition of neutrophils chemotaxis.

CONCLUSIONS

Together, the results herein presented show that PPARγ agonists D1, D2, D3, E2, E3 and E4 displays important *in vitro* anti-inflammatory actions by blocking pathways of neutrophil and macrophages, suggesting its therapeutic application to inflammatory reactions.

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