3rd Brazil-France Symposium on Medicinal Chemistry
Maceió/AL | November 12 -14, 2024

BORNYL ACETATE PROMOTES MACROPHAGE PHAGOCYTOSIS AND INCREASES THE EXPRESSION OF ANTIOXIDANT MOLECULES AND MARKERS OF M2-LIKE MACROPHAGE POLARISATION

Graziele R. S. Silva (PG)[1, 2, 3, 4], Alef B. B. Barros (G)[1, 2, 4], Erick G. A. Ferreira (G)[1, 2, 4], Mark S. P. Fidelix (PG)[1, 2, 3, 4], Jordana R. Santana (Res)[1, 2, 3, 4], Juliane P. Silva (T)[1, 2, 4], Maria D. S. Reis (Prof)[1, 2, 3, 4], Emiliano Barreto (Prof)[1, 2, 3, 4]* graziele.silva@icbs.ufal.br

[1] Universidade Federal de Alagoas (UFAL); [2] Instituto de Ciências Biológicas e da Saúde (ICBS); [3] Programa de Pós-graduação em Ciências da Saúde (PPGCS); [4] Laboratório de Biologia Molecular (LBC).

ABSTRACT

Introduction: Bornyl acetate (BA) is a monoterpene with notable anti-inflammatory properties, able to modulate the production of inflammatory cytokines such as interleukin-6 (IL-6) and interleukin-1β (IL-1β). Previous studies demonstrated inhibition of IL-6 and IL-1β prime macrophages towards the M2-like phenotype. M2 macrophages express both arginase (Arg1) and transforming growth factor beta1 (TGF-β1) are thought to be anti-inflammatory immune cells that help control inflammation. The M2 macrophages have high phagocytosis capacity, producing extracellular matrix (ECM) components, angiogenic and chemotactic factors, and IL-10. In addition to the pathogen defence, M2 macrophages clear apoptotic cells, can mitigate inflammatory responses, and promote wound healing. Objective: In this study, we first investigated the effects of BA on macrophage phagocytosis and examined its effects on the expression of the M2-macrophage markers. **Methods**: The mouse macrophage cell line J774.1 was cultured in Dulbecco's Modified Eagle Medium (DMEM), supplemented with 10% Fetal Bovine Serum (FBS), 0.1% penicillin and streptomycin (PS), 2 mM L-glutamine, and pyruvate, and maintained in an incubator with 5% CO_2 at 37°C. The cytotoxic effects of BA at varying concentrations were evaluated using the MTT assay. Phagocytosis was assessed in macrophages treated for 24 hours with either medium or BA at concentrations of 10, 50, and 100 µM, and subsequently exposed to zymosan particles at a 1:10 ratio. After exposure, the cells were stained with Giemsa for 10 minutes and evaluated under light microscopy. In this assay, the mean number of particles per cell (MNP), the percentage of phagocytic cells (PP), and the phagocytic index (PI) were determined, with the PI calculated as follows: PI = MNP × PP. Production of reactive oxygen species (ROS) was evaluated using the NBT test. Additionally, the expression of oxidative stress markers (SOD1 and Nrf2) and M2-like macrophage molecules (Arg-1 and TGF-β1) was analysed via quantitative PCR (qPCR). **Results and Discussion**: Bornyl acetate (BA), at all concentrations tested, did not exhibit cytotoxicity in the J774 macrophage cell line. In evaluating the effects of BA on phagocytic activity, we observed that treatment with BA enhanced all parameters related to phagocytosis, including the number of particles phagocytosed per cell, the percentage of cells capable of phagocytosis, and the overall phagocytic index. Notably, the increase in reactive oxygen species (ROS) production triggered by zymosan-induced phagocytosis was inhibited only at the highest concentration of BA. Given the observed impact on ROS generation, we further investigated the effects of BA on the expression of antioxidant molecules. We found that BA treatment significantly upregulated the expression of key antioxidant genes, SOD1 and Nrf2. Additionally, BA also promoted the expression of markers associated with the M2 macrophage phenotype, including Arg-1 and TGF-β1. **Conclusion**: These findings suggest that bornyl acetate enhances macrophage phagocytic function, potentially by reprogramming them towards an anti-inflammatory, resolution-promoting profile

Keyword: Bornyl acetate, Macrophage polarization, Anti-inflammatory

Financial Support: FAPEAL, CNPq, CAPES