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ANTI-INFLAMMATORY AND ANTIOXIDANT POTENTIAL OF EPIISOPILOTURINE, AN ALKALOID ISOLATED FROM *PILOCARPUS MICROPHYLLUS* IN HUMAN NEUTROPHILS

ROCHA, T. M.[1,2], LIMA, D. F.[3], LEITE, J. R. S. A[4]., LEAL, L. K. A. M.[2]

[1] *Departamento de Fisiologia e Farmacologia, Faculdade de Medicina, UFC, Fortaleza – CE*
talita_mrocha@yahoo.com.br
[2]*Centro de Estudos Farmacêuticos e Cosméticos (CEFAC), Departamento de Farmácia, UFC, Fortaleza - CE. kalyne@ufc.br*
[3] *Universidade Federal do Vale do São Francisco, UNIVASF, Paulo Afonso – BA*
[4] *Universidade Federal do Piauí, Parnaíba - PI*

Introduction *Pilocarpus microphyllus*, popularly known as jaborandi, is a native species cultivated in Brazil whose leaves are rich in alkaloids, such as pilocarpine, which is a centenary imidazole alkaloid. There are as well other plant alkaloids, such as isopilocarpine, pilocarpidine, isopilocarpidine, pilosine, isopilosine, epiisopilosine and epiisopiloturine. Therefore the objective of the present study was to evaluate the safety and non-clinical efficacy of epiisopiloturine (EPIT) in human neutrophils. **Methods** Polymorphonuclear - PMNs ($2.5x10^6$ cels/mL), predominantly neutrophils (80-90%) with cell viability of 95% (excluding Tripan blue) were isolated from human blood residual product. For evaluation of the cytotoxicity the neutrophils were incubated (37° C) with EPIT (10, 50, 100 and 200 µg/mL), DMSO 1% (vehicle/control), Triton X-100 0.2% (standard cytotoxic) or HBSS (sham) and evaluated by MTT test (620nm) and LDH activity (340 nm). The anti-inflammatory/antioxidant potential was determined by the use of chemiluminescence assay (QL) with the production measurement of Reactive Oxygen Species (ROS). The PMNs ($5x10^6$ cells/mL) were incubated (37° C) for 30 minutes with EPIT (1, 10, 50 and 100 µ g/mL), HBSS (sham), quercetin (Querc, 25µg/mL, standard drug) or DMSO 1% (vehicle/control), plus probe luminol (lum, 280 µM). After stimulation with PMA (0.1 µM), the production of QL (counts photons per minute-cpm) was registered for 20 minutes at 37°C. The results were expressed as a mean of ± standard error, and were analyzed by ANOVA (Tukey, * = $p < 0.05$). **Results** The addition of EPIT (1, 10, 50 and 100 µ g/mL) in neutrophils suspension have not promoted significant increase of LDH activity (5.7 ± 0.8; 6.0 ± 0.4; 8.2 ± 0.9; 8.5 ± 1.4%, respectively) compared to the control group (5.2 ± 0.7%). Similar results were seen in the MTT test, in which EPI did not change the cell viability (95.8 ± 1.9; 96.1 ± 3.28; 101.4 ± 3.9 99.9 ± 2.8%, respectively) when related to the control group (87.1 ± 3.9%). Furthermore, the EPIT also showed anti-inflammatory and antioxidant activities reducing up to 33% the production of ROSs (QL lum) in the respiratory burst of human neutrophils induced by PMA. **Conclusions** The EPIT modulated pro-inflammatory mechanism of human neutrophils through the MPO-H_2O_2-HOCl system and this effect does not seem to be related to a cytotoxic action.

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