Biotechnological potential of IDR-1018 peptide against chronic in vitro hyperglycemia

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INTRODUCTION. Diabetes mellitus (DM) is a metabolic disorder, which results in chronic hyperglycemia consequences leading to cells and tissues damage and also causes overproduction of pro-inflammatory cytokines and leukocytes activity. TNF-α is a pro-inflammatory cytokine produced in response to infection, however in excess, as in DM, could causes cellular damage. OBJECTIVES. In order to verify the IDR-1018 peptide’s immunomodulatory biotechnological potential, TNF-α production was assessed in non-stimulated and LPS with/without IFN-γ-stimulated cultures, in a chronic hyperglycemia in vitro environment. MATERIAL AND METHODS. Peptide was obtained from Peptide 2.0 Inc., USA. Synthesis was performed on solid phase from the F-moc method. Raw 264.7 cells were cultured with D-glucose (8 mM, 12 mM and 24 mM) and/or LPS (0.1 mg.mL⁻¹), IFN-γ (10 U/well) and IDR-1018 (128 μg.mL⁻¹–4 μg.mL⁻¹), per 24h. Cell viability (MTT assay) and TNF-α production (ELISA assay) were analyzed after 24h. RESULTS AND DISCUSSION. Different glucose concentrations as well as the addition of LPS/IFN-γ did not affect cellular viability. However, only when stimulated with LPS or peptide at high concentrations, the cell viability decreased by up to 40% in relation to control group. The combination of the IDR-1018 in cell cultures stimulated with glucose, LPS and IFN-γ decreased the TNF-α production, when compared to control groups (non-stimulated RAW, LPS-stimulated RAW and LPS and IFN-γ-stimulated cells), especially at 12 mM and 24 mM D-glucose concentrations. The peptide concentration of 4 μg.mL⁻¹ induced the smallest TNF-α production, reaching 93 pg.mL⁻¹ for D-glucose-stimulated cells, 126 pg.mL⁻¹ for D-glucose and LPS-stimulated cells and null production for D-glucose and LPS and IFN-γ-stimulated cells.

CONCLUSION. Low TNF-α production by LPS and IFN-γ-stimulated cells in cellular hyperglycemia environment was observed after IDR-1018 addition. Once TNF-α is directly related to tissue damage in the diabetic individual, the downregulation of this cytokine may indicate a potential for IDR-1018 to be used in diabetes mellitus context.

KEY-WORDS: diabetes mellitus, cell culture, peptide.

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