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Withaferin-A in Ameliorating the Effects of High Glucose on Inflammatory and Phagocytic Response of Mouse Macrophages

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ABSTRACT

Rapidly increasing rates of diabetes mellitus (DM) throughout the world represent an emerging epidemic with profound consequences including diabetic nephropathy (DN). Studies indicate that mφ-mediated inflammation correlates with the development of DN. Macrophages exhibit pro- (M1) and anti-inflammatory (M2) phenotypes. Therefore, in the present study, we tested our hypothesis that high glucose suppresses the M2 phenotype and phagocytosis, leading to aberrant cytokine release, and that withaferin-A (an anti-inflammatory molecule) will reduce the pro-inflammatory response of macrophages.

We cultured J-774A.1 macrophage-like cells (ATCC) in RPMI 1640. After reaching 70-80% confluence, the cells were serum starved for 18 hours. Cells were then treated with D-glucose (5, and 25mM) for 24h. We extracted the total protein from the cells to measure the expression level of arginase-1, TGF- beta, LC3 and GPNMB by way of the western blot process. In a second set of experiments, we treated the cells with withaferin-A. In these cells, we will measure the level of secreted pro-inflammatory cytokines in culture media using ELISA.

Preliminary data under our ongoing experiments indicate that high glucose treated macrophages exhibited reduced levels of markers of M2 phenotype (Arginase-1, and TGF- beta) and phagocytosis (GPNMB, and LC3). We are planning to conduct the experiments related to the excretion of pro-inflammatory cytokines in high glucose with and without withaferin-A.

Our results indicate that high glucose modulates the expression of markers of M2 phenotype and phagocytosis in macrophages. We are continuing our experiments to confirm the effects of withaferin-A on the secretion of pro-inflammatory cytokines in high glucose.

Keywords: Withaferin-A, Diabetes Mellitus, High Glucose, Diabetic Nephropathy

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