Fisetin in an in vitro Model of the Diabetic Eye

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Age-related macular degeneration (AMD) impacts the retina through an accumulation of unresolved oxidative stress. Diabetic Nephropathy and AMD have a strong association, with an odds ratio of 3.00. Little research has studied the impact of the AGE-RAGE signaling pathway in diabetic complications in AMD. This pathway increases oxidative stress and inflammation by the irreversible production of advanced glycation end products (AGEs). This research examined the effect of Fisetin on reducing the effects of inflammatory pathways, such as AGE-RAGE, in AMD. This interdisciplinary research is based first on studies that identified common Differentially Expressed Genes (DEGs) in Fisetin-treated and AMD datasets by using public GEO datasets GSE5258 and GSE103060 and suggested the enrichment of inflammatory pathways and protein-protein interactions. This led to examining an in vitro model of 661w photoreceptor cells that was employed and treated with concentrations of fructose to model the diabetic microenvironment and followed by a 48-hour treatment of concentrations of Fisetin. The inflammatory AGE-RAGE, VEGF, IL-1 beta, and TNF-alpha pathways were studied through ELISAs which suggested a decreased secretion of TNF-alpha, IL-1 beta, and VEGF and an increased expression of the AGE-RAGE pathway and ROS at higher concentrations of Fisetin. This research suggests that the AGE-RAGE pathway is connected to ROS production through oxidative stress and TNF alpha, IL-1 beta, and VEGF through inflammatory mechanisms. This research suggests that “antioxidative stress”, a phenomenon where high concentrations of antioxidants can result in additional stress, could have increased secretion of AGE-RAGE and ROS and targeted advantageous ROS molecules with transport and signaling functions.

Awards Won: