Attenuation of Methylglyoxal Cytotoxicity With Fisetin Rescue in Saccharomyces cerevisiae

Jaffery, Zehra (School: Plano West Senior High School)

Methylglyoxal (MGO) is a ubiquitous metabolite produced as a byproduct of glycolysis that spontaneously glycates protein residues to form advanced-glycation end products (AGEs), called fructosamines. AGEs are heavily correlated with age-related diseases such as heart disease and Alzheimer's. The enzymatic network used in MGO metabolism is the glyoxalase system. Glyoxalase I (GLO1), the rate-limiting enzyme, decreases its expression as cells age, allowing for MGO accumulation. Fisetin is a bioactive small molecule with preliminary evidence in mitigating MGO cytotoxicity by increasing GLO1 enzymatic activity and glutathione (GSH) levels, a GLO1 cofactor. However, the efficacy of fisetin in MGO metabolism is largely unknown. This study sees if fisetin will rescue GLO1 in MGO-treated S. cerevisiae (yeast) utilizing three metrics: fructosamine levels, glutathione levels, and viability. It was hypothesized if fisetin increases activity of GLO1 in MGO-treated yeast, there will be decreased fructosamines, increased glutathione, and increased viability compared to MGO-treated yeast without fisetin present. Four experimental groups containing yeast were established: control, fisetin, MGO, and a combination of both. Samples were sonicated to obtain purified protein for assays. Fructosamine and glutathione levels were determined spectrophotometrically with NBT and Ellman’s assays respectively. Viability was evaluated with growth curves measuring optical density and a spot assay. MGO-treated yeast with fisetin were found with decreased fructosamines, increased glutathione, and increased viability compared to MGO-treated yeast, suggesting fisetin increases GLO1 activity, highlighting fisetin as a potential therapeutic and improving morbidity and mortality in age-associated diseases.

Awards Won:

University of Texas at Dallas: Scholarship of $5,000 per year, renewable for up to four years

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