The effect of saffron in two mouse models of hereditary retinal dystrophy

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Introduction

Retinitis pigmentosa (RP) affects 1/4000 people and an earlier form, Leber’s congenital amaurosis (LCA), leads to severe blindness in children. In both RP and LCA, death of photoreceptors by apoptosis occurs as a result of mutations. As the photoreceptor die Müller cells are activated and the retina remodels itself1.

Saffron, an ancient spice, may have the potential to reduce the photoreceptor death due to its documented antioxidant effect. Pre-treatment of albino rats with saffron before exposure to damaging light has demonstrated preservation of the retinal morphology as well as reduction in the photoreceptor death2. In this retinal light damage model, saffron also up-regulates matrix metalloproteinase (MMP) 3 enzyme.

In this project, the Crx +/- mouse, a model for LCA and the rd1 mouse, a model for RP, was used to investigate the effect of early gestational exposure to saffron on photoreceptor degeneration.

Hypothesis: Saffron prevents photoreceptor death, glial proliferation and remodelling in the Crx and rd1 retina.

Methods

- Mice were pre-fed with 25 mg/l of saffron in their drinking water from gestation and during the duration of the study.
- Apoptosis was detected using the TUNEL stain. The number of activated Müller cells and MMP-3 expression was determined by immunohistochemistry using the anti-mouse glial fibrillary acidic protein (GFAP) and anti-rabbit MMP-3 respectively.
- All procedures were carried out on isolated retinas. The retinas were taken from Crx mice at postnatal day (P) 66, from rd1 mice at P31 and from wild type (WT) mice at P30. n = 4 for each model except for WT where n = 2.

Results

- Figure 2. shows retinas from (a) WT, (b) Crx control, (c) Crx with saffron, (d) rd1 control, (e) rd1 with saffron. (i) shows the architecture of the retina with the nuclear stain DAPI. (ii) shows GFAP expression in Müller cells and astrocytes. Müller cells do not express GFAP in WT. (iii) shows MMP-3 expression in the retina. Photoreceptors do not seem to express MMP-3 in WT. n=4.
- Both mouse models have a higher number of photoreceptor layers when treated with saffron compared to control as shown in figure 1 B and 2 C(i) and E(i). There are fewer apoptotic cells in animals treated with saffron compared to control animals as shown in figure 1 A and C (ii) and (iv).
- Fewer activated Müller cells are observed in animals treated with saffron.
- MMP-3 has stronger expression across all retinal layers during degeneration than in WT. Saffron does not appear to significantly affect its expression as shown in figure A-E (iii).

Discussion

- Saffron decreases the rate of photoreceptor degeneration in the Crx and rd1 mouse models by slowing down the pace at which apoptosis occurs.
- Saffron also reduces gliosis in the dystrophic retina as shown by lower numbers of activated Müller cells.
- Photoreceptors and other retinal cells express MMP-3 in the unhealthy retina. Saffron does not appear to change MMP-3 expression patterns.
- Saffron has the potential to slow down photoreceptor cell loss in RP and LCA.

Conclusion

- Saffron does not prevent photoreceptor death in the rd1 and Crx mouse. However it reduces the rate of apoptosis and the amount of gliosis.

References