

Effect of Tocotrienol-Rich Fraction on the Visual-Behaviour Response of rats with Streptozotocin-Induced Diabetic Retinopathy

Muhammad Zulfiqah Sadikan^{1*}, Nurul Alimah Abdul Nasir^{1*}, Igor Nikolayevich Iezhitsa² and Renu Agarwal²

¹ Centre for Neuroscience Research (NeuRon), Faculty of Medicine, University Teknologi MARA, Sungai Buloh, Selangor, 47000, Malaysia.

² School of Medicine, International Medical University, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

*Correspondence Author's email: nurulalimah@uitm.edu.my

ABSTRACT:

Diabetic retinopathy (DR) is the second leading diabetic complication, which impairs vision. Tocotrienol-rich fraction (TRF) has shown to protect against diabetes-induced retinal oxidative stress. Therefore, we investigate TRF effect on the visual-behaviour response in rats with streptozotocin (STZ)-induced DR. Male *Sprague-Dawley* rats (200-250 grams) were divided into diabetic received intraperitoneal 55mg/kg STZ and normal (N) rats received citrate buffer. Diabetic rats were subdivided to diabetic-vehicle (DV) and diabetic-TRF (DT). N and DV received vehicle, whereas DT received 100 mg/kg TRF orally for 12 weeks. The general behaviour in open field arena was assessed at week 12 followed by visual-behaviour response, a mirror and reversed mirror was added. Retinal tissues were collected for haematoxylin and eosin (H&E) staining. In open field, N showed higher zone crossings (3.73-folds, $p<0.001$), travelling (2.02-folds, $p<0.001$), rearing (2.22-folds, $p<0.001$) and grooming (4.33-folds, $p<0.01$) with lower freezing (2.47-folds, $p<0.001$) and faecal pellet (4.17-folds, $p<0.01$) versus DV. Compared to DV, general behaviour in DT was similar to N. N spent more time with higher zone entries toward mirrored compared to non-mirrored and reversed mirror zones ($p<0.05$ and $p<0.01$ respectively). N also showed higher freezing within mirrored zone versus DV (2.00-folds, $p<0.05$). Visual-behaviour response in DT was comparable to N. Retinal morphometry showed reduction in cell count in ganglion cell layer and layer thickness in DV versus N ($p<0.01$). In DT these parameters were greater than DV ($p<0.05$), which correlated with visual-behaviour response. Hence, orally administered TRF improves visual-behaviour response in DR rodent model associated with retinal morphology preservation.

Keyword: diabetic retinopathy; tocotrienol-rich fraction; visual-behaviour response; open field test; mirror test.

Acknowledgement: This work was supported by Universiti Teknologi MARA (UiTM) grants (600-IRMI/DANA 5/3/BESTARI (P) (001/2018) and 600-IRMI/DANA 5/3/BESTARI (P) (012/2018)) and Ministry of Education (MOE), MY grant (600-IRMI/FRGS 5/3 (101/2019)).