Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol8Issue1abst123P.pdf

The anti-inflammatory effect of sulforaphane in the brain

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Introduction: Brain inflammation is involved in several neurological pathologies, such as stroke, multiple sclerosis and Alzheimer's disease[1], which continue to have unmet clinical needs. Consequently, research for efficacious anti-inflammatory agents is ongoing. Sulforaphane (SFN), an isothiocynate derived from cruciferous vegetables, has been widely studied in the field of oncology where its beneficial effects have been numerous [2]. More recently, SFN's protective effects following damage to the brain have indicated similar protective effects [3, 4]. The effect of SFN on leukocyte-endothelial interactions has yet to be visualised.

Aim: To investigate the ability of sulforaphane (i.p, 5mgkg^{-1}) to protect the cerebral microvasculature against experimental endotoxaemia.

Methods and Results: Intra vital microscopy was used to visualise the cerebral microvasculature. C57Bl6 mice were anaesthetised with Ketamine (150mgkg^{-1})/Xylazine(7.5mgkg^{-1}), cannulated via the jugular vein and injected with Rhodamine 6G, a fluorescent dye taken up by leukocytes. Preliminary data indicated neither sham surgery nor systemic saline increased leukocyte-endothelial interactions, whereas; LPS (i.p, 4mgkg^{-1}) caused a significant increase in leukocyte-endothelial measured as indicated by increased cell flux (1.4±0.7 cells/min in sham/1.05±0.3 cells/min in saline treated *vs*. 6.8±1.7 cells/min in LPS treated mice), decreased rolling velocity (431.7±242.6 µm/sec in sham/ 286.1±112.9 µm/sec in saline treated *vs*. 22.8±2.2 µm/sec in LPS treated mice) and increased numbers of adherent cells (0.1±0.1cells/min/100µm in sham/ 0.7±0.5 in saline treated *vs*. 5.2±0.8cells/min/100µm in LPS treated mice). No significant leukocyte-endothelial interaction was observed in arterioles in any mice.

Following this model establishment the effect of systemic prophylactic SFN (4mg/kg) was investigated. SFN significantly reduced cell flux, (6.8 cells/min in LPS treated mice vs. 1.1±0.4 cells/min in SFN/LPS treated mice), increased rolling velocity (22.8 µm/sec in LPS treated mice vs. 79.7±22.6 µm/sec in SFN/LPS treated mice) and decreased cell adhesion (5.2 cells/min/100µm in LPS treated mice vs. 1.7±0.6 cells/min/100µm in SFN/LPS treated mice) in pial venules when compared to mice treated with LPS alone; and significantly reduced cell adhesion (1.7 cells/min/100µm in SFN/LPS treated mice vs. 4.2±0.8 cells/min/100µm in corn oil/LPS treated mice) in SFN/LPS treated mice treated compared with corn oil (SFN vehicle)/LPS treated mice. Statistical analysis was performed using ANOVA and Bonferroni post-hoc test. $P<0.05$. n= 4 sham surgery mice; n=6 mice in all other groups.

Conclusion: These results indicate that systemic LPS infection induces an inflammatory response within the brain. Furthermore, prophylactic systemic administration of SFN reduces leukocyte-endothelial interactions within the cerebral microvasculature. These novel results suggest SFN as a possible therapeutic strategy in the resolution of inflammation.

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