

The Anti-Angiogenic Effect of Tectorigenin in a Mouse Model of Retinopathy of Prematurity

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Abstract : Purpose: Tectorigenin is an isoflavone derived from the rhizome of *Belamacanda chinensis*. In this study, oxygen-induced retinopathy was used to characterize the anti-angiogenic properties of tectorigenin in mice. Methods: ICR neonatal mice were exposed to 75% oxygen from postnatal day P7 until P12 and returned to room air (21% oxygen) for five days (P12 to P17). Mice were subjected to daily intraperitoneal injection of tectorigenin (1 mg/kg, 10 mg/kg) and vehicle from P12 to P17. Retro-orbital injection of FITC-dextran was performed and retinal flat mounts were viewed by fluorescence microscopy. The Central avascular area was quantified from the digital images in a masked fashion using image analysis software (NIH ImageJ). Neovascular tufts were quantified by using SWIFT_NV and neovascular lumens were quantified from a histologic section in a masked fashion. Immunohistochemistry and Western blot analysis were also performed to demonstrate the anti-angiogenic activity of this compound in vivo. Results: In the retina of tectorigenin injected mouse (10mg/kg), the central non-perfusion area was significantly decreased compared to the vehicle injected group (1.76 ± 0.5 mm² vs 2.85 ± 0.6 mm², $P < 0.05$). In vehicle-injected group, $33.45 \pm 5.51\%$ of the total retinal area was avascular, whereas the retinas of pups treated with high-dose (10 mg/kg) tectorigenin showed avascular retinal areas of $21.25 \pm 4.34\%$ ($P < 0.05$). High dose of tectorigenin also significantly reduced the number of vascular lumens in the histologic section. Tectorigenin (10 mg/kg) significantly reduced the expression of vascular endothelial growth factor (VEGF), matrix metalloproteinase-2 (MMP-2), MMP-9, and angiotensin II compared to the vehicle injected group. Tectorigenin did not affect CD31 abundance at any tested dose. Conclusions: Our results show that tectorigenin possesses powerful anti-angiogenic properties and can attenuate new vessel formation in the retina after systemic administration. These results imply that this compound can be considered as a candidate substance for therapeutic inhibition of retinal angiogenesis.

Keywords : tectorigenin, anti-angiogenic, retinopathy, *Belamacanda chinensis*

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